Table 1.1.1.9.24
Proportion of Subjects Achieving Mean Serum Phosphorous Levels Above the Lower Limit of Normal (2.5 mg/dL) at the Mid-Point of the Dose Interval, as Averaged Across Dose Cycles Between Baseline and Week 24 - Sensitivity Analysis
Week 24 Analysis

Statistics	KRN23 (N=68)	Placebo (N=66)
Achieved Mean Serum Phosphorus - n(%)	63 (92.6%)	5 (7.6%)
Difference in achievement (KRN23 vs Placebo) - %	85.1%	
Logistic Regression[1]		
Achieved Mean Serum Phosphorus - %	94.9%	8.5%
95% C.I.	85.6%, 98.3%	3.1%, 21.4%
Odds ratio (KRN23 vs Placebo)	202.021	
95% C.I. of odds ratio	45.880, 889.542	
P-value	<.0001	
RR[3] (95% CI), P-value	12.229 (5.252, 28.479), <.0001	
ARR[3] (95% CI), P-value	202.019 (46.518, 877.344), 0.0000	
ARD[4]		
Difference (95% C.I.)	0.851 (0.762, 0.940)	
P-value	<.0001	

The planned randomization stratification is based on the mean of the 7 days of BPI Worst Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, planned stratification factor, and age group as independent variables
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADSL.sas7bdat, ADPHOS.sas7bdat Program source: t-phos-resp-ARD.sas

Table 1.2.2.9.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness Adjusting for Baseline of BPI Worst Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	68	134
	Mean	61.36	64.71	63.06
	SD, SE	20.770, 2.557	20.253, 2.456	20.500, 1.771
	Median	62.50	62.50	62.50
	Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
	Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0

The planned randomization stratification is based on the mean of the 7 days of BPI Worst Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, region, visit, treatment, planned randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.9.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness Adjusting for Baseline of BPI Worst Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	68	134
	Mean	61.36	64.71	63.06
	SD, SE	20.770, 2.557	20.253, 2.456	20.500, 1.771
	Median	62.50	62.50	62.50
	Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
	Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
	Observed			
	n	66	68	134
	Mean	59.28	54.23	56.72
	SD, SE	19.772, 2.434	25.700, 3.117	23.026, 1.989
	Median	62.50	50.00	62.50
	Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
	Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0

The planned randomization stratification is based on the mean of the 7 days of BPI Worst Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, region, visit, treatment, planned randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.9.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness Adjusting for Baseline of BPI Worst Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	68	134
	Mean	-2.08	-10.48	-6.34
	SD, SE	17.757, 2.186	23.020, 2.792	20.947, 1.810
	Median	0.00	-12.50	0.00
	Q1, Q3	-12.50, 12.50	-25.00, 12.50	-25.00, 12.50
	Min, Max	-37.5, 37.5	-75.0, 37.5	-75.0, 37.5
	GEE Estimates			
	LS Mean (SE)	-3.58 (2.410)	-11.77 (3.114)	
	95% CI	(-8.30, 1.14)	(-17.88, -5.67)	
	LS Mean Difference (SE)		-8.19 (3.111)	
	95% CI		(-14.29, -2.10)	
	p-value		0.0085	

The planned randomization stratification is based on the mean of the 7 days of BPI Worst Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, region, visit, treatment, planned randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.9.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness Adjusting for Baseline of BPI Worst Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	65	67	132
	Mean	61.15	64.37	62.78
	SD, SE	20.861, 2.587	20.209, 2.469	20.517, 1.786
	Median	62.50	62.50	62.50
	Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
	Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
	Observed			
	n	65	67	132
	Mean	60.38	53.73	57.01
	SD, SE	21.827, 2.707	20.759, 2.536	21.471, 1.869
	Median	62.50	50.00	62.50
	Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
	Min, Max	12.5, 100.0	12.5, 87.5	12.5, 100.0

The planned randomization stratification is based on the mean of the 7 days of BPI Worst Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, region, visit, treatment, planned randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.9.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness Adjusting for Baseline of BPI Worst Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	65	67	132
	Mean	-0.77	-10.63	-5.78
	SD, SE	21.749, 2.698	24.450, 2.987	23.596, 2.054
	Median	0.00	-12.50	-12.50
	Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 12.50
	Min, Max	-50.0, 62.5	-75.0, 50.0	-75.0, 62.5
	GEE Estimates			
	LS Mean (SE)	-2.28 (2.645)	-11.94 (2.659)	
	95% CI	(-7.46, 2.91)	(-17.15, -6.73)	
	LS Mean Difference (SE)		-9.66 (3.297)	
	95% CI		(-16.12, -3.20)	
	p-value		0.0034	
	HedgesG (95% CI)		-0.420 (-0.765; -0.075)	

The planned randomization stratification is based on the mean of the 7 days of BPI Worst Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, region, visit, treatment, planned randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.91.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	68	134
	Mean	61.36	64.71	63.06
	SD, SE	20.770, 2.557	20.253, 2.456	20.500, 1.771
	Median	62.50	62.50	62.50
	Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
	Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0

mBOCF = modified Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed using mBOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.91.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	68	134
	Mean	61.36	64.71	63.06
	SD, SE	20.770, 2.557	20.253, 2.456	20.500, 1.771
	Median	62.50	62.50	62.50
	Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
	Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
	Observed			
	n	66	68	134
	Mean	59.28	54.23	56.72
	SD, SE	19.772, 2.434	25.700, 3.117	23.026, 1.989
	Median	62.50	50.00	62.50
	Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
	Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0

mBOCF = modified Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed using mBOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.91.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	68	134
	Mean	-2.08	-10.48	-6.34
	SD, SE	17.757, 2.186	23.020, 2.792	20.947, 1.810
	Median	0.00	-12.50	0.00
	Q1, Q3	-12.50, 12.50	-25.00, 12.50	-25.00, 12.50
	Min, Max	-37.5, 37.5	-75.0, 37.5	-75.0, 37.5
	GEE Estimates			
	LS Mean (SE)	-0.90 (2.782)	-7.77 (3.532)	
	95% CI	(-6.36, 4.55)	(-14.70, -0.85)	
	LS Mean Difference (SE)		-6.87 (3.160)	
	95% CI		(-13.06, -0.68)	
	p-value		0.0297	

mBOCF = modified Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed using mBOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.91.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	66	68	134
	Mean	61.36	64.71	63.06
	SD, SE	20.770, 2.557	20.253, 2.456	20.500, 1.771
	Median	62.50	62.50	62.50
	Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
	Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
	Observed			
	n	66	68	134
	Mean	60.61	54.23	57.37
	SD, SE	21.733, 2.675	21.007, 2.547	21.526, 1.860
	Median	62.50	50.00	62.50
	Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
	Min, Max	12.5, 100.0	12.5, 87.5	12.5, 100.0

mBOCF = modified Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed using mBOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.91.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	66	68	134
	Mean	-0.76	-10.48	-5.69
	SD, SE	21.582, 2.657	24.301, 2.947	23.429, 2.024
	Median	0.00	-12.50	-6.25
	Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 12.50
	Min, Max	-50.0, 62.5	-75.0, 50.0	-75.0, 62.5
	GEE Estimates			
	LS Mean (SE)	0.42 (3.110)	-7.77 (3.022)	
	95% CI	(-5.67, 6.52)	(-13.70, -1.85)	
	LS Mean Difference (SE)		-8.20 (3.221)	
	95% CI		(-14.51, -1.88)	
	p-value		0.0110	
	HedgesG (95% CI)		-0.417 (-0.759; -0.075)	

mBOCF = modified Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed using mBOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.92.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	68	134
	Mean	61.36	64.71	63.06
	SD, SE	20.770, 2.557	20.253, 2.456	20.500, 1.771
	Median	62.50	62.50	62.50
	Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
	Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0

LOCF = Last Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed as LOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.92.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	68	134
	Mean	61.36	64.71	63.06
	SD, SE	20.770, 2.557	20.253, 2.456	20.500, 1.771
	Median	62.50	62.50	62.50
	Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
	Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
	Observed			
	n	66	68	134
	Mean	59.28	54.23	56.72
	SD, SE	19.772, 2.434	25.700, 3.117	23.026, 1.989
	Median	62.50	50.00	62.50
	Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
	Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0

LOCF = Last Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed as LOCF as the dependent variable, region, visit, treatment, actual
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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	68	134
	Mean	-2.08	-10.48	-6.34
	SD, SE	17.757, 2.186	23.020, 2.792	20.947, 1.810
	Median	0.00	-12.50	0.00
	Q1, Q3	-12.50, 12.50	-25.00, 12.50	-25.00, 12.50
	Min, Max	-37.5, 37.5	-75.0, 37.5	-75.0, 37.5
	GEE Estimates			
	LS Mean (SE)	-0.90 (2.782)	-7.77 (3.532)	
	95% CI	(-6.36, 4.55)	(-14.70, -0.85)	
	LS Mean Difference (SE)		-6.87 (3.160)	
	95% CI		(-13.06, -0.68)	
	p-value		0.0297	

LOCF = Last Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed as LOCF as the dependent variable, region, visit, treatment, actual
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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.92.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	66	68	134
	Mean	61.36	64.71	63.06
	SD, SE	20.770, 2.557	20.253, 2.456	20.500, 1.771
	Median	62.50	62.50	62.50
	Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
	Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
	Observed			
	n	66	68	134
	Mean	60.61	54.23	57.37
	SD, SE	21.733, 2.675	21.007, 2.547	21.526, 1.860
	Median	62.50	50.00	62.50
	Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
	Min, Max	12.5, 100.0	12.5, 87.5	12.5, 100.0

LOCF = Last Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed as LOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.92.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	66	68	134
	Mean	-0.76	-10.48	-5.69
	SD, SE	21.582, 2.657	24.301, 2.947	23.429, 2.024
	Median	0.00	-12.50	-6.25
	Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 12.50
	Min, Max	-50.0, 62.5	-75.0, 50.0	-75.0, 62.5
	GEE Estimates			
	LS Mean (SE)	0.42 (3.110)	-7.77 (3.022)	
	95% CI	(-5.67, 6.52)	(-13.70, -1.85)	
	LS Mean Difference (SE)		-8.20 (3.221)	
	95% CI		(-14.51, -1.88)	
	p-value		0.0110	
	HedgesG (95% CI)		-0.417 (-0.759; -0.075)	

LOCF = Last Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed as LOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.93.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	68	134
	Mean	61.36	64.71	63.06
	SD, SE	20.770, 2.557	20.253, 2.456	20.500, 1.771
	Median	62.50	62.50	62.50
	Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
	Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0

BOCF = Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed as BOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.93.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	68	134
	Mean	61.36	64.71	63.06
	SD, SE	20.770, 2.557	20.253, 2.456	20.500, 1.771
	Median	62.50	62.50	62.50
	Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
	Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
	Observed			
	n	66	68	134
	Mean	59.28	54.23	56.72
	SD, SE	19.772, 2.434	25.700, 3.117	23.026, 1.989
	Median	62.50	50.00	62.50
	Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
	Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0

BOCF = Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed as BOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.93.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	68	134
	Mean	-2.08	-10.48	-6.34
	SD, SE	17.757, 2.186	23.020, 2.792	20.947, 1.810
	Median	0.00	-12.50	0.00
	Q1, Q3	-12.50, 12.50	-25.00, 12.50	-25.00, 12.50
	Min, Max	-37.5, 37.5	-75.0, 37.5	-75.0, 37.5
	GEE Estimates			
	LS Mean (SE)	-0.90 (2.782)	-7.77 (3.532)	
	95% CI	(-6.36, 4.55)	(-14.70, -0.85)	
	LS Mean Difference (SE)		-6.87 (3.160)	
	95% CI		(-13.06, -0.68)	
	p-value		0.0297	

BOCF = Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed as BOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.93.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	66	68	134
	Mean	61.36	64.71	63.06
	SD, SE	20.770, 2.557	20.253, 2.456	20.500, 1.771
	Median	62.50	62.50	62.50
	Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
	Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
	Observed			
	n	66	68	134
	Mean	60.61	54.23	57.37
	SD, SE	21.733, 2.675	21.007, 2.547	21.526, 1.860
	Median	62.50	50.00	62.50
	Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
	Min, Max	12.5, 100.0	12.5, 87.5	12.5, 100.0

BOCF = Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed as BOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.2.93.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Stiffness (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	66	68	134
	Mean	-0.76	-10.48	-5.69
	SD, SE	21.582, 2.657	24.301, 2.947	23.429, 2.024
	Median	0.00	-12.50	-6.25
	Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 12.50
	Min, Max	-50.0, 62.5	-75.0, 50.0	-75.0, 62.5
	GEE Estimates			
	LS Mean (SE)	0.42 (3.110)	-7.77 (3.022)	
	95% CI	(-5.67, 6.52)	(-13.70, -1.85)	
	LS Mean Difference (SE)		-8.20 (3.221)	
	95% CI		(-14.51, -1.88)	
	p-value		0.0110	
	HedgesG (95% CI)		-0.417 (-0.759; -0.075)	

BOCF = Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness imputed as BOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-stiff.sas

Table 1.2.3.9.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function Adjusting for Baseline of BPI Worst Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	68	134
	Mean	43.89	50.79	47.40
	SD, SE	19.938, 2.454	19.660, 2.384	20.024, 1.730
	Median	44.12	52.94	47.79
	Q1, Q3	29.41, 60.29	36.76, 64.71	35.29, 61.76
	Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1

The planned randomization stratification is based on the mean of the 7 days of BPI Worst Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function as the dependent variable, region, visit, treatment, planned randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.9.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function Adjusting for Baseline of BPI Worst Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	68	134
	Mean	43.89	50.79	47.40
	SD, SE	19.938, 2.454	19.660, 2.384	20.024, 1.730
	Median	44.12	52.94	47.79
	Q1, Q3	29.41, 60.29	36.76, 64.71	35.29, 61.76
	Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
	Observed			
	n	66	68	134
	Mean	40.49	43.23	41.88
	SD, SE	21.386, 2.632	20.311, 2.463	20.814, 1.798
	Median	38.24	42.65	39.71
	Q1, Q3	26.47, 51.47	29.41, 58.82	27.94, 55.88
	Min, Max	2.9, 100.0	4.4, 82.4	2.9, 100.0

The planned randomization stratification is based on the mean of the 7 days of BPI Worst Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function as the dependent variable, region, visit, treatment, planned randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.9.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function Adjusting for Baseline of BPI Worst Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	68	134
	Mean	-3.41	-7.56	-5.52
	SD, SE	14.047, 1.729	11.358, 1.377	12.875, 1.112
	Median	-2.21	-6.62	-4.41
	Q1, Q3	-10.29, 5.88	-12.50, 1.47	-11.76, 2.94
	Min, Max	-41.2, 26.5	-42.6, 10.3	-42.6, 26.5
	GEE Estimates			
	LS Mean (SE)	-0.90 (2.466)	-4.20 (1.897)	
	95% CI	(-5.73, 3.94)	(-7.92, -0.48)	
	LS Mean Difference (SE)		-3.30 (2.242)	
	95% CI		(-7.70, 1.09)	
	p-value		0.1409	

The planned randomization stratification is based on the mean of the 7 days of BPI Worst Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function as the dependent variable, region, visit, treatment, planned randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.9.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function Adjusting for Baseline of BPI Worst Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	65	66	131
	Mean	43.62	50.33	47.00
	SD, SE	19.967, 2.477	19.336, 2.380	19.863, 1.735
	Median	44.12	52.94	47.06
	Q1, Q3	29.41, 58.82	36.76, 64.71	33.82, 61.76
	Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
	Observed			
	n	65	66	131
	Mean	42.65	43.43	43.04
	SD, SE	22.760, 2.823	19.507, 2.401	21.106, 1.844
	Median	39.71	43.38	41.18
	Q1, Q3	27.94, 55.88	29.41, 60.29	29.41, 57.35
	Min, Max	1.5, 98.5	5.9, 83.8	1.5, 98.5

The planned randomization stratification is based on the mean of the 7 days of BPI Worst Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function as the dependent variable, region, visit, treatment, planned randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.9.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function Adjusting for Baseline of BPI Worst Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	65	66	131
	Mean	-0.97	-6.90	-3.96
	SD, SE	14.718, 1.826	15.322, 1.886	15.260, 1.333
	Median	0.00	-5.88	-4.41
	Q1, Q3	-10.29, 7.35	-14.71, 0.09	-13.24, 4.41
	Min, Max	-29.4, 41.2	-47.1, 55.9	-47.1, 55.9
	GEE Estimates			
	LS Mean (SE)	1.57 (2.512)	-3.55 (2.320)	
	95% CI	(-3.36, 6.49)	(-8.10, 0.99)	
	LS Mean Difference (SE)		-5.12 (2.475)	
	95% CI		(-9.97, -0.27)	
	p-value		0.0386	
	HedgesG (95% CI)		-0.389 (-0.735; -0.043)	

The planned randomization stratification is based on the mean of the 7 days of BPI Worst Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function as the dependent variable, region, visit, treatment, planned randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.91.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	68	134
	Mean	43.89	50.79	47.40
	SD, SE	19.938, 2.454	19.660, 2.384	20.024, 1.730
	Median	44.12	52.94	47.79
	Q1, Q3	29.41, 60.29	36.76, 64.71	35.29, 61.76
	Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1

mBOCF = modified Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as mBOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.91.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	68	134
	Mean	43.89	50.79	47.40
	SD, SE	19.938, 2.454	19.660, 2.384	20.024, 1.730
	Median	44.12	52.94	47.79
	Q1, Q3	29.41, 60.29	36.76, 64.71	35.29, 61.76
	Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
	Observed			
	n	66	68	134
	Mean	40.49	43.23	41.88
	SD, SE	21.386, 2.632	20.311, 2.463	20.814, 1.798
	Median	38.24	42.65	39.71
	Q1, Q3	26.47, 51.47	29.41, 58.82	27.94, 55.88
	Min, Max	2.9, 100.0	4.4, 82.4	2.9, 100.0

mBOCF = modified Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as mBOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.91.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	68	134
	Mean	-3.41	-7.56	-5.52
	SD, SE	14.047, 1.729	11.358, 1.377	12.875, 1.112
	Median	-2.21	-6.62	-4.41
	Q1, Q3	-10.29, 5.88	-12.50, 1.47	-11.76, 2.94
	Min, Max	-41.2, 26.5	-42.6, 10.3	-42.6, 26.5
	GEE Estimates			
	LS Mean (SE)	-0.70 (2.632)	-3.78 (2.071)	
	95% CI	(-5.85, 4.46)	(-7.84, 0.28)	
	LS Mean Difference (SE)		-3.09 (2.234)	
	95% CI		(-7.46, 1.29)	
	p-value		0.1672	

mBOCF = modified Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as mBOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.91.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	66	68	134
	Mean	43.89	50.79	47.40
	SD, SE	19.938, 2.454	19.660, 2.384	20.024, 1.730
	Median	44.12	52.94	47.79
	Q1, Q3	29.41, 60.29	36.76, 64.71	35.29, 61.76
	Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
	Observed			
	n	66	68	134
	Mean	42.96	43.90	43.44
	SD, SE	22.726, 2.797	19.628, 2.380	21.136, 1.826
	Median	39.71	43.38	41.18
	Q1, Q3	27.94, 57.35	29.41, 60.29	29.41, 58.82
	Min, Max	1.5, 98.5	5.9, 83.8	1.5, 98.5

mBOCF = modified Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as mBOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.91.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	66	68	134
	Mean	-0.94	-6.89	-3.96
	SD, SE	14.607, 1.798	15.135, 1.835	15.120, 1.306
	Median	0.00	-5.88	-3.68
	Q1, Q3	-10.29, 7.35	-14.71, 0.05	-13.24, 4.41
	Min, Max	-29.4, 41.2	-47.1, 55.9	-47.1, 55.9
	GEE Estimates			
	LS Mean (SE)	1.78 (2.704)	-3.11 (2.517)	
	95% CI	(-3.52, 7.08)	(-8.04, 1.83)	
	LS Mean Difference (SE)		-4.89 (2.445)	
	95% CI		(-9.68, -0.09)	
	p-value		0.0457	
	HedgesG (95% CI)		-0.395 (-0.737; -0.053)	

mBOCF = modified Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as mBOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.92.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	68	134
	Mean	43.89	50.79	47.40
	SD, SE	19.938, 2.454	19.660, 2.384	20.024, 1.730
	Median	44.12	52.94	47.79
	Q1, Q3	29.41, 60.29	36.76, 64.71	35.29, 61.76
	Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1

LOCF = Last Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as LOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.92.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	68	134
	Mean	43.89	50.79	47.40
	SD, SE	19.938, 2.454	19.660, 2.384	20.024, 1.730
	Median	44.12	52.94	47.79
	Q1, Q3	29.41, 60.29	36.76, 64.71	35.29, 61.76
	Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
	Observed			
	n	66	68	134
	Mean	40.49	43.23	41.88
	SD, SE	21.386, 2.632	20.311, 2.463	20.814, 1.798
	Median	38.24	42.65	39.71
	Q1, Q3	26.47, 51.47	29.41, 58.82	27.94, 55.88
	Min, Max	2.9, 100.0	4.4, 82.4	2.9, 100.0

LOCF = Last Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as LOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.92.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	68	134
	Mean	-3.41	-7.56	-5.52
	SD, SE	14.047, 1.729	11.358, 1.377	12.875, 1.112
	Median	-2.21	-6.62	-4.41
	Q1, Q3	-10.29, 5.88	-12.50, 1.47	-11.76, 2.94
	Min, Max	-41.2, 26.5	-42.6, 10.3	-42.6, 26.5
	GEE Estimates			
	LS Mean (SE)	-0.70 (2.632)	-3.78 (2.071)	
	95% CI	(-5.85, 4.46)	(-7.84, 0.28)	
	LS Mean Difference (SE)		-3.09 (2.234)	
	95% CI		(-7.46, 1.29)	
	p-value		0.1672	

LOCF = Last Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as LOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.92.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	66	68	134
	Mean	43.89	50.79	47.40
	SD, SE	19.938, 2.454	19.660, 2.384	20.024, 1.730
	Median	44.12	52.94	47.79
	Q1, Q3	29.41, 60.29	36.76, 64.71	35.29, 61.76
	Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
	Observed			
	n	66	68	134
	Mean	42.96	43.90	43.44
	SD, SE	22.726, 2.797	19.628, 2.380	21.136, 1.826
	Median	39.71	43.38	41.18
	Q1, Q3	27.94, 57.35	29.41, 60.29	29.41, 58.82
	Min, Max	1.5, 98.5	5.9, 83.8	1.5, 98.5

LOCF = Last Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as LOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.92.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	66	68	134
	Mean	-0.94	-6.89	-3.96
	SD, SE	14.607, 1.798	15.135, 1.835	15.120, 1.306
	Median	0.00	-5.88	-3.68
	Q1, Q3	-10.29, 7.35	-14.71, 0.05	-13.24, 4.41
	Min, Max	-29.4, 41.2	-47.1, 55.9	-47.1, 55.9
	GEE Estimates			
	LS Mean (SE)	1.78 (2.704)	-3.11 (2.517)	
	95% CI	(-3.52, 7.08)	(-8.04, 1.83)	
	LS Mean Difference (SE)		-4.89 (2.445)	
	95% CI		(-9.68, -0.09)	
	p-value		0.0457	
	HedgesG (95% CI)		-0.395 (-0.737; -0.053)	

LOCF = Last Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as LOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.93.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	68	134
	Mean	43.89	50.79	47.40
	SD, SE	19.938, 2.454	19.660, 2.384	20.024, 1.730
	Median	44.12	52.94	47.79
	Q1, Q3	29.41, 60.29	36.76, 64.71	35.29, 61.76
	Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1

BOCF = Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as BOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.93.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	68	134
	Mean	43.89	50.79	47.40
	SD, SE	19.938, 2.454	19.660, 2.384	20.024, 1.730
	Median	44.12	52.94	47.79
	Q1, Q3	29.41, 60.29	36.76, 64.71	35.29, 61.76
	Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
	Observed			
	n	66	68	134
	Mean	40.49	43.23	41.88
	SD, SE	21.386, 2.632	20.311, 2.463	20.814, 1.798
	Median	38.24	42.65	39.71
	Q1, Q3	26.47, 51.47	29.41, 58.82	27.94, 55.88
	Min, Max	2.9, 100.0	4.4, 82.4	2.9, 100.0

BOCF = Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as BOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.93.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	68	134
	Mean	-3.41	-7.56	-5.52
	SD, SE	14.047, 1.729	11.358, 1.377	12.875, 1.112
	Median	-2.21	-6.62	-4.41
	Q1, Q3	-10.29, 5.88	-12.50, 1.47	-11.76, 2.94
	Min, Max	-41.2, 26.5	-42.6, 10.3	-42.6, 26.5
	GEE Estimates			
	LS Mean (SE)	-0.66 (2.628)	-3.78 (2.072)	
	95% CI	(-5.81, 4.49)	(-7.84, 0.28)	
	LS Mean Difference (SE)		-3.12 (2.233)	
	95% CI		(-7.49, 1.26)	
	p-value		0.1628	

BOCF = Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as BOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.93.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	66	68	134
	Mean	43.89	50.79	47.40
	SD, SE	19.938, 2.454	19.660, 2.384	20.024, 1.730
	Median	44.12	52.94	47.79
	Q1, Q3	29.41, 60.29	36.76, 64.71	35.29, 61.76
	Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
	Observed			
	n	66	68	134
	Mean	42.94	44.10	43.53
	SD, SE	22.707, 2.795	20.017, 2.427	21.311, 1.841
	Median	39.71	43.38	41.18
	Q1, Q3	27.94, 57.35	29.41, 60.29	29.41, 58.82
	Min, Max	1.5, 98.5	5.9, 89.7	1.5, 98.5

BOCF = Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as BOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.3.93.24
Summary and Analysis of Change from Baseline to Week 24 in WOMAC Physical Function (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	66	68	134
	Mean	-0.96	-6.69	-3.87
	SD, SE	14.605, 1.798	15.137, 1.836	15.098, 1.304
	Median	0.00	-5.88	-2.94
	Q1, Q3	-10.29, 7.35	-14.71, 0.05	-13.24, 4.41
	Min, Max	-29.4, 41.2	-47.1, 55.9	-47.1, 55.9
	GEE Estimates			
	LS Mean (SE)	1.79 (2.699)	-2.91 (2.530)	
	95% CI	(-3.50, 7.08)	(-7.87, 2.05)	
	LS Mean Difference (SE)		-4.70 (2.450)	
	95% CI		(-9.50, 0.10)	
	p-value		0.0551	
	HedgesG (95% CI)		-0.380 (-0.722; -0.039)	

BOCF = Baseline Observation Carried Forward.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical function imputed as BOCF as the dependent variable, region, visit, treatment, actual
randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical function as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC.sas7bdat Program source: t-womac-pf.sas

Table 1.2.4.24
Summary and Analysis of Change from Baseline to Week 24 in Pain Score of WOMAC (Primary Analysis Set)
24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	67	133
	Mean	47.95	50.67	49.32
	SD, SE	15.541, 1.913	18.005, 2.200	16.819, 1.458
	Median	45.00	55.00	50.00
	Q1, Q3	40.00, 60.00	35.00, 60.00	40.00, 60.00
	Min, Max	10.0, 90.0	10.0, 100.0	10.0, 100.0

N1 = number of subjects in the analysis population of each subgroup.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC_WK96_303.sas7bdat Program source: t-pain-total.sas

Table 1.2.4.24
Summary and Analysis of Change from Baseline to Week 24 in Pain Score of WOMAC (Primary Analysis Set)
24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	67	133
	Mean	47.95	50.67	49.32
	SD, SE	15.541, 1.913	18.005, 2.200	16.819, 1.458
	Median	45.00	55.00	50.00
	Q1, Q3	40.00, 60.00	35.00, 60.00	40.00, 60.00
	Min, Max	10.0, 90.0	10.0, 100.0	10.0, 100.0
	Observed			
	n	66	68	134
	Mean	43.94	43.53	43.73
	SD, SE	17.640, 2.171	18.609, 2.257	18.071, 1.561
	Median	45.00	40.00	45.00
	Q1, Q3	30.00, 55.00	30.00, 60.00	30.00, 60.00
	Min, Max	5.0, 90.0	5.0, 90.0	5.0, 90.0

N1 = number of subjects in the analysis population of each subgroup.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC_WK96_303.sas7bdat Program source: t-pain-total.sas

Table 1.2.4.24
Summary and Analysis of Change from Baseline to Week 24 in Pain Score of WOMAC (Primary Analysis Set)
24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	67	133
	Mean	-4.02	-7.09	-5.56
	SD, SE	14.577, 1.794	13.985, 1.708	14.311, 1.241
	Median	-5.00	-5.00	-5.00
	Q1, Q3	-15.00, 5.00	-15.00, 5.00	-15.00, 5.00
	Min, Max	-35.0, 30.0	-50.0, 20.0	-50.0, 30.0
	GEE Estimates			
	LS Mean (SE)	-4.26 (2.673)	-7.34 (2.329)	
	95% CI	(-9.50, 0.97)	(-11.91, -2.78)	
	LS Mean Difference (SE)		-3.08 (2.235)	
	95% CI		(-7.46, 1.30)	
	p-value		0.1682	

N1 = number of subjects in the analysis population of each subgroup.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC_WK96_303.sas7bdat Program source: t-pain-total.sas

Table 1.2.4.24
Summary and Analysis of Change from Baseline to Week 24 in Pain Score of WOMAC (Primary Analysis Set)
24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	65	66	131
	Mean	47.62	50.08	48.85
	SD, SE	15.414, 1.912	17.464, 2.150	16.462, 1.438
	Median	45.00	55.00	50.00
	Q1, Q3	40.00, 55.00	35.00, 60.00	40.00, 60.00
	Min, Max	10.0, 90.0	10.0, 100.0	10.0, 100.0
	Observed			
	n	65	67	132
	Mean	45.23	43.36	44.28
	SD, SE	18.380, 2.280	17.109, 2.090	17.703, 1.541
	Median	45.00	40.00	45.00
	Q1, Q3	30.00, 55.00	35.00, 55.00	32.50, 55.00
	Min, Max	10.0, 100.0	5.0, 85.0	5.0, 100.0

N1 = number of subjects in the analysis population of each subgroup.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC_WK96_303.sas7bdat Program source: t-pain-total.sas

Table 1.2.4.24
Summary and Analysis of Change from Baseline to Week 24 in Pain Score of WOMAC (Primary Analysis Set)
24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	65	66	131
	Mean	-2.38	-6.67	-4.54
	SD, SE	15.515, 1.924	17.614, 2.168	16.681, 1.457
	Median	0.00	-5.00	0.00
	Q1, Q3	-15.00, 5.00	-15.00, 5.00	-15.00, 5.00
	Min, Max	-35.0, 35.0	-50.0, 50.0	-50.0, 50.0
	GEE Estimates			
	LS Mean (SE)	-2.77 (2.750)	-7.14 (2.544)	
	95% CI	(-8.16, 2.62)	(-12.12, -2.15)	
	LS Mean Difference (SE)		-4.37 (2.533)	
	95% CI		(-9.33, 0.60)	
	p-value		0.0848	

N1 = number of subjects in the analysis population of each subgroup.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC_WK96_303.sas7bdat Program source: t-pain-total.sas

Table 1.2.5.24
Summary and Analysis of Change from Baseline to Week 24 in Total Score of WOMAC (Primary Analysis Set)
24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	67	133
	Mean	46.20	51.88	49.06
	SD, SE	17.733, 2.183	18.402, 2.248	18.229, 1.581
	Median	46.88	53.13	50.00
	Q1, Q3	36.46, 59.38	39.58, 63.54	38.54, 62.50
	Min, Max	6.3, 92.7	11.5, 93.8	6.3, 93.8

N1 = number of subjects in the analysis population of each subgroup.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC_WK96_303.sas7bdat Program source: t-pain-total.sas

Table 1.2.5.24
Summary and Analysis of Change from Baseline to Week 24 in Total Score of WOMAC (Primary Analysis Set)
24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	67	133
	Mean	46.20	51.88	49.06
	SD, SE	17.733, 2.183	18.402, 2.248	18.229, 1.581
	Median	46.88	53.13	50.00
	Q1, Q3	36.46, 59.38	39.58, 63.54	38.54, 62.50
	Min, Max	6.3, 92.7	11.5, 93.8	6.3, 93.8
	Observed			
	n	66	68	134
	Mean	42.77	44.21	43.50
	SD, SE	18.988, 2.337	19.457, 2.360	19.169, 1.656
	Median	41.67	43.23	42.71
	Q1, Q3	32.29, 53.13	30.73, 59.38	31.25, 57.29
	Min, Max	8.3, 95.8	5.2, 84.4	5.2, 95.8

N1 = number of subjects in the analysis population of each subgroup.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC_WK96_303.sas7bdat Program source: t-pain-total.sas

Table 1.2.5.24
Summary and Analysis of Change from Baseline to Week 24 in Total Score of WOMAC (Primary Analysis Set)
24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	67	133
	Mean	-3.42	-7.79	-5.62
	SD, SE	12.462, 1.534	11.567, 1.413	12.173, 1.056
	Median	-3.65	-7.29	-4.17
	Q1, Q3	-9.38, 4.17	-13.54, 1.04	-12.50, 3.13
	Min, Max	-39.6, 21.9	-43.8, 11.5	-43.8, 21.9
	GEE Estimates			
	LS Mean (SE)	-1.40 (2.210)	-5.18 (1.810)	
	95% CI	(-5.73, 2.93)	(-8.73, -1.64)	
	LS Mean Difference (SE)		-3.78 (2.067)	
	95% CI		(-7.83, 0.27)	
	p-value		0.0673	

N1 = number of subjects in the analysis population of each subgroup.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC_WK96_303.sas7bdat Program source: t-pain-total.sas

Table 1.2.5.24
Summary and Analysis of Change from Baseline to Week 24 in Total Score of WOMAC (Primary Analysis Set)
24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	65	66	131
	Mean	45.91	51.31	48.63
	SD, SE	17.720, 2.198	17.935, 2.208	17.965, 1.570
	Median	46.88	52.60	48.96
	Q1, Q3	36.46, 58.33	39.58, 62.50	37.50, 62.50
	Min, Max	6.3, 92.7	11.5, 93.8	6.3, 93.8
	Observed			
	n	65	67	132
	Mean	44.66	43.92	44.29
	SD, SE	20.769, 2.576	17.783, 2.173	19.240, 1.675
	Median	41.67	43.75	41.67
	Q1, Q3	31.25, 58.33	30.21, 57.29	30.21, 57.81
	Min, Max	5.2, 97.9	8.3, 84.4	5.2, 97.9

N1 = number of subjects in the analysis population of each subgroup.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC_WK96_303.sas7bdat Program source: t-pain-total.sas

Table 1.2.5.24
Summary and Analysis of Change from Baseline to Week 24 in Total Score of WOMAC (Primary Analysis Set)
24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	65	66	131
	Mean	-1.25	-7.59	-4.44
	SD, SE	13.659, 1.694	15.072, 1.855	14.682, 1.283
	Median	0.00	-6.25	-4.17
	Q1, Q3	-10.42, 5.21	-14.58, 0.00	-13.54, 3.13
	Min, Max	-28.1, 34.4	-42.7, 54.2	-42.7, 54.2
	GEE Estimates			
	LS Mean (SE)	0.77 (2.324)	-5.09 (2.137)	
	95% CI	(-3.79, 5.32)	(-9.28, -0.90)	
	LS Mean Difference (SE)		-5.85 (2.319)	
	95% CI		(-10.40, -1.31)	
	p-value		0.0116	
	HedgesG (95% CI)		-0.435 (-0.781, -0.088)	

N1 = number of subjects in the analysis population of each subgroup.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADWOMAC_WK96_303.sas7bdat Program source: t-pain-total.sas

Table 1.2.1.9.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain Adjusting for Baseline of BPI Average Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	68	134
	Mean	6.54	6.81	6.68
	SD, SE	1.433, 0.176	1.308, 0.159	1.372, 0.119
	Median	6.50	7.13	6.79
	Q1, Q3	5.75, 7.50	6.19, 7.81	5.88, 7.63
	Min, Max	3.1, 9.1	3.0, 8.9	3.0, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI Worst Pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Average Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.9.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain Adjusting for Baseline of BPI Average Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	68	134
	Mean	6.54	6.81	6.68
	SD, SE	1.433, 0.176	1.308, 0.159	1.372, 0.119
	Median	6.50	7.13	6.79
	Q1, Q3	5.75, 7.50	6.19, 7.81	5.88, 7.63
	Min, Max	3.1, 9.1	3.0, 8.9	3.0, 9.1
	Observed			
	n	66	68	134
	Mean	6.03	5.99	6.01
	SD, SE	1.955, 0.241	1.762, 0.214	1.852, 0.160
	Median	6.40	6.38	6.38
	Q1, Q3	4.63, 7.25	5.00, 7.38	4.75, 7.38
	Min, Max	0.6, 9.9	1.9, 9.6	0.6, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI Worst Pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Average Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.9.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain Adjusting for Baseline of BPI Average Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	68	134
	Mean	-0.52	-0.82	-0.67
	SD, SE	1.561, 0.192	1.462, 0.177	1.513, 0.131
	Median	-0.31	-0.45	-0.38
	Q1, Q3	-1.75, 0.50	-1.23, 0.00	-1.29, 0.25
	Min, Max	-4.0, 2.4	-6.1, 1.4	-6.1, 2.4
	GEE Estimates			
	LS Mean (SE)	-0.38 (0.207)	-0.63 (0.194)	
	95% CI	(-0.79, 0.03)	(-1.01, -0.25)	
	LS Mean Difference (SE)		-0.25 (0.249)	
	95% CI		(-0.74, 0.24)	
	p-value		0.3093	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI Worst Pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Average Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.9.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain Adjusting for Baseline of BPI Average Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	65	67	132
	Mean	6.51	6.80	6.66
	SD, SE	1.417, 0.176	1.316, 0.161	1.369, 0.119
	Median	6.50	7.13	6.75
	Q1, Q3	5.75, 7.50	6.13, 7.88	5.88, 7.63
	Min, Max	3.1, 9.1	3.0, 8.9	3.0, 9.1
	Observed			
	n	65	67	132
	Mean	6.09	5.82	5.95
	SD, SE	2.013, 0.250	1.916, 0.234	1.961, 0.171
	Median	6.25	6.00	6.13
	Q1, Q3	4.63, 7.50	4.38, 7.50	4.63, 7.50
	Min, Max	0.4, 9.9	2.1, 9.3	0.4, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI Worst Pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Average Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.9.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain Adjusting for Baseline of BPI Average Pain - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	65	67	132
	Mean	-0.42	-0.98	-0.70
	SD, SE	1.759, 0.218	1.564, 0.191	1.680, 0.146
	Median	-0.50	-0.75	-0.63
	Q1, Q3	-1.21, 0.50	-1.75, 0.13	-1.60, 0.25
	Min, Max	-4.9, 4.3	-5.9, 1.6	-5.9, 4.3
	GEE Estimates			
	LS Mean (SE)	-0.32 (0.222)	-0.79 (0.211)	
	95% CI	(-0.76, 0.11)	(-1.20, -0.37)	
	LS Mean Difference (SE)		-0.46 (0.275)	
	95% CI		(-1.00, 0.08)	
	p-value		0.0919	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI Worst Pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Average Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.91.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	68	134
	Mean	6.54	6.81	6.68
	SD, SE	1.433, 0.176	1.308, 0.159	1.372, 0.119
	Median	6.50	7.13	6.79
	Q1, Q3	5.75, 7.50	6.19, 7.81	5.88, 7.63
	Min, Max	3.1, 9.1	3.0, 8.9	3.0, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed using mBOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.91.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	68	134
	Mean	6.54	6.81	6.68
	SD, SE	1.433, 0.176	1.308, 0.159	1.372, 0.119
	Median	6.50	7.13	6.79
	Q1, Q3	5.75, 7.50	6.19, 7.81	5.88, 7.63
	Min, Max	3.1, 9.1	3.0, 8.9	3.0, 9.1
	Observed			
	n	66	68	134
	Mean	6.03	5.99	6.01
	SD, SE	1.955, 0.241	1.762, 0.214	1.852, 0.160
	Median	6.40	6.38	6.38
	Q1, Q3	4.63, 7.25	5.00, 7.38	4.75, 7.38
	Min, Max	0.6, 9.9	1.9, 9.6	0.6, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed using mBOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.91.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	68	134
	Mean	-0.52	-0.82	-0.67
	SD, SE	1.561, 0.192	1.462, 0.177	1.513, 0.131
	Median	-0.31	-0.45	-0.38
	Q1, Q3	-1.75, 0.50	-1.23, 0.00	-1.29, 0.25
	Min, Max	-4.0, 2.4	-6.1, 1.4	-6.1, 2.4
	GEE Estimates			
	LS Mean (SE)	-0.38 (0.207)	-0.63 (0.195)	
	95% CI	(-0.79, 0.02)	(-1.02, -0.25)	
	LS Mean Difference (SE)		-0.25 (0.250)	
	95% CI		(-0.74, 0.24)	
	p-value		0.3119	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed using mBOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.91.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	66	68	134
	Mean	6.54	6.81	6.68
	SD, SE	1.433, 0.176	1.308, 0.159	1.372, 0.119
	Median	6.50	7.13	6.79
	Q1, Q3	5.75, 7.50	6.19, 7.81	5.88, 7.63
	Min, Max	3.1, 9.1	3.0, 8.9	3.0, 9.1
	Observed			
	n	66	68	134
	Mean	6.07	5.84	5.95
	SD, SE	2.005, 0.247	1.907, 0.231	1.952, 0.169
	Median	6.25	6.06	6.13
	Q1, Q3	4.63, 7.50	4.38, 7.44	4.63, 7.50
	Min, Max	0.4, 9.9	2.1, 9.3	0.4, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed using mBOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.91.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (mBOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	66	68	134
	Mean	-0.48	-0.97	-0.73
	SD, SE	1.800, 0.222	1.554, 0.188	1.691, 0.146
	Median	-0.50	-0.75	-0.63
	Q1, Q3	-1.38, 0.50	-1.75, 0.13	-1.63, 0.25
	Min, Max	-4.9, 4.3	-5.9, 1.6	-5.9, 4.3
	GEE Estimates			
	LS Mean (SE)	-0.34 (0.223)	-0.78 (0.211)	
	95% CI	(-0.78, 0.10)	(-1.20, -0.37)	
	LS Mean Difference (SE)		-0.44 (0.275)	
	95% CI		(-0.98, 0.10)	
	p-value		0.1085	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed using mBOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.92.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	68	134
	Mean	6.54	6.81	6.68
	SD, SE	1.433, 0.176	1.308, 0.159	1.372, 0.119
	Median	6.50	7.13	6.79
	Q1, Q3	5.75, 7.50	6.19, 7.81	5.88, 7.63
	Min, Max	3.1, 9.1	3.0, 8.9	3.0, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed as LOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.92.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	68	134
	Mean	6.54	6.81	6.68
	SD, SE	1.433, 0.176	1.308, 0.159	1.372, 0.119
	Median	6.50	7.13	6.79
	Q1, Q3	5.75, 7.50	6.19, 7.81	5.88, 7.63
	Min, Max	3.1, 9.1	3.0, 8.9	3.0, 9.1
	Observed			
	n	66	68	134
	Mean	6.03	5.99	6.01
	SD, SE	1.955, 0.241	1.762, 0.214	1.852, 0.160
	Median	6.40	6.38	6.38
	Q1, Q3	4.63, 7.25	5.00, 7.38	4.75, 7.38
	Min, Max	0.6, 9.9	1.9, 9.6	0.6, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed as LOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.92.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	68	134
	Mean	-0.52	-0.82	-0.67
	SD, SE	1.561, 0.192	1.462, 0.177	1.513, 0.131
	Median	-0.31	-0.45	-0.38
	Q1, Q3	-1.75, 0.50	-1.23, 0.00	-1.29, 0.25
	Min, Max	-4.0, 2.4	-6.1, 1.4	-6.1, 2.4
	GEE Estimates			
	LS Mean (SE)	-0.38 (0.207)	-0.63 (0.195)	
	95% CI	(-0.79, 0.02)	(-1.02, -0.25)	
	LS Mean Difference (SE)		-0.25 (0.250)	
	95% CI		(-0.74, 0.24)	
	p-value		0.3119	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed as LOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.92.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	66	68	134
	Mean	6.54	6.81	6.68
	SD, SE	1.433, 0.176	1.308, 0.159	1.372, 0.119
	Median	6.50	7.13	6.79
	Q1, Q3	5.75, 7.50	6.19, 7.81	5.88, 7.63
	Min, Max	3.1, 9.1	3.0, 8.9	3.0, 9.1
	Observed			
	n	66	68	134
	Mean	6.07	5.84	5.95
	SD, SE	2.005, 0.247	1.907, 0.231	1.952, 0.169
	Median	6.25	6.06	6.13
	Q1, Q3	4.63, 7.50	4.38, 7.44	4.63, 7.50
	Min, Max	0.4, 9.9	2.1, 9.3	0.4, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed as LOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.92.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (LOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	66	68	134
	Mean	-0.48	-0.97	-0.73
	SD, SE	1.800, 0.222	1.554, 0.188	1.691, 0.146
	Median	-0.50	-0.75	-0.63
	Q1, Q3	-1.38, 0.50	-1.75, 0.13	-1.63, 0.25
	Min, Max	-4.9, 4.3	-5.9, 1.6	-5.9, 4.3
	GEE Estimates			
	LS Mean (SE)	-0.34 (0.223)	-0.78 (0.211)	
	95% CI	(-0.78, 0.10)	(-1.20, -0.37)	
	LS Mean Difference (SE)		-0.44 (0.275)	
	95% CI		(-0.98, 0.10)	
	p-value		0.1085	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed as LOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.93.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Baseline	n	66	68	134
	Mean	6.54	6.81	6.68
	SD, SE	1.433, 0.176	1.308, 0.159	1.372, 0.119
	Median	6.50	7.13	6.79
	Q1, Q3	5.75, 7.50	6.19, 7.81	5.88, 7.63
	Min, Max	3.1, 9.1	3.0, 8.9	3.0, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed as BOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.93.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Baseline			
	n	66	68	134
	Mean	6.54	6.81	6.68
	SD, SE	1.433, 0.176	1.308, 0.159	1.372, 0.119
	Median	6.50	7.13	6.79
	Q1, Q3	5.75, 7.50	6.19, 7.81	5.88, 7.63
	Min, Max	3.1, 9.1	3.0, 8.9	3.0, 9.1
	Observed			
	n	66	68	134
	Mean	6.03	5.99	6.01
	SD, SE	1.955, 0.241	1.762, 0.214	1.852, 0.160
	Median	6.40	6.38	6.38
	Q1, Q3	4.63, 7.25	5.00, 7.38	4.75, 7.38
	Min, Max	0.6, 9.9	1.9, 9.6	0.6, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed as BOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.93.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 12	Change from Baseline			
	n	66	68	134
	Mean	-0.52	-0.82	-0.67
	SD, SE	1.561, 0.192	1.462, 0.177	1.513, 0.131
	Median	-0.31	-0.45	-0.38
	Q1, Q3	-1.75, 0.50	-1.23, 0.00	-1.29, 0.25
	Min, Max	-4.0, 2.4	-6.1, 1.4	-6.1, 2.4
	GEE Estimates			
	LS Mean (SE)	-0.38 (0.207)	-0.64 (0.194)	
	95% CI	(-0.79, 0.02)	(-1.02, -0.26)	
	LS Mean Difference (SE)		-0.26 (0.249)	
	95% CI		(-0.74, 0.23)	
	p-value		0.3013	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed as BOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.93.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Baseline			
	n	66	68	134
	Mean	6.54	6.81	6.68
	SD, SE	1.433, 0.176	1.308, 0.159	1.372, 0.119
	Median	6.50	7.13	6.79
	Q1, Q3	5.75, 7.50	6.19, 7.81	5.88, 7.63
	Min, Max	3.1, 9.1	3.0, 8.9	3.0, 9.1
	Observed			
	n	66	68	134
	Mean	6.13	5.84	5.98
	SD, SE	2.024, 0.249	1.911, 0.232	1.965, 0.170
	Median	6.25	6.06	6.19
	Q1, Q3	4.63, 7.63	4.38, 7.44	4.63, 7.50
	Min, Max	0.4, 9.9	2.1, 9.3	0.4, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed as BOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 1.2.1.93.24
Summary and Analysis of change from Baseline to Week 24 in BPI Worst Pain (BOCF) - Sensitivity Analysis
Primary Analysis - 24 Weeks Analysis

Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Week 24	Change from Baseline			
	n	66	68	134
	Mean	-0.42	-0.96	-0.69
	SD, SE	1.746, 0.215	1.557, 0.189	1.669, 0.144
	Median	-0.43	-0.75	-0.56
	Q1, Q3	-1.21, 0.50	-1.75, 0.13	-1.58, 0.25
	Min, Max	-4.9, 4.3	-5.9, 1.6	-5.9, 4.3
	GEE Estimates			
	LS Mean (SE)	-0.28 (0.218)	-0.78 (0.211)	
	95% CI	(-0.71, 0.15)	(-1.20, -0.37)	
	LS Mean Difference (SE)		-0.50 (0.271)	
	95% CI		(-1.03, 0.03)	
	p-value		0.0637	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain imputed as BOCF as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADBPI.sas7bdat Program source: t_bpi.sas

Table 2.2.5.2.1.24.1
Summary and Analysis of Change and Percent Change from Baseline to Week 24 in Serum Phosphorus (mg/dL)
Primary Analysis Set_Week 24 Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6		N1	27	17	44
	Baseline	n	27	17	44
		Mean	1.92	2.05	1.97
		SD, SE	0.293, 0.056	0.170, 0.041	0.258, 0.039
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.10	1.90, 2.10	1.85, 2.10
		Min, Max	1.4, 2.4	1.8, 2.4	1.4, 2.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.1
Summary and Analysis of Change and Percent Change from Baseline to Week 24 in Serum Phosphorus (mg/dL)
Primary Analysis Set_Week 24 Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Baseline			
		n	27	17	44
		Mean	1.92	2.05	1.97
		SD, SE	0.293, 0.056	0.170, 0.041	0.258, 0.039
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.10	1.90, 2.10	1.85, 2.10
		Min, Max	1.4, 2.4	1.8, 2.4	1.4, 2.4
		Observed			
		n	27	17	44
		Mean	2.09	2.82	2.37
		SD, SE	0.350, 0.067	0.711, 0.172	0.627, 0.095
		Median	2.10	2.60	2.30
		Q1, Q3	1.80, 2.30	2.40, 3.10	1.95, 2.60
		Min, Max	1.5, 2.7	1.9, 4.6	1.5, 4.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.1
Summary and Analysis of Change and Percent Change from Baseline to Week 24 in Serum Phosphorus (mg/dL)
Primary Analysis Set_Week 24 Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Change from Baseline			
		n	27	17	44
		Mean	0.17	0.78	0.40
		SD, SE	0.243, 0.047	0.703, 0.171	0.557, 0.084
		Median	0.20	0.70	0.30
		Q1, Q3	0.00, 0.30	0.50, 1.00	0.10, 0.60
		Min, Max	-0.4, 0.6	-0.3, 2.6	-0.4, 2.6
		GEE Estimates			
		LS Mean (SE)	0.04 (0.084)	0.69 (0.207)	0.36 (0.131)
		95% CI	(-0.13, 0.20)	(0.28, 1.09)	(0.11, 0.62)
		LS Mean Difference (SE)		0.65 (0.175)	
		95% CI		(0.31, 0.99)	
		p-value		0.0002	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.1
Summary and Analysis of Change and Percent Change from Baseline to Week 24 in Serum Phosphorus (mg/dL)
Primary Analysis Set_Week 24 Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Baseline			
		n	27	17	44
		Mean	1.92	2.05	1.97
		SD, SE	0.293, 0.056	0.170, 0.041	0.258, 0.039
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.10	1.90, 2.10	1.85, 2.10
		Min, Max	1.4, 2.4	1.8, 2.4	1.4, 2.4
		Observed			
		n	27	17	44
		Mean	2.11	2.58	2.30
		SD, SE	0.342, 0.066	0.391, 0.095	0.425, 0.064
		Median	2.10	2.60	2.30
		Q1, Q3	1.90, 2.40	2.30, 2.80	2.00, 2.60
		Min, Max	1.5, 2.8	2.0, 3.6	1.5, 3.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.1
Summary and Analysis of Change and Percent Change from Baseline to Week 24 in Serum Phosphorus (mg/dL)
Primary Analysis Set_Week 24 Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Change from Baseline			
		n	27	17	44
		Mean	0.19	0.54	0.33
		SD, SE	0.345, 0.066	0.412, 0.100	0.405, 0.061
		Median	0.20	0.50	0.30
		Q1, Q3	0.10, 0.40	0.40, 0.70	0.10, 0.55
		Min, Max	-0.6, 1.1	0.0, 1.6	-0.6, 1.6
		GEE Estimates			
		LS Mean (SE)	0.06 (0.084)	0.45 (0.146)	0.26 (0.105)
		95% CI	(-0.10, 0.23)	(0.16, 0.73)	(0.05, 0.46)
		LS Mean Difference (SE)		0.38 (0.111)	
		95% CI		(0.17, 0.60)	
		p-value		0.0005	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.1
Summary and Analysis of Change and Percent Change from Baseline to Week 24 in Serum Phosphorus (mg/dL)
Primary Analysis Set_Week 24 Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6		N1	39	51	90
	Baseline	n	39	51	90
		Mean	1.92	2.03	1.98
		SD, SE	0.334, 0.054	0.338, 0.047	0.339, 0.036
		Median	1.90	2.00	2.00
		Q1, Q3	1.60, 2.20	1.80, 2.20	1.70, 2.20
		Min, Max	1.3, 2.6	1.3, 3.0	1.3, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.1
Summary and Analysis of Change and Percent Change from Baseline to Week 24 in Serum Phosphorus (mg/dL)
Primary Analysis Set_Week 24 Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Baseline			
		n	37	51	88
		Mean	1.91	2.03	1.98
		SD, SE	0.329, 0.054	0.338, 0.047	0.338, 0.036
		Median	1.90	2.00	2.00
		Q1, Q3	1.60, 2.20	1.80, 2.20	1.70, 2.20
		Min, Max	1.3, 2.6	1.3, 3.0	1.3, 3.0
		Observed			
		n	37	51	88
		Mean	2.03	2.63	2.38
		SD, SE	0.364, 0.060	0.515, 0.072	0.544, 0.058
		Median	2.00	2.50	2.30
		Q1, Q3	1.80, 2.20	2.30, 2.90	2.00, 2.70
		Min, Max	1.4, 2.8	1.5, 4.2	1.4, 4.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.1
Summary and Analysis of Change and Percent Change from Baseline to Week 24 in Serum Phosphorus (mg/dL)
Primary Analysis Set_Week 24 Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Change from Baseline			
		n	37	51	88
		Mean	0.12	0.60	0.40
		SD, SE	0.328, 0.054	0.454, 0.064	0.469, 0.050
		Median	0.10	0.60	0.40
		Q1, Q3	-0.10, 0.40	0.30, 0.90	0.05, 0.70
		Min, Max	-0.5, 0.7	-0.2, 1.7	-0.5, 1.7
		GEE Estimates			
		LS Mean (SE)	-0.07 (0.086)	0.48 (0.090)	0.21 (0.078)
		95% CI	(-0.24, 0.10)	(0.31, 0.66)	(0.05, 0.36)
		LS Mean Difference (SE)		0.56 (0.081)	
		95% CI		(0.40, 0.71)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.1
Summary and Analysis of Change and Percent Change from Baseline to Week 24 in Serum Phosphorus (mg/dL)
Primary Analysis Set_Week 24 Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Baseline			
		n	39	51	90
		Mean	1.92	2.03	1.98
		SD, SE	0.334, 0.054	0.338, 0.047	0.339, 0.036
		Median	1.90	2.00	2.00
		Q1, Q3	1.60, 2.20	1.80, 2.20	1.70, 2.20
		Min, Max	1.3, 2.6	1.3, 3.0	1.3, 3.0
		Observed			
		n	39	51	90
		Mean	2.04	2.51	2.30
		SD, SE	0.345, 0.055	0.465, 0.065	0.477, 0.050
		Median	2.00	2.50	2.30
		Q1, Q3	1.80, 2.40	2.20, 2.80	2.00, 2.50
		Min, Max	1.3, 2.7	1.6, 3.7	1.3, 3.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.1
Summary and Analysis of Change and Percent Change from Baseline to Week 24 in Serum Phosphorus (mg/dL)
Primary Analysis Set_Week 24 Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Change from Baseline			
		n	39	51	90
		Mean	0.12	0.48	0.32
		SD, SE	0.347, 0.056	0.392, 0.055	0.413, 0.044
		Median	0.00	0.50	0.30
		Q1, Q3	-0.10, 0.40	0.20, 0.70	0.00, 0.60
		Min, Max	-0.4, 1.0	-0.4, 1.5	-0.4, 1.5
		GEE Estimates			
		LS Mean (SE)	-0.07 (0.084)	0.36 (0.086)	0.14 (0.077)
		95% CI	(-0.24, 0.09)	(0.19, 0.53)	(-0.01, 0.29)
		LS Mean Difference (SE)		0.43 (0.073)	
		95% CI		(0.29, 0.57)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.2
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6		N1	49	48	97
	Baseline	n	49	48	97
		Mean	1.89	1.99	1.94
		SD, SE	0.312, 0.045	0.296, 0.043	0.307, 0.031
		Median	1.90	2.00	1.90
		Q1, Q3	1.70, 2.10	1.80, 2.20	1.70, 2.20
		Min, Max	1.3, 2.6	1.3, 2.7	1.3, 2.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.2
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Baseline			
		n	48	48	96
		Mean	1.89	1.99	1.94
		SD, SE	0.315, 0.046	0.296, 0.043	0.308, 0.031
		Median	1.90	2.00	1.90
		Q1, Q3	1.65, 2.15	1.80, 2.20	1.70, 2.20
		Min, Max	1.3, 2.6	1.3, 2.7	1.3, 2.7
		Observed			
		n	48	48	96
		Mean	2.05	2.64	2.34
		SD, SE	0.374, 0.054	0.557, 0.080	0.557, 0.057
		Median	2.00	2.55	2.30
		Q1, Q3	1.70, 2.30	2.30, 2.90	2.00, 2.60
		Min, Max	1.4, 2.8	1.5, 4.6	1.4, 4.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.2
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Change from Baseline			
		n	48	48	96
		Mean	0.16	0.65	0.40
		SD, SE	0.265, 0.038	0.552, 0.080	0.495, 0.051
		Median	0.15	0.60	0.30
		Q1, Q3	0.00, 0.30	0.30, 0.95	0.10, 0.60
		Min, Max	-0.5, 0.6	-0.3, 2.6	-0.5, 2.6
		GEE Estimates			
		LS Mean (SE)	0.01 (0.069)	0.55 (0.102)	0.28 (0.076)
		95% CI	(-0.13, 0.14)	(0.35, 0.75)	(0.13, 0.43)
		LS Mean Difference (SE)		0.54 (0.086)	
		95% CI		(0.37, 0.71)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.2
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Baseline			
		n	49	48	97
		Mean	1.89	1.99	1.94
		SD, SE	0.312, 0.045	0.296, 0.043	0.307, 0.031
		Median	1.90	2.00	1.90
		Q1, Q3	1.70, 2.10	1.80, 2.20	1.70, 2.20
		Min, Max	1.3, 2.6	1.3, 2.7	1.3, 2.7
		Observed			
		n	49	48	97
		Mean	2.03	2.51	2.26
		SD, SE	0.366, 0.052	0.425, 0.061	0.461, 0.047
		Median	2.00	2.50	2.30
		Q1, Q3	1.80, 2.40	2.20, 2.80	2.00, 2.50
		Min, Max	1.3, 2.8	1.6, 3.7	1.3, 3.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.2
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Change from Baseline			
		n	49	48	97
		Mean	0.14	0.51	0.32
		SD, SE	0.331, 0.047	0.407, 0.059	0.414, 0.042
		Median	0.20	0.50	0.30
		Q1, Q3	-0.10, 0.30	0.20, 0.75	0.00, 0.60
		Min, Max	-0.6, 1.1	-0.4, 1.6	-0.6, 1.6
		GEE Estimates			
		LS Mean (SE)	-0.01 (0.068)	0.42 (0.079)	0.20 (0.065)
		95% CI	(-0.14, 0.12)	(0.26, 0.57)	(0.08, 0.33)
		LS Mean Difference (SE)		0.42 (0.068)	
		95% CI		(0.29, 0.56)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.2
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6		N1	17	20	37
	Baseline	n	17	20	37
		Mean	2.01	2.12	2.07
		SD, SE	0.316, 0.077	0.311, 0.070	0.314, 0.052
		Median	2.00	2.10	2.10
		Q1, Q3	1.90, 2.20	1.95, 2.25	1.90, 2.20
		Min, Max	1.4, 2.5	1.6, 3.0	1.4, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.2
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Baseline			
		n	16	20	36
		Mean	1.98	2.12	2.06
		SD, SE	0.299, 0.075	0.311, 0.070	0.310, 0.052
		Median	2.00	2.10	2.05
		Q1, Q3	1.85, 2.20	1.95, 2.25	1.90, 2.20
		Min, Max	1.4, 2.4	1.6, 3.0	1.4, 3.0
		Observed			
		n	16	20	36
		Mean	2.08	2.77	2.46
		SD, SE	0.309, 0.077	0.607, 0.136	0.604, 0.101
		Median	2.05	2.60	2.40
		Q1, Q3	1.80, 2.20	2.40, 3.10	2.00, 2.70
		Min, Max	1.7, 2.7	2.0, 4.2	1.7, 4.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.2
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Change from Baseline			
		n	16	20	36
		Mean	0.09	0.65	0.40
		SD, SE	0.373, 0.093	0.475, 0.106	0.511, 0.085
		Median	0.05	0.60	0.45
		Q1, Q3	-0.25, 0.40	0.40, 1.00	0.00, 0.70
		Min, Max	-0.5, 0.7	-0.2, 1.7	-0.5, 1.7
		GEE Estimates			
		LS Mean (SE)	0.13 (0.100)	0.72 (0.064)	0.43 (0.049)
		95% CI	(-0.06, 0.33)	(0.60, 0.85)	(0.33, 0.52)
		LS Mean Difference (SE)		0.59 (0.136)	
		95% CI		(0.32, 0.86)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.2
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Baseline			
		n	17	20	37
		Mean	2.01	2.12	2.07
		SD, SE	0.316, 0.077	0.311, 0.070	0.314, 0.052
		Median	2.00	2.10	2.10
		Q1, Q3	1.90, 2.20	1.95, 2.25	1.90, 2.20
		Min, Max	1.4, 2.5	1.6, 3.0	1.4, 3.0
		Observed			
		n	17	20	37
		Mean	2.18	2.58	2.39
		SD, SE	0.243, 0.059	0.501, 0.112	0.445, 0.073
		Median	2.20	2.60	2.30
		Q1, Q3	2.00, 2.40	2.10, 3.05	2.00, 2.60
		Min, Max	1.8, 2.6	1.8, 3.4	1.8, 3.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.2
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Change from Baseline			
		n	17	20	37
		Mean	0.17	0.45	0.32
		SD, SE	0.395, 0.096	0.372, 0.083	0.403, 0.066
		Median	0.20	0.45	0.40
		Q1, Q3	-0.10, 0.40	0.15, 0.70	0.00, 0.60
		Min, Max	-0.4, 1.0	-0.2, 1.1	-0.4, 1.1
		GEE Estimates			
		LS Mean (SE)	0.23 (0.099)	0.52 (0.064)	0.37 (0.060)
		95% CI	(0.03, 0.42)	(0.40, 0.65)	(0.26, 0.49)
		LS Mean Difference (SE)		0.30 (0.116)	
		95% CI		(0.07, 0.52)	
		p-value		0.0111	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.3
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU		N1	58	58	116
	Baseline	n	58	58	116
		Mean	1.94	2.06	2.00
		SD, SE	0.317, 0.042	0.292, 0.038	0.309, 0.029
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.6	1.4, 3.0	1.3, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.3
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Baseline			
		n	56	58	114
		Mean	1.93	2.06	1.99
		SD, SE	0.313, 0.042	0.292, 0.038	0.308, 0.029
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.6	1.4, 3.0	1.3, 3.0
		Observed			
		n	56	58	114
		Mean	2.07	2.68	2.38
		SD, SE	0.363, 0.049	0.526, 0.069	0.546, 0.051
		Median	2.05	2.60	2.30
		Q1, Q3	1.80, 2.30	2.30, 2.90	2.00, 2.60
		Min, Max	1.4, 2.8	1.9, 4.2	1.4, 4.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.3
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Change from Baseline			
		n	56	58	114
		Mean	0.14	0.62	0.38
		SD, SE	0.298, 0.040	0.491, 0.064	0.473, 0.044
		Median	0.10	0.60	0.30
		Q1, Q3	0.00, 0.30	0.30, 1.00	0.00, 0.60
		Min, Max	-0.5, 0.7	-0.3, 1.9	-0.5, 1.9
		GEE Estimates			
		LS Mean (SE)	0.10 (0.039)	0.64 (0.066)	0.37 (0.040)
		95% CI	(0.02, 0.18)	(0.51, 0.77)	(0.29, 0.45)
		LS Mean Difference (SE)		0.54 (0.072)	
		95% CI		(0.40, 0.68)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.5.2.1.24.3
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Baseline			
		n	58	58	116
		Mean	1.94	2.06	2.00
		SD, SE	0.317, 0.042	0.292, 0.038	0.309, 0.029
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.6	1.4, 3.0	1.3, 3.0
		Observed			
		n	58	58	116
		Mean	2.07	2.54	2.31
		SD, SE	0.352, 0.046	0.414, 0.054	0.449, 0.042
		Median	2.10	2.50	2.30
		Q1, Q3	1.80, 2.40	2.20, 2.80	2.00, 2.60
		Min, Max	1.3, 2.8	1.8, 3.7	1.3, 3.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.5.2.1.24.3
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Change from Baseline			
		n	58	58	116
		Mean	0.14	0.49	0.31
		SD, SE	0.351, 0.046	0.377, 0.049	0.403, 0.037
		Median	0.15	0.50	0.30
		Q1, Q3	-0.10, 0.40	0.20, 0.70	0.00, 0.60
		Min, Max	-0.6, 1.1	-0.4, 1.5	-0.6, 1.5
		GEE Estimates			
		LS Mean (SE)	0.11 (0.042)	0.51 (0.049)	0.31 (0.034)
		95% CI	(0.03, 0.19)	(0.41, 0.60)	(0.24, 0.37)
		LS Mean Difference (SE)		0.40 (0.062)	
		95% CI		(0.28, 0.52)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.5.2.1.24.3
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia		N1	8	10	18
	Baseline	n	8	10	18
		Mean	1.81	1.90	1.86
		SD, SE	0.300, 0.106	0.356, 0.113	0.326, 0.077
		Median	1.85	2.00	1.95
		Q1, Q3	1.55, 2.05	1.50, 2.20	1.50, 2.10
		Min, Max	1.4, 2.2	1.3, 2.4	1.3, 2.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.3
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Baseline			
		n	8	10	18
		Mean	1.81	1.90	1.86
		SD, SE	0.300, 0.106	0.356, 0.113	0.326, 0.077
		Median	1.85	2.00	1.95
		Q1, Q3	1.55, 2.05	1.50, 2.20	1.50, 2.10
		Min, Max	1.4, 2.2	1.3, 2.4	1.3, 2.4
		Observed			
		n	8	10	18
		Mean	1.99	2.69	2.38
		SD, SE	0.314, 0.111	0.820, 0.259	0.725, 0.171
		Median	1.95	2.65	2.30
		Q1, Q3	1.70, 2.30	2.30, 2.80	1.90, 2.80
		Min, Max	1.6, 2.4	1.5, 4.6	1.5, 4.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.3
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Change from Baseline			
		n	8	10	18
		Mean	0.17	0.79	0.52
		SD, SE	0.276, 0.098	0.717, 0.227	0.635, 0.150
		Median	0.20	0.70	0.45
		Q1, Q3	0.10, 0.35	0.50, 0.90	0.20, 0.80
		Min, Max	-0.4, 0.5	-0.1, 2.6	-0.4, 2.6
		GEE Estimates			
		LS Mean (SE)	0.26 (0.211)	0.86 (0.176)	0.56 (0.139)
		95% CI	(-0.15, 0.67)	(0.51, 1.21)	(0.29, 0.83)
		LS Mean Difference (SE)		0.60 (0.271)	
		95% CI		(0.07, 1.13)	
		p-value		0.0265	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.3
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Baseline			
		n	8	10	18
		Mean	1.81	1.90	1.86
		SD, SE	0.300, 0.106	0.356, 0.113	0.326, 0.077
		Median	1.85	2.00	1.95
		Q1, Q3	1.55, 2.05	1.50, 2.20	1.50, 2.10
		Min, Max	1.4, 2.2	1.3, 2.4	1.3, 2.4
		Observed			
		n	8	10	18
		Mean	2.03	2.43	2.25
		SD, SE	0.287, 0.101	0.618, 0.196	0.528, 0.125
		Median	2.05	2.30	2.10
		Q1, Q3	1.80, 2.25	2.00, 2.80	1.80, 2.40
		Min, Max	1.6, 2.4	1.6, 3.6	1.6, 3.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.3
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Change from Baseline			
		n	8	10	18
		Mean	0.21	0.53	0.39
		SD, SE	0.318, 0.113	0.512, 0.162	0.455, 0.107
		Median	0.20	0.50	0.35
		Q1, Q3	0.10, 0.45	0.10, 0.60	0.10, 0.60
		Min, Max	-0.4, 0.6	-0.1, 1.6	-0.4, 1.6
		GEE Estimates			
		LS Mean (SE)	0.30 (0.198)	0.60 (0.155)	0.45 (0.152)
		95% CI	(-0.09, 0.68)	(0.30, 0.90)	(0.15, 0.75)
		LS Mean Difference (SE)		0.30 (0.182)	
		95% CI		(-0.05, 0.66)	
		p-value		0.0965	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.4
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male		N1	23	24	47
	Baseline	n	23	24	47
		Mean	1.77	1.97	1.87
		SD, SE	0.329, 0.069	0.260, 0.053	0.309, 0.045
		Median	1.70	1.95	1.90
		Q1, Q3	1.50, 2.00	1.90, 2.20	1.60, 2.10
		Min, Max	1.3, 2.4	1.3, 2.4	1.3, 2.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.4
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Baseline			
		n	22	24	46
		Mean	1.77	1.97	1.88
		SD, SE	0.337, 0.072	0.260, 0.053	0.312, 0.046
		Median	1.70	1.95	1.90
		Q1, Q3	1.50, 2.00	1.90, 2.20	1.60, 2.10
		Min, Max	1.3, 2.4	1.3, 2.4	1.3, 2.4
		Observed			
		n	22	24	46
		Mean	1.88	2.48	2.19
		SD, SE	0.341, 0.073	0.550, 0.112	0.550, 0.081
		Median	1.85	2.35	2.10
		Q1, Q3	1.60, 2.00	2.15, 2.65	1.80, 2.50
		Min, Max	1.4, 2.7	1.5, 4.2	1.4, 4.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.4
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Change from Baseline			
		n	22	24	46
		Mean	0.10	0.51	0.32
		SD, SE	0.320, 0.068	0.501, 0.102	0.467, 0.069
		Median	0.10	0.50	0.30
		Q1, Q3	0.00, 0.30	0.20, 0.75	0.00, 0.60
		Min, Max	-0.5, 0.6	-0.2, 1.9	-0.5, 1.9
		GEE Estimates			
		LS Mean (SE)	-0.16 (0.099)	0.36 (0.114)	0.10 (0.091)
		95% CI	(-0.35, 0.04)	(0.14, 0.59)	(-0.08, 0.28)
		LS Mean Difference (SE)		0.52 (0.114)	
		95% CI		(0.30, 0.74)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.4
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Baseline			
		n	23	24	47
		Mean	1.77	1.97	1.87
		SD, SE	0.329, 0.069	0.260, 0.053	0.309, 0.045
		Median	1.70	1.95	1.90
		Q1, Q3	1.50, 2.00	1.90, 2.20	1.60, 2.10
		Min, Max	1.3, 2.4	1.3, 2.4	1.3, 2.4
		Observed			
		n	23	24	47
		Mean	1.84	2.36	2.10
		SD, SE	0.274, 0.057	0.437, 0.089	0.448, 0.065
		Median	1.90	2.30	2.00
		Q1, Q3	1.60, 2.00	2.00, 2.60	1.80, 2.50
		Min, Max	1.3, 2.5	1.8, 3.7	1.3, 3.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.4
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Change from Baseline			
		n	23	24	47
		Mean	0.07	0.39	0.23
		SD, SE	0.313, 0.065	0.384, 0.078	0.383, 0.056
		Median	0.10	0.40	0.20
		Q1, Q3	-0.10, 0.20	0.05, 0.60	0.00, 0.50
		Min, Max	-0.6, 0.6	-0.2, 1.5	-0.6, 1.5
		GEE Estimates			
		LS Mean (SE)	-0.19 (0.101)	0.24 (0.095)	0.02 (0.087)
		95% CI	(-0.39, 0.01)	(0.05, 0.42)	(-0.15, 0.19)
		LS Mean Difference (SE)		0.43 (0.091)	
		95% CI		(0.25, 0.61)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.4
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female		N1	43	44	87
	Baseline	n	43	44	87
		Mean	2.00	2.07	2.03
		SD, SE	0.281, 0.043	0.323, 0.049	0.303, 0.033
		Median	2.00	2.00	2.00
		Q1, Q3	1.80, 2.20	1.85, 2.25	1.80, 2.20
		Min, Max	1.4, 2.6	1.4, 3.0	1.4, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.4
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Baseline			
		n	42	44	86
		Mean	1.99	2.07	2.03
		SD, SE	0.273, 0.042	0.323, 0.049	0.301, 0.032
		Median	2.00	2.00	2.00
		Q1, Q3	1.80, 2.20	1.85, 2.25	1.80, 2.20
		Min, Max	1.4, 2.6	1.4, 3.0	1.4, 3.0
		Observed			
		n	42	44	86
		Mean	2.15	2.79	2.48
		SD, SE	0.331, 0.051	0.559, 0.084	0.560, 0.060
		Median	2.15	2.70	2.40
		Q1, Q3	1.90, 2.40	2.45, 3.05	2.10, 2.70
		Min, Max	1.5, 2.8	2.0, 4.6	1.5, 4.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.4
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Change from Baseline			
		n	42	44	86
		Mean	0.16	0.72	0.45
		SD, SE	0.281, 0.043	0.532, 0.080	0.510, 0.055
		Median	0.20	0.70	0.35
		Q1, Q3	0.00, 0.30	0.35, 1.00	0.10, 0.70
		Min, Max	-0.4, 0.7	-0.3, 2.6	-0.4, 2.6
		GEE Estimates			
		LS Mean (SE)	0.11 (0.094)	0.72 (0.125)	0.42 (0.102)
		95% CI	(-0.07, 0.30)	(0.47, 0.96)	(0.22, 0.62)
		LS Mean Difference (SE)		0.60 (0.085)	
		95% CI		(0.44, 0.77)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.4
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Baseline			
		n	43	44	87
		Mean	2.00	2.07	2.03
		SD, SE	0.281, 0.043	0.323, 0.049	0.303, 0.033
		Median	2.00	2.00	2.00
		Q1, Q3	1.80, 2.20	1.85, 2.25	1.80, 2.20
		Min, Max	1.4, 2.6	1.4, 3.0	1.4, 3.0
		Observed			
		n	43	44	87
		Mean	2.19	2.62	2.41
		SD, SE	0.315, 0.048	0.428, 0.065	0.432, 0.046
		Median	2.30	2.55	2.40
		Q1, Q3	2.00, 2.40	2.30, 2.95	2.10, 2.60
		Min, Max	1.5, 2.8	1.6, 3.6	1.5, 3.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.4
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Change from Baseline			
		n	43	44	87
		Mean	0.19	0.55	0.37
		SD, SE	0.358, 0.055	0.393, 0.059	0.416, 0.045
		Median	0.20	0.60	0.40
		Q1, Q3	-0.10, 0.40	0.30, 0.80	0.10, 0.70
		Min, Max	-0.4, 1.1	-0.4, 1.6	-0.4, 1.6
		GEE Estimates			
		LS Mean (SE)	0.15 (0.096)	0.55 (0.116)	0.35 (0.100)
		95% CI	(-0.04, 0.34)	(0.32, 0.78)	(0.15, 0.55)
		LS Mean Difference (SE)		0.40 (0.070)	
		95% CI		(0.26, 0.54)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.5
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White		N1	53	55	108
	Baseline	n	53	55	108
		Mean	1.91	2.05	1.98
		SD, SE	0.305, 0.042	0.292, 0.039	0.305, 0.029
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.5	1.4, 3.0	1.3, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.5
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Baseline			
		n	51	55	106
		Mean	1.90	2.05	1.98
		SD, SE	0.299, 0.042	0.292, 0.039	0.303, 0.029
		Median	1.90	2.00	2.00
		Q1, Q3	1.60, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.4	1.4, 3.0	1.3, 3.0
		Observed			
		n	51	55	106
		Mean	2.06	2.68	2.38
		SD, SE	0.350, 0.049	0.540, 0.073	0.551, 0.054
		Median	2.10	2.60	2.30
		Q1, Q3	1.80, 2.30	2.30, 3.00	2.00, 2.60
		Min, Max	1.4, 2.8	1.9, 4.2	1.4, 4.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.5
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Change from Baseline			
		n	51	55	106
		Mean	0.16	0.63	0.41
		SD, SE	0.286, 0.040	0.502, 0.068	0.473, 0.046
		Median	0.10	0.60	0.30
		Q1, Q3	0.00, 0.40	0.30, 1.00	0.10, 0.70
		Min, Max	-0.5, 0.7	-0.3, 1.9	-0.5, 1.9
		GEE Estimates			
		LS Mean (SE)	0.12 (0.041)	0.65 (0.069)	0.38 (0.043)
		95% CI	(0.04, 0.20)	(0.51, 0.79)	(0.30, 0.47)
		LS Mean Difference (SE)		0.53 (0.075)	
		95% CI		(0.39, 0.68)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.5
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Baseline			
		n	53	55	108
		Mean	1.91	2.05	1.98
		SD, SE	0.305, 0.042	0.292, 0.039	0.305, 0.029
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.5	1.4, 3.0	1.3, 3.0
		Observed			
		n	53	55	108
		Mean	2.08	2.55	2.32
		SD, SE	0.357, 0.049	0.408, 0.055	0.448, 0.043
		Median	2.10	2.50	2.35
		Q1, Q3	1.80, 2.40	2.20, 2.80	2.00, 2.60
		Min, Max	1.3, 2.8	1.8, 3.7	1.3, 3.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.5
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Change from Baseline			
		n	53	55	108
		Mean	0.17	0.50	0.34
		SD, SE	0.345, 0.047	0.377, 0.051	0.396, 0.038
		Median	0.20	0.50	0.30
		Q1, Q3	-0.10, 0.40	0.20, 0.80	0.05, 0.60
		Min, Max	-0.6, 1.1	-0.4, 1.5	-0.6, 1.5
		GEE Estimates			
		LS Mean (SE)	0.14 (0.046)	0.52 (0.050)	0.33 (0.036)
		95% CI	(0.05, 0.23)	(0.42, 0.62)	(0.26, 0.40)
		LS Mean Difference (SE)		0.38 (0.064)	
		95% CI		(0.26, 0.51)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.5
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White		N1	13	13	26
	Baseline	n	13	13	26
		Mean	1.97	1.96	1.97
		SD, SE	0.366, 0.102	0.352, 0.098	0.352, 0.069
		Median	2.00	2.00	2.00
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.70, 2.20
		Min, Max	1.4, 2.6	1.3, 2.5	1.3, 2.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.5
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Baseline			
		n	13	13	26
		Mean	1.97	1.96	1.97
		SD, SE	0.366, 0.102	0.352, 0.098	0.352, 0.069
		Median	2.00	2.00	2.00
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.70, 2.20
		Min, Max	1.4, 2.6	1.3, 2.5	1.3, 2.6
		Observed			
		n	13	13	26
		Mean	2.02	2.68	2.35
		SD, SE	0.394, 0.109	0.713, 0.198	0.656, 0.129
		Median	1.90	2.60	2.30
		Q1, Q3	1.70, 2.30	2.30, 2.80	1.80, 2.70
		Min, Max	1.5, 2.7	1.5, 4.6	1.5, 4.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.5
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Change from Baseline			
		n	13	13	26
		Mean	0.05	0.72	0.38
		SD, SE	0.318, 0.088	0.640, 0.178	0.599, 0.117
		Median	0.20	0.60	0.30
		Q1, Q3	-0.20, 0.30	0.50, 0.80	0.00, 0.60
		Min, Max	-0.5, 0.5	-0.1, 2.6	-0.5, 2.6
		GEE Estimates			
		LS Mean (SE)	0.09 (0.107)	0.74 (0.142)	0.42 (0.086)
		95% CI	(-0.12, 0.30)	(0.47, 1.02)	(0.25, 0.59)
		LS Mean Difference (SE)		0.65 (0.183)	
		95% CI		(0.29, 1.01)	
		p-value		0.0004	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.5
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Baseline			
		n	13	13	26
		Mean	1.97	1.96	1.97
		SD, SE	0.366, 0.102	0.352, 0.098	0.352, 0.069
		Median	2.00	2.00	2.00
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.70, 2.20
		Min, Max	1.4, 2.6	1.3, 2.5	1.3, 2.6
		Observed			
		n	13	13	26
		Mean	2.01	2.42	2.22
		SD, SE	0.287, 0.080	0.590, 0.164	0.502, 0.098
		Median	2.00	2.30	2.10
		Q1, Q3	1.80, 2.10	2.00, 2.80	2.00, 2.40
		Min, Max	1.5, 2.4	1.6, 3.6	1.5, 3.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.5
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Change from Baseline			
		n	13	13	26
		Mean	0.04	0.46	0.25
		SD, SE	0.340, 0.094	0.481, 0.133	0.462, 0.091
		Median	0.10	0.50	0.15
		Q1, Q3	-0.20, 0.20	0.10, 0.60	-0.10, 0.60
		Min, Max	-0.4, 0.6	-0.1, 1.6	-0.4, 1.6
		GEE Estimates			
		LS Mean (SE)	0.08 (0.090)	0.49 (0.118)	0.28 (0.079)
		95% CI	(-0.10, 0.25)	(0.26, 0.72)	(0.13, 0.44)
		LS Mean Difference (SE)		0.41 (0.139)	
		95% CI		(0.14, 0.69)	
		p-value		0.0028	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.6
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years		N1	36	31	67
	Baseline	n	36	31	67
		Mean	1.91	1.97	1.94
		SD, SE	0.369, 0.062	0.294, 0.053	0.335, 0.041
		Median	1.90	2.00	1.90
		Q1, Q3	1.60, 2.25	1.80, 2.20	1.70, 2.20
		Min, Max	1.3, 2.6	1.3, 2.6	1.3, 2.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.6
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Baseline			
		n	34	31	65
		Mean	1.90	1.97	1.93
		SD, SE	0.366, 0.063	0.294, 0.053	0.333, 0.041
		Median	1.90	2.00	1.90
		Q1, Q3	1.60, 2.20	1.80, 2.20	1.70, 2.20
		Min, Max	1.3, 2.6	1.3, 2.6	1.3, 2.6
		Observed			
		n	34	31	65
		Mean	2.07	2.49	2.27
		SD, SE	0.354, 0.061	0.400, 0.072	0.429, 0.053
		Median	2.05	2.50	2.30
		Q1, Q3	1.80, 2.30	2.30, 2.70	2.00, 2.50
		Min, Max	1.4, 2.7	1.5, 3.6	1.4, 3.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.6
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Change from Baseline			
		n	34	31	65
		Mean	0.17	0.52	0.34
		SD, SE	0.338, 0.058	0.380, 0.068	0.397, 0.049
		Median	0.15	0.50	0.30
		Q1, Q3	0.00, 0.50	0.30, 0.70	0.10, 0.60
		Min, Max	-0.5, 0.7	-0.2, 1.6	-0.5, 1.6
		GEE Estimates			
		LS Mean (SE)	0.00 (0.074)	0.39 (0.076)	0.20 (0.063)
		95% CI	(-0.14, 0.15)	(0.24, 0.54)	(0.07, 0.32)
		LS Mean Difference (SE)		0.39 (0.082)	
		95% CI		(0.23, 0.55)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.6
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Baseline			
		n	36	31	67
		Mean	1.91	1.97	1.94
		SD, SE	0.369, 0.062	0.294, 0.053	0.335, 0.041
		Median	1.90	2.00	1.90
		Q1, Q3	1.60, 2.25	1.80, 2.20	1.70, 2.20
		Min, Max	1.3, 2.6	1.3, 2.6	1.3, 2.6
		Observed			
		n	36	31	67
		Mean	2.04	2.44	2.22
		SD, SE	0.323, 0.054	0.401, 0.072	0.411, 0.050
		Median	2.10	2.50	2.20
		Q1, Q3	1.80, 2.35	2.10, 2.70	2.00, 2.50
		Min, Max	1.3, 2.5	1.8, 3.3	1.3, 3.3

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.6
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Change from Baseline			
		n	36	31	67
		Mean	0.13	0.47	0.29
		SD, SE	0.342, 0.057	0.323, 0.058	0.373, 0.046
		Median	0.15	0.50	0.30
		Q1, Q3	-0.10, 0.35	0.30, 0.70	0.00, 0.60
		Min, Max	-0.6, 1.0	-0.4, 1.0	-0.6, 1.0
		GEE Estimates			
		LS Mean (SE)	-0.03 (0.071)	0.34 (0.068)	0.16 (0.059)
		95% CI	(-0.17, 0.11)	(0.21, 0.47)	(0.04, 0.27)
		LS Mean Difference (SE)		0.37 (0.074)	
		95% CI		(0.22, 0.51)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.6
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years		N1	30	37	67
	Baseline	n	30	37	67
		Mean	1.93	2.09	2.02
		SD, SE	0.241, 0.044	0.306, 0.050	0.287, 0.035
		Median	1.95	2.00	2.00
		Q1, Q3	1.80, 2.10	1.90, 2.30	1.80, 2.20
		Min, Max	1.4, 2.4	1.5, 3.0	1.4, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.6
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Baseline			
		n	30	37	67
		Mean	1.93	2.09	2.02
		SD, SE	0.241, 0.044	0.306, 0.050	0.287, 0.035
		Median	1.95	2.00	2.00
		Q1, Q3	1.80, 2.10	1.90, 2.30	1.80, 2.20
		Min, Max	1.4, 2.4	1.5, 3.0	1.4, 3.0
		Observed			
		n	30	37	67
		Mean	2.04	2.84	2.48
		SD, SE	0.365, 0.067	0.644, 0.106	0.666, 0.081
		Median	2.00	2.80	2.30
		Q1, Q3	1.80, 2.30	2.30, 3.10	2.00, 2.80
		Min, Max	1.4, 2.8	2.0, 4.6	1.4, 4.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.6
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Change from Baseline			
		n	30	37	67
		Mean	0.11	0.75	0.47
		SD, SE	0.235, 0.043	0.609, 0.100	0.575, 0.070
		Median	0.10	0.80	0.30
		Q1, Q3	0.00, 0.20	0.40, 1.00	0.00, 0.80
		Min, Max	-0.4, 0.6	-0.3, 2.6	-0.4, 2.6
		GEE Estimates			
		LS Mean (SE)	0.04 (0.123)	0.74 (0.159)	0.39 (0.133)
		95% CI	(-0.20, 0.28)	(0.42, 1.05)	(0.13, 0.65)
		LS Mean Difference (SE)		0.69 (0.099)	
		95% CI		(0.50, 0.89)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.6
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Baseline			
		n	30	37	67
		Mean	1.93	2.09	2.02
		SD, SE	0.241, 0.044	0.306, 0.050	0.287, 0.035
		Median	1.95	2.00	2.00
		Q1, Q3	1.80, 2.10	1.90, 2.30	1.80, 2.20
		Min, Max	1.4, 2.4	1.5, 3.0	1.4, 3.0
		Observed			
		n	30	37	67
		Mean	2.10	2.60	2.38
		SD, SE	0.369, 0.067	0.474, 0.078	0.494, 0.060
		Median	2.10	2.50	2.40
		Q1, Q3	1.80, 2.40	2.30, 2.80	2.00, 2.70
		Min, Max	1.5, 2.8	1.6, 3.7	1.5, 3.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.6
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Change from Baseline			
		n	30	37	67
		Mean	0.17	0.51	0.36
		SD, SE	0.354, 0.065	0.450, 0.074	0.442, 0.054
		Median	0.20	0.50	0.30
		Q1, Q3	-0.10, 0.40	0.10, 0.80	0.10, 0.70
		Min, Max	-0.4, 1.1	-0.2, 1.6	-0.4, 1.6
		GEE Estimates			
		LS Mean (SE)	0.10 (0.128)	0.50 (0.143)	0.30 (0.129)
		95% CI	(-0.15, 0.35)	(0.22, 0.78)	(0.05, 0.55)
		LS Mean Difference (SE)		0.39 (0.088)	
		95% CI		(0.22, 0.57)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.7
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5		N1	41	39	80
	Baseline	n	41	39	80
		Mean	1.91	2.03	1.97
		SD, SE	0.316, 0.049	0.301, 0.048	0.312, 0.035
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.10	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.6	1.3, 2.7	1.3, 2.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.7
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline			
		n	39	39	78
		Mean	1.90	2.03	1.96
		SD, SE	0.309, 0.049	0.301, 0.048	0.310, 0.035
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.10	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.6	1.3, 2.7	1.3, 2.7
		Observed			
		n	39	39	78
		Mean	2.09	2.67	2.38
		SD, SE	0.371, 0.059	0.552, 0.088	0.551, 0.062
		Median	2.10	2.60	2.30
		Q1, Q3	1.70, 2.40	2.30, 3.00	2.10, 2.60
		Min, Max	1.4, 2.7	1.5, 4.6	1.4, 4.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.7
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline			
		n	39	39	78
		Mean	0.19	0.64	0.41
		SD, SE	0.259, 0.041	0.532, 0.085	0.474, 0.054
		Median	0.20	0.60	0.30
		Q1, Q3	0.00, 0.30	0.30, 1.00	0.10, 0.60
		Min, Max	-0.4, 0.7	-0.3, 2.6	-0.4, 2.6
		GEE Estimates			
		LS Mean (SE)	0.02 (0.082)	0.55 (0.122)	0.28 (0.093)
		95% CI	(-0.14, 0.18)	(0.31, 0.79)	(0.10, 0.47)
		LS Mean Difference (SE)		0.53 (0.094)	
		95% CI		(0.34, 0.71)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.7
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline			
		n	41	39	80
		Mean	1.91	2.03	1.97
		SD, SE	0.316, 0.049	0.301, 0.048	0.312, 0.035
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.10	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.6	1.3, 2.7	1.3, 2.7
		Observed			
		n	41	39	80
		Mean	2.07	2.57	2.32
		SD, SE	0.346, 0.054	0.478, 0.077	0.484, 0.054
		Median	2.10	2.60	2.30
		Q1, Q3	1.80, 2.40	2.20, 2.80	2.00, 2.60
		Min, Max	1.3, 2.8	1.6, 3.7	1.3, 3.7

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Table 2.2.5.2.1.24.7
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline			
		n	41	39	80
		Mean	0.16	0.55	0.35
		SD, SE	0.355, 0.055	0.424, 0.068	0.434, 0.049
		Median	0.20	0.60	0.35
		Q1, Q3	-0.10, 0.40	0.20, 0.80	0.05, 0.60
		Min, Max	-0.6, 1.1	-0.4, 1.6	-0.6, 1.6
		GEE Estimates			
		LS Mean (SE)	0.01 (0.078)	0.46 (0.100)	0.23 (0.080)
		95% CI	(-0.15, 0.16)	(0.26, 0.65)	(0.07, 0.39)
		LS Mean Difference (SE)		0.45 (0.079)	
		95% CI		(0.30, 0.60)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.7
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5		N1	25	29	54
	Baseline	n	25	29	54
		Mean	1.94	2.04	1.99
		SD, SE	0.321, 0.064	0.313, 0.058	0.318, 0.043
		Median	2.00	2.00	2.00
		Q1, Q3	1.70, 2.20	1.80, 2.20	1.80, 2.20
		Min, Max	1.4, 2.4	1.4, 3.0	1.4, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline			
		n	25	29	54
		Mean	1.94	2.04	1.99
		SD, SE	0.321, 0.064	0.313, 0.058	0.318, 0.043
		Median	2.00	2.00	2.00
		Q1, Q3	1.70, 2.20	1.80, 2.20	1.80, 2.20
		Min, Max	1.4, 2.4	1.4, 3.0	1.4, 3.0
		Observed			
		n	25	29	54
		Mean	2.01	2.70	2.38
		SD, SE	0.333, 0.067	0.605, 0.112	0.603, 0.082
		Median	2.00	2.50	2.30
		Q1, Q3	1.80, 2.20	2.30, 2.80	2.00, 2.70
		Min, Max	1.4, 2.8	2.0, 4.2	1.4, 4.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline			
		n	25	29	54
		Mean	0.07	0.66	0.39
		SD, SE	0.335, 0.067	0.529, 0.098	0.534, 0.073
		Median	0.00	0.60	0.30
		Q1, Q3	-0.20, 0.30	0.30, 0.90	0.00, 0.60
		Min, Max	-0.5, 0.6	-0.2, 1.9	-0.5, 1.9
		GEE Estimates			
		LS Mean (SE)	0.04 (0.089)	0.68 (0.103)	0.36 (0.078)
		95% CI	(-0.13, 0.22)	(0.48, 0.88)	(0.21, 0.52)
		LS Mean Difference (SE)		0.64 (0.111)	
		95% CI		(0.42, 0.86)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline			
		n	25	29	54
		Mean	1.94	2.04	1.99
		SD, SE	0.321, 0.064	0.313, 0.058	0.318, 0.043
		Median	2.00	2.00	2.00
		Q1, Q3	1.70, 2.20	1.80, 2.20	1.80, 2.20
		Min, Max	1.4, 2.4	1.4, 3.0	1.4, 3.0
		Observed			
		n	25	29	54
		Mean	2.06	2.46	2.28
		SD, SE	0.346, 0.069	0.399, 0.074	0.422, 0.057
		Median	2.00	2.40	2.30
		Q1, Q3	1.80, 2.40	2.20, 2.70	2.00, 2.50
		Min, Max	1.5, 2.6	1.8, 3.2	1.5, 3.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline			
		n	25	29	54
		Mean	0.13	0.42	0.29
		SD, SE	0.336, 0.067	0.347, 0.064	0.370, 0.050
		Median	0.10	0.40	0.20
		Q1, Q3	-0.10, 0.30	0.20, 0.70	0.00, 0.50
		Min, Max	-0.4, 1.0	-0.2, 1.1	-0.4, 1.1
		GEE Estimates			
		LS Mean (SE)	0.10 (0.096)	0.45 (0.081)	0.27 (0.078)
		95% CI	(-0.09, 0.29)	(0.29, 0.61)	(0.12, 0.43)
		LS Mean Difference (SE)		0.35 (0.087)	
		95% CI		(0.18, 0.52)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.8
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8		N1	37	30	67
	Baseline	n	37	30	67
		Mean	1.85	1.98	1.91
		SD, SE	0.323, 0.053	0.270, 0.049	0.305, 0.037
		Median	1.90	2.00	1.90
		Q1, Q3	1.60, 2.00	1.90, 2.20	1.70, 2.10
		Min, Max	1.3, 2.6	1.4, 2.5	1.3, 2.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline			
		n	37	30	67
		Mean	1.85	1.98	1.91
		SD, SE	0.323, 0.053	0.270, 0.049	0.305, 0.037
		Median	1.90	2.00	1.90
		Q1, Q3	1.60, 2.00	1.90, 2.20	1.70, 2.10
		Min, Max	1.3, 2.6	1.4, 2.5	1.3, 2.6
		Observed			
		n	37	30	67
		Mean	2.04	2.70	2.34
		SD, SE	0.386, 0.063	0.614, 0.112	0.595, 0.073
		Median	2.00	2.50	2.30
		Q1, Q3	1.70, 2.30	2.30, 3.10	2.00, 2.60
		Min, Max	1.4, 2.7	1.9, 4.6	1.4, 4.6

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The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline			
		n	37	30	67
		Mean	0.19	0.72	0.43
		SD, SE	0.283, 0.046	0.596, 0.109	0.519, 0.063
		Median	0.20	0.60	0.40
		Q1, Q3	0.00, 0.40	0.40, 1.00	0.10, 0.60
		Min, Max	-0.5, 0.7	-0.3, 2.6	-0.5, 2.6
		GEE Estimates			
		LS Mean (SE)	0.06 (0.098)	0.63 (0.145)	0.34 (0.108)
		95% CI	(-0.14, 0.25)	(0.35, 0.92)	(0.13, 0.56)
		LS Mean Difference (SE)		0.58 (0.119)	
		95% CI		(0.34, 0.81)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline			
		n	37	30	67
		Mean	1.85	1.98	1.91
		SD, SE	0.323, 0.053	0.270, 0.049	0.305, 0.037
		Median	1.90	2.00	1.90
		Q1, Q3	1.60, 2.00	1.90, 2.20	1.70, 2.10
		Min, Max	1.3, 2.6	1.4, 2.5	1.3, 2.6
		Observed			
		n	37	30	67
		Mean	2.04	2.53	2.26
		SD, SE	0.359, 0.059	0.463, 0.085	0.475, 0.058
		Median	2.10	2.50	2.20
		Q1, Q3	1.80, 2.40	2.20, 2.80	1.90, 2.50
		Min, Max	1.3, 2.7	1.6, 3.7	1.3, 3.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline			
		n	37	30	67
		Mean	0.18	0.55	0.34
		SD, SE	0.328, 0.054	0.399, 0.073	0.403, 0.049
		Median	0.20	0.50	0.30
		Q1, Q3	0.00, 0.40	0.30, 0.70	0.10, 0.60
		Min, Max	-0.6, 1.0	0.0, 1.6	-0.6, 1.6
		GEE Estimates			
		LS Mean (SE)	0.05 (0.094)	0.46 (0.121)	0.25 (0.100)
		95% CI	(-0.14, 0.23)	(0.22, 0.70)	(0.06, 0.45)
		LS Mean Difference (SE)		0.41 (0.086)	
		95% CI		(0.25, 0.58)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8		N1	29	38	67
	Baseline	n	29	38	67
		Mean	2.01	2.07	2.04
		SD, SE	0.289, 0.054	0.326, 0.053	0.310, 0.038
		Median	2.00	2.05	2.00
		Q1, Q3	1.80, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.4, 2.5	1.3, 3.0	1.3, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.8
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline			
		n	27	38	65
		Mean	2.00	2.07	2.04
		SD, SE	0.281, 0.054	0.326, 0.053	0.308, 0.038
		Median	2.00	2.05	2.00
		Q1, Q3	1.80, 2.20	1.90, 2.20	1.90, 2.20
		Min, Max	1.4, 2.4	1.3, 3.0	1.3, 3.0
		Observed			
		n	27	38	65
		Mean	2.07	2.67	2.42
		SD, SE	0.318, 0.061	0.542, 0.088	0.545, 0.068
		Median	2.00	2.60	2.30
		Q1, Q3	1.80, 2.30	2.30, 2.90	2.00, 2.70
		Min, Max	1.6, 2.8	1.5, 4.2	1.5, 4.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.8
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline			
		n	27	38	65
		Mean	0.08	0.59	0.38
		SD, SE	0.302, 0.058	0.466, 0.076	0.477, 0.059
		Median	0.10	0.60	0.30
		Q1, Q3	-0.10, 0.20	0.20, 0.90	0.00, 0.70
		Min, Max	-0.5, 0.7	-0.2, 1.7	-0.5, 1.7
		GEE Estimates			
		LS Mean (SE)	-0.09 (0.121)	0.49 (0.125)	0.20 (0.114)
		95% CI	(-0.33, 0.15)	(0.25, 0.74)	(-0.02, 0.42)
		LS Mean Difference (SE)		0.58 (0.093)	
		95% CI		(0.40, 0.76)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.8
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline			
		n	29	38	67
		Mean	2.01	2.07	2.04
		SD, SE	0.289, 0.054	0.326, 0.053	0.310, 0.038
		Median	2.00	2.05	2.00
		Q1, Q3	1.80, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.4, 2.5	1.3, 3.0	1.3, 3.0
		Observed			
		n	29	38	67
		Mean	2.11	2.53	2.35
		SD, SE	0.323, 0.060	0.438, 0.071	0.442, 0.054
		Median	2.10	2.50	2.30
		Q1, Q3	1.90, 2.40	2.20, 2.80	2.00, 2.60
		Min, Max	1.5, 2.8	1.8, 3.4	1.5, 3.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.8
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline			
		n	29	38	67
		Mean	0.10	0.45	0.30
		SD, SE	0.368, 0.068	0.392, 0.064	0.417, 0.051
		Median	0.10	0.50	0.20
		Q1, Q3	-0.10, 0.40	0.20, 0.70	0.00, 0.60
		Min, Max	-0.4, 1.1	-0.4, 1.1	-0.4, 1.1
		GEE Estimates			
		LS Mean (SE)	-0.05 (0.122)	0.35 (0.115)	0.15 (0.111)
		95% CI	(-0.29, 0.19)	(0.13, 0.58)	(-0.07, 0.37)
		LS Mean Difference (SE)		0.40 (0.086)	
		95% CI		(0.23, 0.57)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.9
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat <= 50		N1	42	32	74
	Baseline	n	42	32	74
		Mean	1.89	2.00	1.93
		SD, SE	0.293, 0.045	0.282, 0.050	0.292, 0.034
		Median	1.90	2.00	1.90
		Q1, Q3	1.70, 2.00	1.90, 2.15	1.70, 2.10
		Min, Max	1.4, 2.6	1.3, 2.6	1.3, 2.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.9
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat <= 50	Week 12	Baseline			
		n	41	32	73
		Mean	1.89	2.00	1.94
		SD, SE	0.297, 0.046	0.282, 0.050	0.294, 0.034
		Median	1.90	2.00	1.90
		Q1, Q3	1.70, 2.00	1.90, 2.15	1.70, 2.10
		Min, Max	1.4, 2.6	1.3, 2.6	1.3, 2.6
		Observed			
		n	41	32	73
		Mean	2.06	2.68	2.33
		SD, SE	0.360, 0.056	0.616, 0.109	0.575, 0.067
		Median	2.00	2.65	2.30
		Q1, Q3	1.80, 2.30	2.30, 2.95	2.00, 2.60
		Min, Max	1.4, 2.7	1.5, 4.6	1.4, 4.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.9
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat <= 50	Week 12	Change from Baseline			
		n	41	32	73
		Mean	0.18	0.68	0.40
		SD, SE	0.261, 0.041	0.566, 0.100	0.490, 0.057
		Median	0.20	0.60	0.30
		Q1, Q3	0.00, 0.30	0.30, 1.00	0.10, 0.60
		Min, Max	-0.5, 0.7	-0.3, 2.6	-0.5, 2.6
		GEE Estimates			
		LS Mean (SE)	0.04 (0.084)	0.62 (0.126)	0.33 (0.093)
		95% CI	(-0.13, 0.20)	(0.37, 0.87)	(0.15, 0.51)
		LS Mean Difference (SE)		0.58 (0.107)	
		95% CI		(0.37, 0.79)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.9
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat <= 50	Week 24	Baseline			
		n	42	32	74
		Mean	1.89	2.00	1.93
		SD, SE	0.293, 0.045	0.282, 0.050	0.292, 0.034
		Median	1.90	2.00	1.90
		Q1, Q3	1.70, 2.00	1.90, 2.15	1.70, 2.10
		Min, Max	1.4, 2.6	1.3, 2.6	1.3, 2.6
		Observed			
		n	42	32	74
		Mean	2.05	2.50	2.24
		SD, SE	0.358, 0.055	0.476, 0.084	0.468, 0.054
		Median	2.05	2.50	2.20
		Q1, Q3	1.80, 2.40	2.10, 2.80	1.90, 2.50
		Min, Max	1.5, 2.8	1.6, 3.7	1.5, 3.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.9
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat <= 50	Week 24	Change from Baseline			
		n	42	32	74
		Mean	0.16	0.50	0.31
		SD, SE	0.365, 0.056	0.419, 0.074	0.422, 0.049
		Median	0.20	0.50	0.30
		Q1, Q3	-0.10, 0.40	0.15, 0.70	0.00, 0.60
		Min, Max	-0.6, 1.1	-0.4, 1.6	-0.6, 1.6
		GEE Estimates			
		LS Mean (SE)	0.03 (0.084)	0.43 (0.101)	0.23 (0.082)
		95% CI	(-0.14, 0.19)	(0.24, 0.63)	(0.07, 0.39)
		LS Mean Difference (SE)		0.41 (0.088)	
		95% CI		(0.24, 0.58)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.9
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat > 50		N1	24	35	59
	Baseline	n	24	35	59
		Mean	1.98	2.07	2.04
		SD, SE	0.348, 0.071	0.324, 0.055	0.334, 0.043
		Median	2.10	2.10	2.10
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.5	1.4, 3.0	1.3, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.9
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat > 50	Week 12	Baseline			
		n	23	35	58
		Mean	1.96	2.07	2.03
		SD, SE	0.338, 0.070	0.324, 0.055	0.331, 0.044
		Median	2.10	2.10	2.10
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.4	1.4, 3.0	1.3, 3.0
		Observed			
		n	23	35	58
		Mean	2.04	2.69	2.43
		SD, SE	0.357, 0.074	0.542, 0.092	0.570, 0.075
		Median	2.10	2.60	2.35
		Q1, Q3	1.80, 2.30	2.30, 2.90	2.10, 2.80
		Min, Max	1.4, 2.8	2.0, 4.2	1.4, 4.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.9
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat > 50	Week 12	Change from Baseline			
		n	23	35	58
		Mean	0.08	0.61	0.40
		SD, SE	0.343, 0.072	0.502, 0.085	0.515, 0.068
		Median	0.10	0.60	0.35
		Q1, Q3	-0.20, 0.30	0.20, 0.90	0.00, 0.70
		Min, Max	-0.5, 0.7	-0.2, 1.7	-0.5, 1.7
		GEE Estimates			
		LS Mean (SE)	-0.09 (0.093)	0.53 (0.102)	0.22 (0.082)
		95% CI	(-0.27, 0.09)	(0.33, 0.73)	(0.06, 0.38)
		LS Mean Difference (SE)		0.62 (0.106)	
		95% CI		(0.41, 0.82)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.9
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat > 50	Week 24	Baseline			
		n	24	35	59
		Mean	1.98	2.07	2.04
		SD, SE	0.348, 0.071	0.324, 0.055	0.334, 0.043
		Median	2.10	2.10	2.10
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.5	1.4, 3.0	1.3, 3.0
		Observed			
		n	24	35	59
		Mean	2.11	2.56	2.38
		SD, SE	0.320, 0.065	0.425, 0.072	0.444, 0.058
		Median	2.10	2.50	2.40
		Q1, Q3	2.00, 2.40	2.20, 3.00	2.00, 2.60
		Min, Max	1.3, 2.6	1.8, 3.4	1.3, 3.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.9
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat > 50	Week 24	Change from Baseline			
		n	24	35	59
		Mean	0.13	0.49	0.34
		SD, SE	0.315, 0.064	0.384, 0.065	0.398, 0.052
		Median	0.10	0.50	0.30
		Q1, Q3	-0.10, 0.40	0.20, 0.80	0.00, 0.70
		Min, Max	-0.4, 0.6	-0.2, 1.1	-0.4, 1.1
		GEE Estimates			
		LS Mean (SE)	-0.03 (0.095)	0.40 (0.093)	0.19 (0.084)
		95% CI	(-0.22, 0.15)	(0.22, 0.59)	(0.02, 0.35)
		LS Mean Difference (SE)		0.44 (0.085)	
		95% CI		(0.27, 0.60)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.10
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5		N1	37	30	67
	Baseline	n	37	30	67
		Mean	1.85	2.00	1.92
		SD, SE	0.323, 0.053	0.286, 0.052	0.313, 0.038
		Median	1.90	2.00	1.90
		Q1, Q3	1.60, 2.00	1.80, 2.20	1.70, 2.10
		Min, Max	1.3, 2.6	1.4, 2.6	1.3, 2.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.10
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Baseline			
		n	37	30	67
		Mean	1.85	2.00	1.92
		SD, SE	0.323, 0.053	0.286, 0.052	0.313, 0.038
		Median	1.90	2.00	1.90
		Q1, Q3	1.60, 2.00	1.80, 2.20	1.70, 2.10
		Min, Max	1.3, 2.6	1.4, 2.6	1.3, 2.6
		Observed			
		n	37	30	67
		Mean	2.04	2.74	2.35
		SD, SE	0.386, 0.063	0.603, 0.110	0.601, 0.073
		Median	2.00	2.65	2.30
		Q1, Q3	1.70, 2.30	2.30, 3.10	2.00, 2.60
		Min, Max	1.4, 2.7	1.9, 4.6	1.4, 4.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.10
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Change from Baseline			
		n	37	30	67
		Mean	0.19	0.74	0.43
		SD, SE	0.283, 0.046	0.605, 0.111	0.529, 0.065
		Median	0.20	0.65	0.40
		Q1, Q3	0.00, 0.40	0.40, 1.00	0.10, 0.60
		Min, Max	-0.5, 0.7	-0.3, 2.6	-0.5, 2.6
		GEE Estimates			
		LS Mean (SE)	0.05 (0.099)	0.66 (0.146)	0.35 (0.109)
		95% CI	(-0.15, 0.24)	(0.37, 0.95)	(0.14, 0.57)
		LS Mean Difference (SE)		0.61 (0.119)	
		95% CI		(0.38, 0.85)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.10
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Baseline			
		n	37	30	67
		Mean	1.85	2.00	1.92
		SD, SE	0.323, 0.053	0.286, 0.052	0.313, 0.038
		Median	1.90	2.00	1.90
		Q1, Q3	1.60, 2.00	1.80, 2.20	1.70, 2.10
		Min, Max	1.3, 2.6	1.4, 2.6	1.3, 2.6
		Observed			
		n	37	30	67
		Mean	2.04	2.52	2.25
		SD, SE	0.359, 0.059	0.466, 0.085	0.474, 0.058
		Median	2.10	2.50	2.20
		Q1, Q3	1.80, 2.40	2.20, 2.80	1.90, 2.50
		Min, Max	1.3, 2.7	1.6, 3.7	1.3, 3.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.10
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Change from Baseline			
		n	37	30	67
		Mean	0.18	0.52	0.33
		SD, SE	0.328, 0.054	0.427, 0.078	0.410, 0.050
		Median	0.20	0.50	0.30
		Q1, Q3	0.00, 0.40	0.30, 0.70	0.00, 0.60
		Min, Max	-0.6, 1.0	-0.4, 1.6	-0.6, 1.6
		GEE Estimates			
		LS Mean (SE)	0.04 (0.093)	0.44 (0.123)	0.24 (0.100)
		95% CI	(-0.15, 0.22)	(0.20, 0.68)	(0.04, 0.44)
		LS Mean Difference (SE)		0.41 (0.086)	
		95% CI		(0.24, 0.58)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.10
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5		N1	29	38	67
	Baseline	n	29	38	67
		Mean	2.01	2.06	2.04
		SD, SE	0.289, 0.054	0.318, 0.052	0.305, 0.037
		Median	2.00	2.05	2.00
		Q1, Q3	1.80, 2.20	1.90, 2.20	1.90, 2.20
		Min, Max	1.4, 2.5	1.3, 3.0	1.3, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.10
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Baseline			
		n	27	38	65
		Mean	2.00	2.06	2.03
		SD, SE	0.281, 0.054	0.318, 0.052	0.303, 0.038
		Median	2.00	2.05	2.00
		Q1, Q3	1.80, 2.20	1.90, 2.20	1.90, 2.20
		Min, Max	1.4, 2.4	1.3, 3.0	1.3, 3.0
		Observed			
		n	27	38	65
		Mean	2.07	2.63	2.40
		SD, SE	0.318, 0.061	0.548, 0.089	0.540, 0.067
		Median	2.00	2.55	2.30
		Q1, Q3	1.80, 2.30	2.30, 2.80	2.00, 2.70
		Min, Max	1.6, 2.8	1.5, 4.2	1.5, 4.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.10
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Change from Baseline			
		n	27	38	65
		Mean	0.08	0.58	0.37
		SD, SE	0.302, 0.058	0.451, 0.073	0.465, 0.058
		Median	0.10	0.60	0.30
		Q1, Q3	-0.10, 0.20	0.20, 0.90	0.00, 0.60
		Min, Max	-0.5, 0.7	-0.2, 1.7	-0.5, 1.7
		GEE Estimates			
		LS Mean (SE)	-0.08 (0.121)	0.47 (0.124)	0.20 (0.114)
		95% CI	(-0.32, 0.16)	(0.23, 0.72)	(-0.03, 0.42)
		LS Mean Difference (SE)		0.56 (0.091)	
		95% CI		(0.38, 0.74)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.10
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Baseline			
		n	29	38	67
		Mean	2.01	2.06	2.04
		SD, SE	0.289, 0.054	0.318, 0.052	0.305, 0.037
		Median	2.00	2.05	2.00
		Q1, Q3	1.80, 2.20	1.90, 2.20	1.90, 2.20
		Min, Max	1.4, 2.5	1.3, 3.0	1.3, 3.0
		Observed			
		n	29	38	67
		Mean	2.11	2.53	2.35
		SD, SE	0.323, 0.060	0.436, 0.071	0.442, 0.054
		Median	2.10	2.50	2.30
		Q1, Q3	1.90, 2.40	2.20, 2.80	2.00, 2.60
		Min, Max	1.5, 2.8	1.8, 3.4	1.5, 3.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.10
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Change from Baseline			
		n	29	38	67
		Mean	0.10	0.47	0.31
		SD, SE	0.368, 0.068	0.372, 0.060	0.412, 0.050
		Median	0.10	0.50	0.30
		Q1, Q3	-0.10, 0.40	0.20, 0.80	0.00, 0.60
		Min, Max	-0.4, 1.1	-0.2, 1.1	-0.4, 1.1
		GEE Estimates			
		LS Mean (SE)	-0.04 (0.123)	0.37 (0.114)	0.16 (0.111)
		95% CI	(-0.28, 0.20)	(0.15, 0.59)	(-0.05, 0.38)
		LS Mean Difference (SE)		0.41 (0.086)	
		95% CI		(0.25, 0.58)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.11
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes		N1	44	47	91
	Baseline	n	44	47	91
		Mean	1.95	2.05	2.00
		SD, SE	0.319, 0.048	0.304, 0.044	0.313, 0.033
		Median	2.00	2.00	2.00
		Q1, Q3	1.70, 2.20	1.80, 2.20	1.80, 2.20
		Min, Max	1.3, 2.6	1.4, 3.0	1.3, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.5.2.1.24.11
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	43	47	90
		Mean	1.94	2.05	2.00
		SD, SE	0.311, 0.047	0.304, 0.044	0.311, 0.033
		Median	2.00	2.00	2.00
		Q1, Q3	1.70, 2.20	1.80, 2.20	1.80, 2.20
		Min, Max	1.3, 2.6	1.4, 3.0	1.3, 3.0
		Observed			
		n	43	47	90
		Mean	2.09	2.68	2.40
		SD, SE	0.353, 0.054	0.507, 0.074	0.528, 0.056
		Median	2.10	2.60	2.30
		Q1, Q3	1.80, 2.40	2.30, 2.90	2.00, 2.70
		Min, Max	1.4, 2.8	2.0, 4.2	1.4, 4.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.11
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	43	47	90
		Mean	0.15	0.63	0.40
		SD, SE	0.296, 0.045	0.470, 0.069	0.461, 0.049
		Median	0.10	0.60	0.30
		Q1, Q3	0.00, 0.40	0.30, 1.00	0.10, 0.70
		Min, Max	-0.5, 0.7	-0.3, 1.7	-0.5, 1.7
		GEE Estimates			
		LS Mean (SE)	0.08 (0.056)	0.60 (0.060)	0.34 (0.042)
		95% CI	(-0.03, 0.19)	(0.49, 0.72)	(0.26, 0.42)
		LS Mean Difference (SE)		0.53 (0.080)	
		95% CI		(0.37, 0.68)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.11
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	44	47	91
		Mean	1.95	2.05	2.00
		SD, SE	0.319, 0.048	0.304, 0.044	0.313, 0.033
		Median	2.00	2.00	2.00
		Q1, Q3	1.70, 2.20	1.80, 2.20	1.80, 2.20
		Min, Max	1.3, 2.6	1.4, 3.0	1.3, 3.0
		Observed			
		n	44	47	91
		Mean	2.13	2.54	2.34
		SD, SE	0.366, 0.055	0.423, 0.062	0.446, 0.047
		Median	2.15	2.50	2.40
		Q1, Q3	1.90, 2.40	2.20, 2.80	2.10, 2.60
		Min, Max	1.3, 2.8	1.8, 3.7	1.3, 3.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.11
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	44	47	91
		Mean	0.18	0.50	0.34
		SD, SE	0.351, 0.053	0.389, 0.057	0.402, 0.042
		Median	0.20	0.50	0.30
		Q1, Q3	-0.10, 0.40	0.20, 0.80	0.10, 0.60
		Min, Max	-0.4, 1.1	-0.4, 1.5	-0.4, 1.5
		GEE Estimates			
		LS Mean (SE)	0.11 (0.059)	0.47 (0.047)	0.29 (0.039)
		95% CI	(-0.01, 0.22)	(0.38, 0.56)	(0.21, 0.37)
		LS Mean Difference (SE)		0.36 (0.073)	
		95% CI		(0.22, 0.50)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.11
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No		N1	22	21	43
	Baseline	n	22	21	43
		Mean	1.86	2.00	1.93
		SD, SE	0.307, 0.065	0.307, 0.067	0.311, 0.047
		Median	1.90	2.00	1.90
		Q1, Q3	1.60, 2.10	1.90, 2.20	1.70, 2.20
		Min, Max	1.4, 2.4	1.3, 2.5	1.3, 2.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.11
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Baseline			
		n	21	21	42
		Mean	1.86	2.00	1.93
		SD, SE	0.314, 0.068	0.307, 0.067	0.314, 0.048
		Median	1.90	2.00	1.90
		Q1, Q3	1.60, 2.10	1.90, 2.20	1.70, 2.20
		Min, Max	1.4, 2.4	1.3, 2.5	1.3, 2.5
		Observed			
		n	21	21	42
		Mean	1.98	2.68	2.33
		SD, SE	0.359, 0.078	0.708, 0.154	0.658, 0.101
		Median	2.00	2.60	2.25
		Q1, Q3	1.70, 2.10	2.30, 2.90	1.90, 2.60
		Min, Max	1.4, 2.7	1.5, 4.6	1.4, 4.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.11
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Change from Baseline			
		n	21	21	42
		Mean	0.12	0.69	0.40
		SD, SE	0.294, 0.064	0.648, 0.141	0.574, 0.089
		Median	0.20	0.60	0.30
		Q1, Q3	0.00, 0.30	0.40, 0.90	0.00, 0.60
		Min, Max	-0.5, 0.6	-0.2, 2.6	-0.5, 2.6
		GEE Estimates			
		LS Mean (SE)	0.03 (0.090)	0.68 (0.154)	0.36 (0.100)
		95% CI	(-0.14, 0.21)	(0.37, 0.98)	(0.16, 0.55)
		LS Mean Difference (SE)		0.64 (0.155)	
		95% CI		(0.34, 0.95)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.11
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Baseline			
		n	22	21	43
		Mean	1.86	2.00	1.93
		SD, SE	0.307, 0.065	0.307, 0.067	0.311, 0.047
		Median	1.90	2.00	1.90
		Q1, Q3	1.60, 2.10	1.90, 2.20	1.70, 2.20
		Min, Max	1.4, 2.4	1.3, 2.5	1.3, 2.5
		Observed			
		n	22	21	43
		Mean	1.95	2.49	2.21
		SD, SE	0.260, 0.055	0.502, 0.110	0.478, 0.073
		Median	2.00	2.50	2.10
		Q1, Q3	1.80, 2.10	2.10, 2.80	1.80, 2.50
		Min, Max	1.5, 2.4	1.6, 3.6	1.5, 3.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.11
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Change from Baseline			
		n	22	21	43
		Mean	0.09	0.49	0.28
		SD, SE	0.334, 0.071	0.418, 0.091	0.425, 0.065
		Median	0.10	0.50	0.30
		Q1, Q3	-0.10, 0.30	0.10, 0.70	0.00, 0.60
		Min, Max	-0.6, 0.6	-0.1, 1.6	-0.6, 1.6
		GEE Estimates			
		LS Mean (SE)	0.01 (0.089)	0.48 (0.121)	0.24 (0.093)
		95% CI	(-0.17, 0.18)	(0.24, 0.72)	(0.06, 0.43)
		LS Mean Difference (SE)		0.47 (0.104)	
		95% CI		(0.27, 0.68)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.12
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes		N1	13	17	30
	Baseline	n	13	17	30
		Mean	1.85	2.11	2.00
		SD, SE	0.250, 0.069	0.398, 0.096	0.360, 0.066
		Median	1.80	2.10	2.00
		Q1, Q3	1.70, 2.00	1.90, 2.30	1.70, 2.20
		Min, Max	1.5, 2.3	1.4, 3.0	1.4, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.12
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	13	17	30
		Mean	1.85	2.11	2.00
		SD, SE	0.250, 0.069	0.398, 0.096	0.360, 0.066
		Median	1.80	2.10	2.00
		Q1, Q3	1.70, 2.00	1.90, 2.30	1.70, 2.20
		Min, Max	1.5, 2.3	1.4, 3.0	1.4, 3.0
		Observed			
		n	13	17	30
		Mean	2.11	2.79	2.50
		SD, SE	0.330, 0.092	0.589, 0.143	0.597, 0.109
		Median	2.20	2.50	2.35
		Q1, Q3	2.00, 2.30	2.50, 3.10	2.20, 2.60
		Min, Max	1.5, 2.6	2.1, 4.2	1.5, 4.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.12
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	13	17	30
		Mean	0.25	0.69	0.50
		SD, SE	0.279, 0.077	0.479, 0.116	0.455, 0.083
		Median	0.20	0.70	0.50
		Q1, Q3	0.00, 0.50	0.30, 1.10	0.20, 0.80
		Min, Max	-0.1, 0.6	-0.1, 1.6	-0.1, 1.6
		GEE Estimates			
		LS Mean (SE)	0.20 (0.072)	0.71 (0.110)	0.46 (0.066)
		95% CI	(0.06, 0.34)	(0.50, 0.93)	(0.33, 0.59)
		LS Mean Difference (SE)		0.51 (0.131)	
		95% CI		(0.26, 0.77)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.12
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	13	17	30
		Mean	1.85	2.11	2.00
		SD, SE	0.250, 0.069	0.398, 0.096	0.360, 0.066
		Median	1.80	2.10	2.00
		Q1, Q3	1.70, 2.00	1.90, 2.30	1.70, 2.20
		Min, Max	1.5, 2.3	1.4, 3.0	1.4, 3.0
		Observed			
		n	13	17	30
		Mean	2.24	2.68	2.49
		SD, SE	0.320, 0.089	0.453, 0.110	0.452, 0.083
		Median	2.30	2.60	2.50
		Q1, Q3	1.90, 2.50	2.50, 2.80	2.10, 2.60
		Min, Max	1.8, 2.7	2.0, 3.7	1.8, 3.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.12
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	13	17	30
		Mean	0.38	0.57	0.49
		SD, SE	0.279, 0.077	0.434, 0.105	0.381, 0.070
		Median	0.30	0.60	0.45
		Q1, Q3	0.20, 0.50	0.30, 0.90	0.20, 0.70
		Min, Max	-0.1, 1.0	-0.1, 1.5	-0.1, 1.5
		GEE Estimates			
		LS Mean (SE)	0.33 (0.080)	0.59 (0.092)	0.46 (0.060)
		95% CI	(0.17, 0.49)	(0.41, 0.78)	(0.35, 0.58)
		LS Mean Difference (SE)		0.26 (0.125)	
		95% CI		(0.02, 0.51)	
		p-value		0.0351	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.12
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No		N1	53	51	104
	Baseline	n	53	51	104
		Mean	1.94	2.01	1.97
		SD, SE	0.329, 0.045	0.266, 0.037	0.301, 0.029
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.6	1.3, 2.6	1.3, 2.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.12
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Baseline			
		n	51	51	102
		Mean	1.93	2.01	1.97
		SD, SE	0.326, 0.046	0.266, 0.037	0.299, 0.030
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.6	1.3, 2.6	1.3, 2.6
		Observed			
		n	51	51	102
		Mean	2.04	2.64	2.34
		SD, SE	0.365, 0.051	0.565, 0.079	0.561, 0.056
		Median	2.00	2.60	2.30
		Q1, Q3	1.80, 2.30	2.30, 2.90	2.00, 2.70
		Min, Max	1.4, 2.8	1.5, 4.6	1.4, 4.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.12
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Change from Baseline			
		n	51	51	102
		Mean	0.11	0.63	0.37
		SD, SE	0.293, 0.041	0.545, 0.076	0.508, 0.050
		Median	0.10	0.60	0.30
		Q1, Q3	0.00, 0.30	0.30, 0.90	0.00, 0.60
		Min, Max	-0.5, 0.7	-0.3, 2.6	-0.5, 2.6
		GEE Estimates			
		LS Mean (SE)	0.02 (0.072)	0.58 (0.103)	0.30 (0.079)
		95% CI	(-0.12, 0.16)	(0.38, 0.79)	(0.15, 0.46)
		LS Mean Difference (SE)		0.56 (0.083)	
		95% CI		(0.40, 0.73)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.12
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Baseline			
		n	53	51	104
		Mean	1.94	2.01	1.97
		SD, SE	0.329, 0.045	0.266, 0.037	0.301, 0.029
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.20	1.90, 2.20	1.80, 2.20
		Min, Max	1.3, 2.6	1.3, 2.6	1.3, 2.6
		Observed			
		n	53	51	104
		Mean	2.03	2.48	2.25
		SD, SE	0.339, 0.047	0.437, 0.061	0.449, 0.044
		Median	2.10	2.50	2.20
		Q1, Q3	1.80, 2.40	2.10, 2.80	2.00, 2.50
		Min, Max	1.3, 2.8	1.6, 3.6	1.3, 3.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.12
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Change from Baseline			
		n	53	51	104
		Mean	0.09	0.47	0.28
		SD, SE	0.337, 0.046	0.382, 0.054	0.406, 0.040
		Median	0.10	0.50	0.20
		Q1, Q3	-0.20, 0.30	0.20, 0.70	0.00, 0.55
		Min, Max	-0.6, 1.1	-0.4, 1.6	-0.6, 1.6
		GEE Estimates			
		LS Mean (SE)	0.00 (0.070)	0.42 (0.087)	0.21 (0.072)
		95% CI	(-0.14, 0.14)	(0.25, 0.59)	(0.07, 0.35)
		LS Mean Difference (SE)		0.42 (0.064)	
		95% CI		(0.29, 0.54)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.14
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes		N1	38	32	70
	Baseline	n	38	32	70
		Mean	1.86	2.06	1.95
		SD, SE	0.324, 0.053	0.287, 0.051	0.321, 0.038
		Median	1.80	2.10	1.90
		Q1, Q3	1.60, 2.10	1.90, 2.20	1.70, 2.20
		Min, Max	1.3, 2.6	1.5, 3.0	1.3, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.14
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Baseline			
		n	36	32	68
		Mean	1.85	2.06	1.95
		SD, SE	0.315, 0.052	0.287, 0.051	0.318, 0.039
		Median	1.80	2.10	1.90
		Q1, Q3	1.60, 2.10	1.90, 2.20	1.70, 2.20
		Min, Max	1.3, 2.6	1.5, 3.0	1.3, 3.0
		Observed			
		n	36	32	68
		Mean	2.02	2.66	2.32
		SD, SE	0.333, 0.056	0.571, 0.101	0.557, 0.068
		Median	2.00	2.60	2.25
		Q1, Q3	1.75, 2.30	2.25, 2.80	2.00, 2.60
		Min, Max	1.4, 2.6	1.9, 4.2	1.4, 4.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.14
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Change from Baseline			
		n	36	32	68
		Mean	0.17	0.60	0.38
		SD, SE	0.313, 0.052	0.473, 0.084	0.448, 0.054
		Median	0.20	0.60	0.35
		Q1, Q3	0.00, 0.45	0.30, 0.85	0.10, 0.60
		Min, Max	-0.5, 0.7	-0.3, 1.9	-0.5, 1.9
		GEE Estimates			
		LS Mean (SE)	0.04 (0.077)	0.57 (0.108)	0.30 (0.080)
		95% CI	(-0.11, 0.19)	(0.36, 0.78)	(0.15, 0.46)
		LS Mean Difference (SE)		0.53 (0.096)	
		95% CI		(0.34, 0.72)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.14
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Baseline			
		n	38	32	70
		Mean	1.86	2.06	1.95
		SD, SE	0.324, 0.053	0.287, 0.051	0.321, 0.038
		Median	1.80	2.10	1.90
		Q1, Q3	1.60, 2.10	1.90, 2.20	1.70, 2.20
		Min, Max	1.3, 2.6	1.5, 3.0	1.3, 3.0
		Observed			
		n	38	32	70
		Mean	2.06	2.55	2.29
		SD, SE	0.335, 0.054	0.452, 0.080	0.462, 0.055
		Median	2.10	2.55	2.30
		Q1, Q3	1.80, 2.40	2.25, 2.80	2.00, 2.50
		Min, Max	1.3, 2.8	1.6, 3.7	1.3, 3.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.14
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Change from Baseline			
		n	38	32	70
		Mean	0.20	0.50	0.33
		SD, SE	0.360, 0.058	0.397, 0.070	0.404, 0.048
		Median	0.20	0.50	0.30
		Q1, Q3	-0.10, 0.50	0.15, 0.75	0.00, 0.60
		Min, Max	-0.4, 1.1	-0.2, 1.5	-0.4, 1.5
		GEE Estimates			
		LS Mean (SE)	0.07 (0.083)	0.47 (0.103)	0.27 (0.082)
		95% CI	(-0.09, 0.24)	(0.27, 0.67)	(0.11, 0.43)
		LS Mean Difference (SE)		0.39 (0.090)	
		95% CI		(0.22, 0.57)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.14
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No		N1	28	36	64
	Baseline	n	28	36	64
		Mean	2.00	2.01	2.01
		SD, SE	0.291, 0.055	0.321, 0.053	0.305, 0.038
		Median	2.00	2.00	2.00
		Q1, Q3	1.90, 2.25	1.80, 2.25	1.80, 2.25
		Min, Max	1.4, 2.4	1.3, 2.7	1.3, 2.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.14
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Baseline			
		n	28	36	64
		Mean	2.00	2.01	2.01
		SD, SE	0.291, 0.055	0.321, 0.053	0.305, 0.038
		Median	2.00	2.00	2.00
		Q1, Q3	1.90, 2.25	1.80, 2.25	1.80, 2.25
		Min, Max	1.4, 2.4	1.3, 2.7	1.3, 2.7
		Observed			
		n	28	36	64
		Mean	2.10	2.70	2.44
		SD, SE	0.386, 0.073	0.578, 0.096	0.582, 0.073
		Median	2.10	2.55	2.40
		Q1, Q3	1.80, 2.35	2.30, 3.00	2.10, 2.70
		Min, Max	1.5, 2.8	1.5, 4.6	1.5, 4.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.14
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Change from Baseline			
		n	28	36	64
		Mean	0.10	0.69	0.43
		SD, SE	0.267, 0.050	0.574, 0.096	0.548, 0.068
		Median	0.10	0.65	0.30
		Q1, Q3	0.00, 0.30	0.25, 1.00	0.05, 0.75
		Min, Max	-0.5, 0.6	-0.2, 2.6	-0.5, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.03 (0.114)	0.58 (0.152)	0.28 (0.122)
		95% CI	(-0.25, 0.19)	(0.29, 0.88)	(0.04, 0.52)
		LS Mean Difference (SE)		0.61 (0.110)	
		95% CI		(0.40, 0.83)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.14
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Baseline			
		n	28	36	64
		Mean	2.00	2.01	2.01
		SD, SE	0.291, 0.055	0.321, 0.053	0.305, 0.038
		Median	2.00	2.00	2.00
		Q1, Q3	1.90, 2.25	1.80, 2.25	1.80, 2.25
		Min, Max	1.4, 2.4	1.3, 2.7	1.3, 2.7
		Observed			
		n	28	36	64
		Mean	2.08	2.50	2.32
		SD, SE	0.360, 0.068	0.446, 0.074	0.459, 0.057
		Median	2.05	2.50	2.30
		Q1, Q3	1.80, 2.40	2.20, 2.80	2.00, 2.60
		Min, Max	1.5, 2.7	1.8, 3.6	1.5, 3.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.14
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Change from Baseline			
		n	28	36	64
		Mean	0.08	0.49	0.31
		SD, SE	0.319, 0.060	0.399, 0.066	0.418, 0.052
		Median	0.10	0.50	0.30
		Q1, Q3	-0.20, 0.35	0.20, 0.70	0.00, 0.55
		Min, Max	-0.6, 0.7	-0.4, 1.6	-0.6, 1.6
		GEE Estimates			
		LS Mean (SE)	-0.05 (0.110)	0.39 (0.123)	0.17 (0.107)
		95% CI	(-0.26, 0.17)	(0.15, 0.63)	(-0.04, 0.38)
		LS Mean Difference (SE)		0.44 (0.091)	
		95% CI		(0.26, 0.62)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.15
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = High		N1	29	37	66
	Baseline	n	29	37	66
		Mean	1.92	2.08	2.01
		SD, SE	0.343, 0.064	0.338, 0.055	0.346, 0.043
		Median	1.90	2.00	2.00
		Q1, Q3	1.60, 2.20	1.90, 2.30	1.80, 2.20
		Min, Max	1.3, 2.6	1.3, 3.0	1.3, 3.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.15
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = High	Week 12	Baseline			
		n	27	37	64
		Mean	1.90	2.08	2.00
		SD, SE	0.336, 0.065	0.338, 0.055	0.345, 0.043
		Median	1.90	2.00	2.00
		Q1, Q3	1.60, 2.20	1.90, 2.30	1.80, 2.20
		Min, Max	1.3, 2.6	1.3, 3.0	1.3, 3.0
		Observed			
		n	27	37	64
		Mean	2.00	2.59	2.34
		SD, SE	0.322, 0.062	0.551, 0.091	0.551, 0.069
		Median	2.00	2.50	2.30
		Q1, Q3	1.70, 2.30	2.20, 2.80	2.00, 2.60
		Min, Max	1.4, 2.6	1.5, 4.2	1.4, 4.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Primary Analysis Set_Week 24 Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = High	Week 12	Change from Baseline			
		n	27	37	64
		Mean	0.09	0.51	0.33
		SD, SE	0.292, 0.056	0.466, 0.077	0.450, 0.056
		Median	0.10	0.50	0.30
		Q1, Q3	-0.10, 0.30	0.20, 0.80	0.00, 0.60
		Min, Max	-0.5, 0.7	-0.3, 1.7	-0.5, 1.7
		GEE Estimates			
		LS Mean (SE)	-0.08 (0.093)	0.46 (0.111)	0.19 (0.091)
		95% CI	(-0.26, 0.11)	(0.24, 0.67)	(0.01, 0.37)
		LS Mean Difference (SE)		0.53 (0.096)	
		95% CI		(0.34, 0.72)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = High	Week 24	Baseline			
		n	29	37	66
		Mean	1.92	2.08	2.01
		SD, SE	0.343, 0.064	0.338, 0.055	0.346, 0.043
		Median	1.90	2.00	2.00
		Q1, Q3	1.60, 2.20	1.90, 2.30	1.80, 2.20
		Min, Max	1.3, 2.6	1.3, 3.0	1.3, 3.0
		Observed			
		n	29	37	66
		Mean	2.03	2.47	2.28
		SD, SE	0.348, 0.065	0.478, 0.079	0.478, 0.059
		Median	2.00	2.50	2.25
		Q1, Q3	1.80, 2.40	2.10, 2.80	2.00, 2.50
		Min, Max	1.3, 2.6	1.6, 3.7	1.3, 3.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = High	Week 24	Change from Baseline			
		n	29	37	66
		Mean	0.11	0.39	0.27
		SD, SE	0.354, 0.066	0.430, 0.071	0.421, 0.052
		Median	0.20	0.30	0.20
		Q1, Q3	-0.10, 0.40	0.00, 0.70	0.00, 0.60
		Min, Max	-0.4, 1.0	-0.4, 1.5	-0.4, 1.5
		GEE Estimates			
		LS Mean (SE)	-0.05 (0.091)	0.34 (0.097)	0.14 (0.083)
		95% CI	(-0.23, 0.13)	(0.15, 0.53)	(-0.02, 0.31)
		LS Mean Difference (SE)		0.39 (0.087)	
		95% CI		(0.22, 0.56)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Table 2.2.5.2.1.24.15
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = Low		N1	36	30	66
	Baseline	n	36	30	66
		Mean	1.92	1.98	1.95
		SD, SE	0.302, 0.050	0.255, 0.047	0.281, 0.035
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.15	1.90, 2.20	1.70, 2.20
		Min, Max	1.4, 2.4	1.4, 2.5	1.4, 2.5

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Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = Low	Week 12	Baseline			
		n	36	30	66
		Mean	1.92	1.98	1.95
		SD, SE	0.302, 0.050	0.255, 0.047	0.281, 0.035
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.15	1.90, 2.20	1.70, 2.20
		Min, Max	1.4, 2.4	1.4, 2.5	1.4, 2.5
		Observed			
		n	36	30	66
		Mean	2.11	2.80	2.42
		SD, SE	0.382, 0.064	0.590, 0.108	0.596, 0.073
		Median	2.10	2.75	2.30
		Q1, Q3	1.80, 2.35	2.30, 3.10	2.00, 2.70
		Min, Max	1.4, 2.8	1.9, 4.6	1.4, 4.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Table 2.2.5.2.1.24.15
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = Low	Week 12	Change from Baseline			
		n	36	30	66
		Mean	0.18	0.82	0.47
		SD, SE	0.296, 0.049	0.564, 0.103	0.539, 0.066
		Median	0.20	0.80	0.40
		Q1, Q3	0.00, 0.35	0.40, 1.00	0.10, 0.80
		Min, Max	-0.5, 0.7	-0.2, 2.6	-0.5, 2.6
		GEE Estimates			
		LS Mean (SE)	0.05 (0.069)	0.72 (0.117)	0.39 (0.078)
		95% CI	(-0.08, 0.19)	(0.49, 0.95)	(0.23, 0.54)
		LS Mean Difference (SE)		0.67 (0.114)	
		95% CI		(0.45, 0.89)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
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Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = Low	Week 24	Baseline			
		n	36	30	66
		Mean	1.92	1.98	1.95
		SD, SE	0.302, 0.050	0.255, 0.047	0.281, 0.035
		Median	1.90	2.00	2.00
		Q1, Q3	1.70, 2.15	1.90, 2.20	1.70, 2.20
		Min, Max	1.4, 2.4	1.4, 2.5	1.4, 2.5
		Observed			
		n	36	30	66
		Mean	2.11	2.60	2.33
		SD, SE	0.342, 0.057	0.403, 0.074	0.444, 0.055
		Median	2.10	2.60	2.40
		Q1, Q3	1.90, 2.40	2.40, 2.80	2.00, 2.60
		Min, Max	1.5, 2.8	1.8, 3.6	1.5, 3.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.5.2.1.24.15
Subgroup Analysis: Change from baseline and Percent change from baseline in Serum phosphorus
Primary Analysis Set_Week 24 Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = Low	Week 24	Change from Baseline			
		n	36	30	66
		Mean	0.19	0.62	0.38
		SD, SE	0.342, 0.057	0.319, 0.058	0.394, 0.049
		Median	0.20	0.60	0.40
		Q1, Q3	-0.05, 0.40	0.50, 0.80	0.10, 0.60
		Min, Max	-0.6, 1.1	0.0, 1.6	-0.6, 1.6
		GEE Estimates			
		LS Mean (SE)	0.05 (0.068)	0.53 (0.083)	0.29 (0.065)
		95% CI	(-0.08, 0.19)	(0.36, 0.69)	(0.16, 0.42)
		LS Mean Difference (SE)		0.47 (0.077)	
		95% CI		(0.32, 0.62)	
		p-value		<.0001	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline or percent change from baseline for serum phosphorus as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of serum phosphorus as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADLB.sas7bdat, ADSL.sas7bdat Program source: s_lab-gee.sas

Table 2.2.1.1.24.1

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Baseline BPI Worst Pain

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
BPI Worst Pain at BL <= 6	N1	17	27
	Achieved Mean Serum Phosphorus - n(%)	17 (100.0%)	3 (11.1%)
	Difference in responder (KRN23 vs Placebo) - %	88.9%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	100.0%	12.7%
	95% C.I.	0.0%, 100.0%	3.7%, 35.6%
	Odds ratio (KRN23 vs Placebo)	>999.999	
	95% C.I. of odds ratio	<0.001, >999.999	
	P-value	0.9624	
	RR[3] (95% CI), P-value	9.000 (3.097, 26.156), <.0001	
	ARR[3] (95% CI), P-value	0.000 (0.000, 464E143), 0.9318	
	ARD[4]		
	Difference (95% C.I.)	0.889 (0.770, 1.000)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.1

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Baseline BPI Worst Pain

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
BPI Worst Pain at BL > 6	N1	51	39
	Achieved Mean Serum Phosphorus - n(%)	46 (90.2%)	2 (5.1%)
	Difference in responder (KRN23 vs Placebo) - %	85.1%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	93.0%	7.2%
	95% C.I.	77.9%, 98.0%	1.6%, 27.6%
	Odds ratio (KRN23 vs Placebo)	170.780	
	95% C.I. of odds ratio	29.651, 983.629	
	P-value	<.0001	
	RR[3] (95% CI), P-value	17.588 (4.546, 68.044), <.0001	
	ARR[3] (95% CI), P-value	170.780 (30.382, 959.960), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.851 (0.744, 0.958)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.2

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Baseline BPI Average Pain

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
BPI Average Pain at BL <= 6	N1	48	49
	Achieved Mean Serum Phosphorus - n(%)	45 (93.8%)	4 (8.2%)
	Difference in responder (KRN23 vs Placebo) - %	85.6%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	96.8%	11.0%
	95% C.I.	87.2%, 99.3%	4.0%, 26.6%
	Odds ratio (KRN23 vs Placebo)	245.190	
	95% C.I. of odds ratio	39.685, >999.999	
	P-value	<.0001	
	RR[3] (95% CI), P-value	11.484 (4.477, 29.458), <.0001	
	ARR[3] (95% CI), P-value	245.185 (40.625, 1479.76), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.856 (0.753, 0.959)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.2

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Baseline BPI Average Pain

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
BPI Average Pain at BL > 6	N1	20	17
	Achieved Mean Serum Phosphorus - n(%)	18 (90.0%)	1 (5.9%)
	Difference in responder (KRN23 vs Placebo) - %	84.1%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	88.2%	3.3%
	95% C.I.	61.4%, 97.2%	0.3%, 30.6%
	Odds ratio (KRN23 vs Placebo)	218.133	
	95% C.I. of odds ratio	11.502, >999.999	
	P-value	0.0007	
	RR[3] (95% CI), P-value	15.300 (2.272, 103.02), <.0001	
	ARR[3] (95% CI), P-value	218.132 (12.771, 3725.76), 0.0002	
	ARD[4]		
	Difference (95% C.I.)	0.841 (0.669, 1.000)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.3

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Region

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
North America/EU	N1	58	58
	Achieved Mean Serum Phosphorus - n(%)	55 (94.8%)	5 (8.6%)
	Difference in responder (KRN23 vs Placebo) - %	86.2%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	96.0%	10.8%
	95% C.I.	86.1%, 98.9%	4.2%, 25.2%
	Odds ratio (KRN23 vs Placebo)	196.332	
	95% C.I. of odds ratio	43.026, 895.891	
	P-value	<.0001	
	RR[3] (95% CI), P-value	11.000 (4.749, 25.481), <.0001	
	ARR[3] (95% CI), P-value	196.332 (43.731, 881.442), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.862 (0.770, 0.954)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.3

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Region

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Asia	N1	10	8
	Achieved Mean Serum Phosphorus - n(%)	8 (80.0%)	0 (0.0%)
	Difference in responder (KRN23 vs Placebo) - %	80.0%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	99.8%	0.0%
	95% C.I.	0.0%, 100.0%	0.0%, 100.0%
	Odds ratio (KRN23 vs Placebo)	>999.999	
	95% C.I. of odds ratio	<0.001, >999.999	
	P-value	0.9535	
	RR[3] (95% CI), P-value		
	ARR[3] (95% CI), P-value	3.483E8 (0.000, 614E170), 0.9188	
	ARD[4]		
	Difference (95% C.I.)	0.800 (0.552, 1.000)	
	P-value	0.0011	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.4

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Gender

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Sex = Male	N1	24	23
	Achieved Mean Serum Phosphorus - n(%)	21 (87.5%)	1 (4.3%)
	Difference in responder (KRN23 vs Placebo) - %	83.2%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	85.1%	3.1%
	95% C.I.	60.1%, 95.6%	0.3%, 25.1%
	Odds ratio (KRN23 vs Placebo)	178.633	
	95% C.I. of odds ratio	14.579, >999.999	
	P-value	0.0001	
	RR[3] (95% CI), P-value	20.125 (2.942, 137.66), <.0001	
	ARR[3] (95% CI), P-value	178.632 (15.619, 2043.02), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.832 (0.675, 0.988)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.4

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Gender

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Sex = Female	N1	44	43
	Achieved Mean Serum Phosphorus - n(%)	42 (95.5%)	4 (9.3%)
	Difference in responder (KRN23 vs Placebo) - %	86.2%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	97.8%	13.4%
	95% C.I.	88.8%, 99.6%	4.9%, 31.8%
	Odds ratio (KRN23 vs Placebo)	290.033	
	95% C.I. of odds ratio	39.127, >999.999	
	P-value	<.0001	
	RR[3] (95% CI), P-value	10.261 (4.026, 26.151), <.0001	
	ARR[3] (95% CI), P-value	290.024 (40.272, 2088.65), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.862 (0.755, 0.968)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.5

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Race

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Race = White	N1	55	53
	Achieved Mean Serum Phosphorus - n(%)	52 (94.5%)	5 (9.4%)
	Difference in responder (KRN23 vs Placebo) - %	85.1%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	95.6%	11.5%
	95% C.I.	85.2%, 98.8%	4.5%, 26.5%
	Odds ratio (KRN23 vs Placebo)	167.532	
	95% C.I. of odds ratio	36.617, 766.501	
	P-value	<.0001	
	RR[3] (95% CI), P-value	10.022 (4.341, 23.135), <.0001	
	ARR[3] (95% CI), P-value	167.532 (37.265, 753.184), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.851 (0.752, 0.950)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.5

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Race

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Race = Non-White	N1	13	13
	Achieved Mean Serum Phosphorus - n(%)	11 (84.6%)	0 (0.0%)
	Difference in responder (KRN23 vs Placebo) - %	84.6%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	99.8%	0.0%
	95% C.I.	0.0%, 100.0%	0.0%, 100.0%
	Odds ratio (KRN23 vs Placebo)	>999.999	
	95% C.I. of odds ratio	<0.001, >999.999	
	P-value	0.9428	
	RR[3] (95% CI), P-value		
	ARR[3] (95% CI), P-value	1.35E8 (0.000, 169E135), 0.9018	
	ARD[4]		
	Difference (95% C.I.)	0.846 (0.650, 1.000)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.6

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Age

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Age <= 41 Years	N1	31	36
	Achieved Mean Serum Phosphorus - n(%)	29 (93.5%)	2 (5.6%)
	Difference in responder (KRN23 vs Placebo) - %	88.0%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	93.5%	5.6%
	95% C.I.	77.1%, 98.4%	1.4%, 20.1%
	Odds ratio (KRN23 vs Placebo)	246.500	
	95% C.I. of odds ratio	31.419, >999.999	
	P-value	<.0001	
	RR[3] (95% CI), P-value	16.839 (4.365, 64.956), <.0001	
	ARR[3] (95% CI), P-value	246.500 (32.647, 1861.19), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.880 (0.766, 0.994)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.6

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Age

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Age > 41 Years	N1	37	30
	Achieved Mean Serum Phosphorus - n(%)	34 (91.9%)	3 (10.0%)
	Difference in responder (KRN23 vs Placebo) - %	81.9%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	93.1%	10.7%
	95% C.I.	78.5%, 98.0%	3.4%, 29.1%
	Odds ratio (KRN23 vs Placebo)	113.075	
	95% C.I. of odds ratio	18.471, 692.213	
	P-value	<.0001	
	RR[3] (95% CI), P-value	9.189 (3.128, 26.999), <.0001	
	ARR[3] (95% CI), P-value	113.075 (19.115, 668.905), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.819 (0.680, 0.958)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.7

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: WOMAC Stiffness at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Stiffness at BL cat <= 62.5	N1	39	41
	Achieved Mean Serum Phosphorus - n(%)	35 (89.7%)	5 (12.2%)
	Difference in responder (KRN23 vs Placebo) - %	77.5%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	96.0%	23.5%
	95% C.I.	84.6%, 99.1%	8.8%, 49.3%
	Odds ratio (KRN23 vs Placebo)	78.796	
	95% C.I. of odds ratio	16.210, 383.033	
	P-value	<.0001	
	RR[3] (95% CI), P-value	7.359 (3.215, 16.846), <.0001	
	ARR[3] (95% CI), P-value	78.796 (16.617, 373.632), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.775 (0.637, 0.914)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.7

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: WOMAC Stiffness at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Stiffness at BL cat > 62.5	N1	29	25
	Achieved Mean Serum Phosphorus - n(%)	28 (96.6%)	0 (0.0%)
	Difference in responder (KRN23 vs Placebo) - %	96.6%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	100.0%	0.0%
	95% C.I.	0.0%, 100.0%	0.0%, 100.0%
	Odds ratio (KRN23 vs Placebo)	>999.999	
	95% C.I. of odds ratio	<0.001, >999.999	
	P-value	0.9407	
	RR[3] (95% CI), P-value		
	ARR[3] (95% CI), P-value	1.46E11 (0.000, 602E173), 0.8943	
	ARD[4]		
	Difference (95% C.I.)	0.966 (0.899, 1.000)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.8

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: WOMAC Physical Function at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Physical Function at BL cat <= 47.8	N1	30	37
	Achieved Mean Serum Phosphorus - n(%)	27 (90.0%)	3 (8.1%)
	Difference in responder (KRN23 vs Placebo) - %	81.9%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	94.9%	13.3%
	95% C.I.	78.2%, 99.0%	3.9%, 36.6%
	Odds ratio (KRN23 vs Placebo)	121.801	
	95% C.I. of odds ratio	18.858, 786.688	
	P-value	<.0001	
	RR[3] (95% CI), P-value	11.100 (3.727, 33.057), <.0001	
	ARR[3] (95% CI), P-value	121.801 (19.535, 759.428), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.819 (0.680, 0.958)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.8

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: WOMAC Physical Function at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Physical Function at BL cat > 47.8	N1	38	29
	Achieved Mean Serum Phosphorus - n(%)	36 (94.7%)	2 (6.9%)
	Difference in responder (KRN23 vs Placebo) - %	87.8%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	94.9%	7.2%
	95% C.I.	79.3%, 98.9%	1.5%, 27.9%
	Odds ratio (KRN23 vs Placebo)	241.785	
	95% C.I. of odds ratio	30.762, >999.999	
	P-value	<.0001	
	RR[3] (95% CI), P-value	13.737 (3.599, 52.428), <.0001	
	ARR[3] (95% CI), P-value	241.785 (31.985, 1827.75), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.878 (0.762, 0.995)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.9

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: WOMAC Pain Score at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Pain Score at BL cat <= 50	N1	32	42
	Achieved Mean Serum Phosphorus - n(%)	28 (87.5%)	4 (9.5%)
	Difference in responder (KRN23 vs Placebo) - %	78.0%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	91.5%	13.2%
	95% C.I.	74.2%, 97.6%	4.7%, 32.2%
	Odds ratio (KRN23 vs Placebo)	70.954	
	95% C.I. of odds ratio	14.847, 339.094	
	P-value	<.0001	
	RR[3] (95% CI), P-value	9.188 (3.584, 23.550), <.0001	
	ARR[3] (95% CI), P-value	70.939 (15.246, 330.074), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.780 (0.635, 0.925)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.9

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: WOMAC Pain Score at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Pain Score at BL cat > 50	N1	35	24
	Achieved Mean Serum Phosphorus - n(%)	34 (97.1%)	1 (4.2%)
	Difference in responder (KRN23 vs Placebo) - %	93.0%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	97.3%	4.4%
	95% C.I.	78.1%, 99.7%	0.4%, 32.3%
	Odds ratio (KRN23 vs Placebo)	776.901	
	95% C.I. of odds ratio	43.415, >999.999	
	P-value	<.0001	
	RR[3] (95% CI), P-value	23.314 (3.420, 158.95), <.0001	
	ARR[3] (95% CI), P-value	776.818 (46.205, 13060.1), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.930 (0.833, 1.000)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.10

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: WOMAC Total Score at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Total Score at BL cat <= 49.5	N1	30	37
	Achieved Mean Serum Phosphorus - n(%)	27 (90.0%)	3 (8.1%)
	Difference in responder (KRN23 vs Placebo) - %	81.9%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	94.8%	13.4%
	95% C.I.	78.2%, 98.9%	4.0%, 36.7%
	Odds ratio (KRN23 vs Placebo)	118.407	
	95% C.I. of odds ratio	18.388, 762.452	
	P-value	<.0001	
	RR[3] (95% CI), P-value	11.100 (3.727, 33.057), <.0001	
	ARR[3] (95% CI), P-value	118.407 (19.047, 736.073), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.819 (0.680, 0.958)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.10

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: WOMAC Total Score at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Total Score at BL cat > 49.5	N1	38	29
	Achieved Mean Serum Phosphorus - n(%)	36 (94.7%)	2 (6.9%)
	Difference in responder (KRN23 vs Placebo) - %	87.8%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	94.9%	7.1%
	95% C.I.	78.7%, 98.9%	1.5%, 27.8%
	Odds ratio (KRN23 vs Placebo)	242.642	
	95% C.I. of odds ratio	30.878, >999.999	
	P-value	<.0001	
	RR[3] (95% CI), P-value	13.737 (3.599, 52.428), <.0001	
	ARR[3] (95% CI), P-value	242.642 (32.105, 1833.83), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.878 (0.762, 0.995)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.11

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Pain Medication Use at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Pain Medication Use at BL = Yes	N1	47	44
	Achieved Mean Serum Phosphorus - n(%)	45 (95.7%)	3 (6.8%)
	Difference in responder (KRN23 vs Placebo) - %	88.9%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	97.1%	8.8%
	95% C.I.	86.1%, 99.4%	2.7%, 24.9%
	Odds ratio (KRN23 vs Placebo)	343.544	
	95% C.I. of odds ratio	48.065, >999.999	
	P-value	<.0001	
	RR[3] (95% CI), P-value	14.043 (4.703, 41.933), <.0001	
	ARR[3] (95% CI), P-value	343.532 (49.381, 2389.85), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.889 (0.795, 0.983)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.11

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Pain Medication Use at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Pain Medication Use at BL cat=No	N1	21	22
	Achieved Mean Serum Phosphorus - n(%)	18 (85.7%)	2 (9.1%)
	Difference in responder (KRN23 vs Placebo) - %	76.6%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	88.1%	11.0%
	95% C.I.	56.0%, 97.7%	1.9%, 44.6%
	Odds ratio (KRN23 vs Placebo)	59.700	
	95% C.I. of odds ratio	8.375, 425.569	
	P-value	0.0001	
	RR[3] (95% CI), P-value	9.429 (2.486, 35.753), <.0001	
	ARR[3] (95% CI), P-value	59.698 (8.887, 401.013), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.766 (0.574, 0.958)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.12

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Opioid Pain Medication Use at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Opioid Pain Medication Use at BL = Yes	N1	17	13
	Achieved Mean Serum Phosphorus - n(%)	17 (100.0%)	3 (23.1%)
	Difference in responder (KRN23 vs Placebo) - %	76.9%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	100.0%	32.0%
	95% C.I.	0.0%, 100.0%	8.2%, 71.2%
	Odds ratio (KRN23 vs Placebo)	>999.999	
	95% C.I. of odds ratio	<0.001, >999.999	
	P-value	0.9610	
	RR[3] (95% CI), P-value	4.333 (1.606, 11.691), <.0001	
	ARR[3] (95% CI), P-value	0.000 (0.000, 865E146), 0.9337	
	ARD[4]		
	Difference (95% C.I.)	0.769 (0.540, 0.998)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.12

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Opioid Pain Medication Use at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Opioid Pain Medication Use at BL cat = No	N1	51	53
	Achieved Mean Serum Phosphorus - n(%)	46 (90.2%)	2 (3.8%)
	Difference in responder (KRN23 vs Placebo) - %	86.4%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	90.0%	3.7%
	95% C.I.	75.8%, 96.3%	0.8%, 15.9%
	Odds ratio (KRN23 vs Placebo)	236.860	
	95% C.I. of odds ratio	42.204, >999.999	
	P-value	<.0001	
	RR[3] (95% CI), P-value	23.902 (6.119, 93.361), <.0001	
	ARR[3] (95% CI), P-value	236.857 (43.085, 1302.10), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.864 (0.768, 0.961)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.14

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Active Fractures and Pseudo-Fractures at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Active fractures and pseudo-fractures at BL = Yes	N1	32	38
	Achieved Mean Serum Phosphorus - n(%)	30 (93.8%)	0 (0.0%)
	Difference in responder (KRN23 vs Placebo) - %	93.8%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	90.0%	0.0%
	95% C.I.	65.9%, 97.7%	0.0%, 100.0%
	Odds ratio (KRN23 vs Placebo)	>999.999	
	95% C.I. of odds ratio	<0.001, >999.999	
	P-value	0.9610	
	RR[3] (95% CI), P-value		
	ARR[3] (95% CI), P-value	3.491E7 (0.000, 434E172), 0.9295	
	ARD[4]		
	Difference (95% C.I.)	0.938 (0.854, 1.000)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.14

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: Active Fractures and Pseudo-Fractures at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Active fractures and pseudo-fractures at BL = No	N1	36	28
	Achieved Mean Serum Phosphorus - n(%)	33 (91.7%)	5 (17.9%)
	Difference in responder (KRN23 vs Placebo) - %	73.8%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	95.0%	25.0%
	95% C.I.	81.5%, 98.8%	10.1%, 49.9%
	Odds ratio (KRN23 vs Placebo)	56.979	
	95% C.I. of odds ratio	10.633, 305.334	
	P-value	<.0001	
	RR[3] (95% CI), P-value	5.133 (2.305, 11.430), <.0001	
	ARR[3] (95% CI), P-value	56.979 (10.993, 295.335), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.738 (0.570, 0.906)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.15

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: 6MWT at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
6MWT score at BL = High	N1	37	29
	Achieved Mean Serum Phosphorus - n(%)	33 (89.2%)	0 (0.0%)
	Difference in responder (KRN23 vs Placebo) - %	89.2%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	89.1%	0.0%
	95% C.I.	70.6%, 96.5%	0.0%, 100.0%
	Odds ratio (KRN23 vs Placebo)	>999.999	
	95% C.I. of odds ratio	<0.001, >999.999	
	P-value	0.9685	
	RR[3] (95% CI), P-value		
	ARR[3] (95% CI), P-value	1.222E7 (0.000, 855E196), 0.9423	
	ARD[4]		
	Difference (95% C.I.)	0.892 (0.792, 0.992)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.1.1.24.15

Subgroup Analysis: proportion of subjects achieving mean serum phosphorus levels above the lower limit of normal (LLN; 2.5 mg/dL [0.81 mmol/L]) at the mid-point of the dose interval, as averaged across dose cycles between between Baseline and Week 24.

Subgroup: 6MWT at Baseline

(Primary Analysis Set - Week 24)

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
6MWT score at BL = Low	N1	30	36
	Achieved Mean Serum Phosphorus - n(%)	29 (96.7%)	5 (13.9%)
	Difference in responder (KRN23 vs Placebo) - %	82.8%	
	Logistic Regression[1]		
	Achieved Mean Serum Phosphorus - %	98.1%	19.3%
	95% C.I.	84.8%, 99.8%	7.7%, 40.6%
	Odds ratio (KRN23 vs Placebo)	216.409	
	95% C.I. of odds ratio	20.878, >999.999	
	P-value	<.0001	
	RR[3] (95% CI), P-value	6.960 (3.077, 15.741), <.0001	
	ARR[3] (95% CI), P-value	216.393 (21.836, 2144.40), 0.0000	
	ARD[4]		
	Difference (95% C.I.)	0.828 (0.698, 0.958)	
	P-value	<.0001	

N=The number of subjects in each treatment group. N1=The number of subjects in the analysis population of each subgroup.

1. A logistic regression model includes treatment group and baseline age and baseline BPI Average Pain as stratification factor , baseline value as a continuous covariate. The estimated responder rate, 95% CI, and odds ratio are from the logistic regression model.

2. RR: Relative Risk

3. ARR: Adjusted Relative Risk

4. ARD: Absolute Risk Difference (KRN23 minus Placebo)

Data source: ADPHOS.sas7bdat, ADSL.sas7bdat Program source: t-phos-SUB.sas

Table 2.2.2.2.24.1
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6		N_1	27	17	44
	Baseline	n	27	17	44
		Mean	54.17	50.74	52.84
		SD, SE	22.734, 4.375	14.968, 3.630	19.968, 3.010
		Median	62.50	50.00	50.00
		Q1, Q3	37.50, 75.00	37.50, 62.50	37.50, 62.50
		Min, Max	0.0, 100.0	25.0, 75.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.1
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Baseline			
		n	27	17	44
		Mean	54.17	50.74	52.84
		SD, SE	22.734, 4.375	14.968, 3.630	19.968, 3.010
		Median	62.50	50.00	50.00
		Q1, Q3	37.50, 75.00	37.50, 62.50	37.50, 62.50
		Min, Max	0.0, 100.0	25.0, 75.0	0.0, 100.0
		Observed			
		n	27	17	44
		Mean	49.54	33.82	43.47
		SD, SE	19.452, 3.744	18.095, 4.389	20.261, 3.055
		Median	50.00	37.50	37.50
		Q1, Q3	37.50, 62.50	25.00, 50.00	31.25, 62.50
		Min, Max	0.0, 87.5	0.0, 62.5	0.0, 87.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.1
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Change from Baseline			
		n	27	17	44
		Mean	-4.63	-16.91	-9.38
		SD, SE	17.386, 3.346	21.168, 5.134	19.649, 2.962
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 0.00	-25.00, -12.50	-25.00, 0.00
		Min, Max	-37.5, 37.5	-50.0, 25.0	-50.0, 37.5
		GEE Estimates			
		LS Mean (SE)	-6.62 (2.566)	-21.60 (4.115)	
		95% CI	(-11.65, -1.59)	(-29.67, -13.53)	
		LS Mean Difference (SE)		-14.98 (4.779)	
		95% CI		(-24.34, -5.61)	
		p-value		0.0017	
		HedgesG (95% CI)		-0.623 (-1.244, -0.002)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.1
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Baseline			
		n	27	17	44
		Mean	54.17	50.74	52.84
		SD, SE	22.734, 4.375	14.968, 3.630	19.968, 3.010
		Median	62.50	50.00	50.00
		Q1, Q3	37.50, 75.00	37.50, 62.50	37.50, 62.50
		Min, Max	0.0, 100.0	25.0, 75.0	0.0, 100.0
		Observed			
		n	27	17	44
		Mean	51.85	42.65	48.30
		SD, SE	16.879, 3.248	15.970, 3.873	16.962, 2.557
		Median	50.00	50.00	50.00
		Q1, Q3	37.50, 62.50	25.00, 50.00	37.50, 62.50
		Min, Max	12.5, 87.5	12.5, 62.5	12.5, 87.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.1
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Change from Baseline			
		n	27	17	44
		Mean	-2.31	-8.09	-4.55
		SD, SE	19.001, 3.657	23.361, 5.666	20.723, 3.124
		Median	0.00	-12.50	0.00
		Q1, Q3	-12.50, 0.00	-12.50, 0.00	-12.50, 0.00
		Min, Max	-37.5, 62.5	-50.0, 25.0	-50.0, 62.5
		GEE Estimates			
		LS Mean (SE)	-4.31 (2.339)	-12.78 (3.893)	
		95% CI	(-8.89, 0.28)	(-20.41, -5.15)	
		LS Mean Difference (SE)		-8.47 (4.226)	
		95% CI		(-16.75, -0.19)	
		p-value		0.0451	
		HedgesG (95% CI)		-0.267 (-0.876, 0.343)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.1
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6		N_1	39	51	90
	Baseline	n	39	51	90
		Mean	66.35	69.36	68.06
		SD, SE	17.944, 2.873	19.735, 2.763	18.935, 1.996
		Median	62.50	75.00	68.75
		Q1, Q3	50.00, 75.00	62.50, 87.50	62.50, 75.00
		Min, Max	12.5, 100.0	12.5, 100.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.1
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Baseline			
		n	39	51	90
		Mean	66.35	69.36	68.06
		SD, SE	17.944, 2.873	19.735, 2.763	18.935, 1.996
		Median	62.50	75.00	68.75
		Q1, Q3	50.00, 75.00	62.50, 87.50	62.50, 75.00
		Min, Max	12.5, 100.0	12.5, 100.0	12.5, 100.0
		Observed			
		n	39	51	90
		Mean	66.03	61.03	63.19
		SD, SE	17.194, 2.753	24.322, 3.406	21.558, 2.272
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	37.50, 75.00	50.00, 75.00
		Min, Max	37.5, 100.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.1
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Change from Baseline			
		n	39	51	90
		Mean	-0.32	-8.33	-4.86
		SD, SE	18.020, 2.886	23.408, 3.278	21.504, 2.267
		Median	0.00	-12.50	0.00
		Q1, Q3	-12.50, 12.50	-25.00, 12.50	-25.00, 12.50
		Min, Max	-37.5, 37.5	-75.0, 37.5	-75.0, 37.5
		GEE Estimates			
		LS Mean (SE)	3.34 (3.230)	-2.96 (3.390)	
		95% CI	(-2.99, 9.67)	(-9.60, 3.69)	
		LS Mean Difference (SE)		-6.30 (3.889)	
		95% CI		(-13.92, 1.32)	
		p-value		0.1052	
		HedgesG (95% CI)		-0.370 (-0.790, 0.051)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.1
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Baseline			
		n	38	50	88
		Mean	66.12	69.00	67.76
		SD, SE	18.128, 2.941	19.763, 2.795	19.021, 2.028
		Median	62.50	75.00	62.50
		Q1, Q3	50.00, 75.00	62.50, 75.00	62.50, 75.00
		Min, Max	12.5, 100.0	12.5, 100.0	12.5, 100.0
		Observed			
		n	38	50	88
		Mean	66.45	57.50	61.36
		SD, SE	23.086, 3.745	20.977, 2.967	22.235, 2.370
		Median	68.75	62.50	62.50
		Q1, Q3	50.00, 87.50	37.50, 75.00	50.00, 75.00
		Min, Max	12.5, 100.0	25.0, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.1
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Change from Baseline			
		n	38	50	88
		Mean	0.33	-11.50	-6.39
		SD, SE	23.697, 3.844	24.980, 3.533	25.000, 2.665
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-25.00, 12.50
		Min, Max	-50.0, 50.0	-75.0, 50.0	-75.0, 50.0
		GEE Estimates			
		LS Mean (SE)	3.96 (3.666)	-6.09 (2.785)	
		95% CI	(-3.23, 11.14)	(-11.55, -0.63)	
		LS Mean Difference (SE)		-10.05 (4.355)	
		95% CI		(-18.58, -1.51)	
		p-value		0.0210	
		HedgesG (95% CI)		-0.474 (-0.902, -0.047)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.2
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6		N_1	49	48	97
	Baseline	n	49	48	97
		Mean	59.44	59.90	59.66
		SD, SE	21.429, 3.061	18.765, 2.708	20.051, 2.036
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	43.75, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.2
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Baseline			
		n	49	48	97
		Mean	59.44	59.90	59.66
		SD, SE	21.429, 3.061	18.765, 2.708	20.051, 2.036
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	43.75, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
		Observed			
		n	49	48	97
		Mean	55.87	49.74	52.84
		SD, SE	18.768, 2.681	23.702, 3.421	21.462, 2.179
		Median	62.50	50.00	50.00
		Q1, Q3	37.50, 75.00	31.25, 75.00	37.50, 75.00
		Min, Max	0.0, 87.5	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.2
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Change from Baseline			
		n	49	48	97
		Mean	-3.57	-10.16	-6.83
		SD, SE	19.264, 2.752	22.428, 3.237	21.042, 2.137
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 0.00	-25.00, 6.25	-25.00, 0.00
		Min, Max	-37.5, 37.5	-50.0, 37.5	-50.0, 37.5
		GEE Estimates			
		LS Mean (SE)	-4.00 (2.917)	-10.30 (4.089)	
		95% CI	(-9.72, 1.71)	(-18.31, -2.28)	
		LS Mean Difference (SE)		-6.30 (3.736)	
		95% CI		(-13.62, 1.03)	
		p-value		0.0920	
		HedgesG (95% CI)		-0.309 (-0.710, 0.091)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.2
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Baseline			
		n	49	48	97
		Mean	59.44	59.90	59.66
		SD, SE	21.429, 3.061	18.765, 2.708	20.051, 2.036
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	43.75, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
		Observed			
		n	49	48	97
		Mean	58.16	51.04	54.64
		SD, SE	21.126, 3.018	19.609, 2.830	20.597, 2.091
		Median	62.50	50.00	62.50
		Q1, Q3	50.00, 75.00	37.50, 62.50	37.50, 62.50
		Min, Max	12.5, 100.0	12.5, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.2
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Change from Baseline			
		n	49	48	97
		Mean	-1.28	-8.85	-5.03
		SD, SE	23.140, 3.306	24.457, 3.530	23.981, 2.435
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 12.50
		Min, Max	-50.0, 62.5	-50.0, 50.0	-50.0, 62.5
		GEE Estimates			
		LS Mean (SE)	-1.71 (3.390)	-9.00 (3.398)	
		95% CI	(-8.35, 4.94)	(-15.66, -2.34)	
		LS Mean Difference (SE)		-7.29 (3.732)	
		95% CI		(-14.60, 0.03)	
		p-value		0.0508	
		HedgesG (95% CI)		-0.313 (-0.713, 0.088)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.2
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6		N_1	17	20	37
	Baseline	n	17	20	37
		Mean	66.91	76.25	71.96
		SD, SE	18.190, 4.412	19.407, 4.340	19.186, 3.154
		Median	62.50	75.00	75.00
		Q1, Q3	50.00, 75.00	62.50, 87.50	62.50, 87.50
		Min, Max	37.5, 100.0	25.0, 100.0	25.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.2
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Baseline			
		n	17	20	37
		Mean	66.91	76.25	71.96
		SD, SE	18.190, 4.412	19.407, 4.340	19.186, 3.154
		Median	62.50	75.00	75.00
		Q1, Q3	50.00, 75.00	62.50, 87.50	62.50, 87.50
		Min, Max	37.5, 100.0	25.0, 100.0	25.0, 100.0
		Observed			
		n	17	20	37
		Mean	69.12	65.00	66.89
		SD, SE	19.822, 4.808	27.685, 6.191	24.155, 3.971
		Median	62.50	68.75	62.50
		Q1, Q3	62.50, 75.00	50.00, 87.50	50.00, 87.50
		Min, Max	37.5, 100.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.2
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Change from Baseline			
		n	17	20	37
		Mean	2.21	-11.25	-5.07
		SD, SE	11.888, 2.883	24.967, 5.583	20.929, 3.441
		Median	0.00	-6.25	0.00
		Q1, Q3	0.00, 12.50	-25.00, 12.50	-12.50, 12.50
		Min, Max	-12.5, 25.0	-75.0, 12.5	-75.0, 25.0
		GEE Estimates			
		LS Mean (SE)	2.80 (4.829)	-8.09 (3.357)	
		95% CI	(-6.67, 12.26)	(-14.67, -1.51)	
		LS Mean Difference (SE)		-10.88 (5.794)	
		95% CI		(-22.24, 0.47)	
		p-value		0.0603	
		HedgesG (95% CI)		-0.638 (-1.301, 0.025)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.2
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Baseline			
		n	16	19	35
		Mean	66.41	75.66	71.43
		SD, SE	18.663, 4.666	19.753, 4.532	19.547, 3.304
		Median	62.50	75.00	75.00
		Q1, Q3	50.00, 75.00	62.50, 87.50	62.50, 87.50
		Min, Max	37.5, 100.0	25.0, 100.0	25.0, 100.0
		Observed			
		n	16	19	35
		Mean	67.19	60.53	63.57
		SD, SE	23.218, 5.804	22.540, 5.171	22.762, 3.848
		Median	68.75	50.00	62.50
		Q1, Q3	50.00, 87.50	37.50, 87.50	50.00, 87.50
		Min, Max	25.0, 100.0	25.0, 87.5	25.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.2
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Change from Baseline			
		n	16	19	35
		Mean	0.78	-15.13	-7.86
		SD, SE	17.362, 4.340	24.502, 5.621	22.704, 3.838
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 12.50
		Min, Max	-25.0, 37.5	-75.0, 12.5	-75.0, 37.5
		GEE Estimates			
		LS Mean (SE)	1.23 (5.790)	-11.62 (2.500)	
		95% CI	(-10.12, 12.58)	(-16.52, -6.72)	
		LS Mean Difference (SE)		-12.85 (6.322)	
		95% CI		(-25.24, -0.46)	
		p-value		0.0421	
		HedgesG (95% CI)		-0.701 (-1.386, -0.016)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.3
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU		N_1	58	58	116
	Baseline	n	58	58	116
		Mean	63.58	65.09	64.33
		SD, SE	19.063, 2.503	19.131, 2.512	19.029, 1.767
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.3
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Baseline			
		n	58	58	116
		Mean	63.58	65.09	64.33
		SD, SE	19.063, 2.503	19.131, 2.512	19.029, 1.767
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0
		Observed			
		n	58	58	116
		Mean	60.78	55.39	58.08
		SD, SE	19.513, 2.562	24.346, 3.197	22.132, 2.055
		Median	62.50	56.25	62.50
		Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.3
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Change from Baseline			
		n	58	58	116
		Mean	-2.80	-9.70	-6.25
		SD, SE	17.053, 2.239	21.845, 2.868	19.816, 1.840
		Median	0.00	-12.50	-6.25
		Q1, Q3	-12.50, 0.00	-25.00, 12.50	-25.00, 6.25
		Min, Max	-37.5, 37.5	-75.0, 37.5	-75.0, 37.5
		GEE Estimates			
		LS Mean (SE)	-1.95 (2.108)	-8.11 (2.901)	
		95% CI	(-6.08, 2.18)	(-13.80, -2.42)	
		LS Mean Difference (SE)		-6.16 (3.371)	
		95% CI		(-12.77, 0.45)	
		p-value		0.0676	
		HedgesG (95% CI)		-0.347 (-0.713, 0.020)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.3
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Baseline			
		n	57	57	114
		Mean	63.38	64.69	64.04
		SD, SE	19.171, 2.539	19.063, 2.525	19.044, 1.784
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0
		Observed			
		n	57	57	114
		Mean	62.28	53.29	57.79
		SD, SE	20.113, 2.664	19.838, 2.628	20.394, 1.910
		Median	62.50	50.00	62.50
		Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	12.5, 100.0	25.0, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.3
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Change from Baseline			
		n	57	57	114
		Mean	-1.10	-11.40	-6.25
		SD, SE	22.195, 2.940	24.353, 3.226	23.767, 2.226
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 0.00
		Min, Max	-50.0, 62.5	-75.0, 50.0	-75.0, 62.5
		GEE Estimates			
		LS Mean (SE)	-0.23 (2.560)	-9.79 (2.765)	
		95% CI	(-5.25, 4.78)	(-15.21, -4.37)	
		LS Mean Difference (SE)		-9.56 (3.555)	
		95% CI		(-16.53, -2.59)	
		p-value		0.0072	
		HedgesG (95% CI)		-0.436 (-0.807, -0.064)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.3
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia		N_1	8	10	18
	Baseline	n	8	10	18
		Mean	45.31	62.50	54.86
		SD, SE	26.674, 9.431	27.003, 8.539	27.500, 6.482
		Median	37.50	62.50	62.50
		Q1, Q3	25.00, 68.75	37.50, 87.50	37.50, 75.00
		Min, Max	12.5, 87.5	12.5, 100.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.3
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Baseline			
		n	8	10	18
		Mean	45.31	62.50	54.86
		SD, SE	26.674, 9.431	27.003, 8.539	27.500, 6.482
		Median	37.50	62.50	62.50
		Q1, Q3	25.00, 68.75	37.50, 87.50	37.50, 75.00
		Min, Max	12.5, 87.5	12.5, 100.0	12.5, 100.0
		Observed			
		n	8	10	18
		Mean	48.44	47.50	47.92
		SD, SE	19.408, 6.862	33.229, 10.508	27.201, 6.411
		Median	50.00	31.25	37.50
		Q1, Q3	31.25, 62.50	25.00, 75.00	25.00, 75.00
		Min, Max	25.0, 75.0	12.5, 100.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.3
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Change from Baseline			
		n	8	10	18
		Mean	3.13	-15.00	-6.94
		SD, SE	22.903, 8.097	29.930, 9.465	27.859, 6.567
		Median	0.00	-12.50	0.00
		Q1, Q3	-6.25, 18.75	-50.00, 12.50	-12.50, 12.50
		Min, Max	-37.5, 37.5	-62.5, 25.0	-62.5, 37.5
		GEE Estimates			
		LS Mean (SE)	6.18 (6.389)	-6.21 (6.793)	
		95% CI	(-6.34, 18.70)	(-19.53, 7.10)	
		LS Mean Difference (SE)		-12.39 (9.414)	
		95% CI		(-30.85, 6.06)	
		p-value		0.1880	
		HedgesG (95% CI)		-0.601 (-1.551, 0.349)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.3
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Baseline			
		n	8	10	18
		Mean	45.31	62.50	54.86
		SD, SE	26.674, 9.431	27.003, 8.539	27.500, 6.482
		Median	37.50	62.50	62.50
		Q1, Q3	25.00, 68.75	37.50, 87.50	37.50, 75.00
		Min, Max	12.5, 87.5	12.5, 100.0	12.5, 100.0
		Observed			
		n	8	10	18
		Mean	46.88	56.25	52.08
		SD, SE	29.693, 10.498	26.517, 8.385	27.537, 6.490
		Median	37.50	62.50	62.50
		Q1, Q3	25.00, 68.75	25.00, 75.00	25.00, 75.00
		Min, Max	12.5, 100.0	12.5, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.3
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Change from Baseline			
		n	8	10	18
		Mean	1.56	-6.25	-2.78
		SD, SE	19.408, 6.862	25.853, 8.176	22.911, 5.400
		Median	6.25	-12.50	0.00
		Q1, Q3	-6.25, 12.50	-12.50, 0.00	-12.50, 12.50
		Min, Max	-37.5, 25.0	-50.0, 50.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	4.62 (7.588)	2.54 (3.900)	
		95% CI	(-10.25, 19.49)	(-5.11, 10.18)	
		LS Mean Difference (SE)		-2.08 (8.139)	
		95% CI		(-18.03, 13.87)	
		p-value		0.7981	
		HedgesG (95% CI)		-0.302 (-1.237, 0.633)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.4
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male		N_1	23	24	47
	Baseline	n	23	24	47
		Mean	59.78	61.46	60.64
		SD, SE	22.912, 4.777	21.467, 4.382	21.959, 3.203
		Median	62.50	62.50	62.50
		Q1, Q3	37.50, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.4
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Baseline			
		n	23	24	47
		Mean	59.78	61.46	60.64
		SD, SE	22.912, 4.777	21.467, 4.382	21.959, 3.203
		Median	62.50	62.50	62.50
		Q1, Q3	37.50, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0
		Observed			
		n	23	24	47
		Mean	61.96	48.96	55.32
		SD, SE	21.807, 4.547	23.578, 4.813	23.421, 3.416
		Median	62.50	43.75	62.50
		Q1, Q3	50.00, 75.00	37.50, 62.50	37.50, 75.00
		Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.4
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Change from Baseline			
		n	23	24	47
		Mean	2.17	-12.50	-5.32
		SD, SE	19.819, 4.133	21.493, 4.387	21.767, 3.175
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 25.00	-25.00, 0.00	-25.00, 12.50
		Min, Max	-25.0, 37.5	-62.5, 25.0	-62.5, 37.5
		GEE Estimates			
		LS Mean (SE)	4.93 (4.956)	-9.24 (5.507)	
		95% CI	(-4.78, 14.65)	(-20.03, 1.56)	
		LS Mean Difference (SE)		-14.17 (5.431)	
		95% CI		(-24.82, -3.53)	
		p-value		0.0091	
		HedgesG (95% CI)		-0.682 (-1.271, -0.094)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.4
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Baseline			
		n	23	23	46
		Mean	59.78	60.33	60.05
		SD, SE	22.912, 4.777	21.204, 4.421	21.829, 3.219
		Median	62.50	62.50	62.50
		Q1, Q3	37.50, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0
		Observed			
		n	23	23	46
		Mean	62.50	48.91	55.71
		SD, SE	22.925, 4.780	19.185, 4.000	22.002, 3.244
		Median	62.50	50.00	56.25
		Q1, Q3	50.00, 75.00	37.50, 62.50	37.50, 62.50
		Min, Max	12.5, 100.0	25.0, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.4
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Change from Baseline			
		n	23	23	46
		Mean	2.72	-11.41	-4.35
		SD, SE	25.550, 5.327	20.613, 4.298	24.040, 3.544
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-12.50, 0.00	-12.50, 12.50
		Min, Max	-50.0, 62.5	-75.0, 25.0	-75.0, 62.5
		GEE Estimates			
		LS Mean (SE)	5.48 (5.469)	-8.24 (4.766)	
		95% CI	(-5.24, 16.20)	(-17.58, 1.10)	
		LS Mean Difference (SE)		-13.72 (5.466)	
		95% CI		(-24.43, -3.01)	
		p-value		0.0121	
		HedgesG (95% CI)		-0.585 (-1.175, 0.005)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.4
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female		N_1	43	44	87
	Baseline	n	43	44	87
		Mean	62.21	66.48	64.37
		SD, SE	19.762, 3.014	19.584, 2.952	19.675, 2.109
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	62.50, 75.00	50.00, 75.00
		Min, Max	12.5, 100.0	12.5, 100.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.4
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Baseline			
		n	43	44	87
		Mean	62.21	66.48	64.37
		SD, SE	19.762, 3.014	19.584, 2.952	19.675, 2.109
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	62.50, 75.00	50.00, 75.00
		Min, Max	12.5, 100.0	12.5, 100.0	12.5, 100.0
		Observed			
		n	43	44	87
		Mean	57.85	57.10	57.47
		SD, SE	18.705, 2.852	26.605, 4.011	22.911, 2.456
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	25.0, 100.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.4
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Change from Baseline			
		n	43	44	87
		Mean	-4.36	-9.38	-6.90
		SD, SE	16.340, 2.492	23.980, 3.615	20.598, 2.208
		Median	0.00	-12.50	0.00
		Q1, Q3	-12.50, 0.00	-25.00, 12.50	-25.00, 12.50
		Min, Max	-37.5, 37.5	-75.0, 37.5	-75.0, 37.5
		GEE Estimates			
		LS Mean (SE)	-4.33 (3.161)	-7.30 (4.047)	
		95% CI	(-10.53, 1.86)	(-15.23, 0.64)	
		LS Mean Difference (SE)		-2.96 (3.996)	
		95% CI		(-10.79, 4.87)	
		p-value		0.4584	
		HedgesG (95% CI)		-0.239 (-0.661, 0.183)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.4
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Baseline			
		n	42	44	86
		Mean	61.90	66.48	64.24
		SD, SE	19.899, 3.071	19.584, 2.952	19.756, 2.130
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	62.50, 75.00	50.00, 75.00
		Min, Max	12.5, 100.0	12.5, 100.0	12.5, 100.0
		Observed			
		n	42	44	86
		Mean	59.23	56.25	57.70
		SD, SE	21.396, 3.301	21.312, 3.213	21.280, 2.295
		Median	62.50	56.25	62.50
		Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	12.5, 100.0	12.5, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.4
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Change from Baseline			
		n	42	44	86
		Mean	-2.68	-10.23	-6.54
		SD, SE	19.431, 2.998	26.451, 3.988	23.462, 2.530
		Median	0.00	-12.50	0.00
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-25.00, 0.00
		Min, Max	-37.5, 50.0	-50.0, 50.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	-2.61 (3.386)	-8.15 (3.557)	
		95% CI	(-9.25, 4.02)	(-15.12, -1.18)	
		LS Mean Difference (SE)		-5.53 (3.940)	
		95% CI		(-13.26, 2.19)	
		p-value		0.1601	
		HedgesG (95% CI)		-0.317 (-0.743, 0.108)	

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The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.5
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White		N_1	53	55	108
	Baseline	n	53	55	108
		Mean	63.44	64.77	64.12
		SD, SE	19.741, 2.712	19.408, 2.617	19.492, 1.876
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.5
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Baseline			
		n	53	55	108
		Mean	63.44	64.77	64.12
		SD, SE	19.741, 2.712	19.408, 2.617	19.492, 1.876
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0
		Observed			
		n	53	55	108
		Mean	59.20	55.23	57.18
		SD, SE	19.170, 2.633	24.496, 3.303	22.032, 2.120
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.5
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Change from Baseline			
		n	53	55	108
		Mean	-4.25	-9.55	-6.94
		SD, SE	16.796, 2.307	22.304, 3.007	19.881, 1.913
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 0.00	-25.00, 12.50	-25.00, 0.00
		Min, Max	-37.5, 37.5	-75.0, 37.5	-75.0, 37.5
		GEE Estimates			
		LS Mean (SE)	-3.53 (2.206)	-8.29 (3.035)	
		95% CI	(-7.86, 0.79)	(-14.24, -2.34)	
		LS Mean Difference (SE)		-4.76 (3.484)	
		95% CI		(-11.59, 2.07)	
		p-value		0.1720	
		HedgesG (95% CI)		-0.263 (-0.642, 0.116)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.5
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Baseline			
		n	53	55	108
		Mean	63.44	64.77	64.12
		SD, SE	19.741, 2.712	19.408, 2.617	19.492, 1.876
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0
		Observed			
		n	53	55	108
		Mean	62.03	53.64	57.75
		SD, SE	19.910, 2.735	20.080, 2.708	20.344, 1.958
		Median	62.50	50.00	62.50
		Q1, Q3	50.00, 75.00	37.50, 75.00	43.75, 75.00
		Min, Max	12.5, 100.0	25.0, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.5
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Change from Baseline			
		n	53	55	108
		Mean	-1.42	-11.14	-6.37
		SD, SE	22.422, 3.080	24.729, 3.334	24.017, 2.311
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 0.00
		Min, Max	-50.0, 62.5	-75.0, 50.0	-75.0, 62.5
		GEE Estimates			
		LS Mean (SE)	-0.70 (2.700)	-9.88 (2.846)	
		95% CI	(-5.99, 4.59)	(-15.46, -4.31)	
		LS Mean Difference (SE)		-9.18 (3.665)	
		95% CI		(-16.36, -2.00)	
		p-value		0.0123	
		HedgesG (95% CI)		-0.405 (-0.786, -0.024)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.5
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White		N_1	13	13	26
	Baseline	n	13	13	26
		Mean	52.88	64.42	58.65
		SD, SE	23.471, 6.510	24.392, 6.765	24.179, 4.742
		Median	62.50	62.50	62.50
		Q1, Q3	37.50, 75.00	62.50, 87.50	37.50, 75.00
		Min, Max	12.5, 87.5	12.5, 100.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.5
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Baseline			
		n	13	13	26
		Mean	52.88	64.42	58.65
		SD, SE	23.471, 6.510	24.392, 6.765	24.179, 4.742
		Median	62.50	62.50	62.50
		Q1, Q3	37.50, 75.00	62.50, 87.50	37.50, 75.00
		Min, Max	12.5, 87.5	12.5, 100.0	12.5, 100.0
		Observed			
		n	13	13	26
		Mean	59.62	50.00	54.81
		SD, SE	22.909, 6.354	31.041, 8.609	27.175, 5.329
		Median	62.50	37.50	62.50
		Q1, Q3	37.50, 75.00	25.00, 75.00	25.00, 75.00
		Min, Max	25.0, 100.0	12.5, 100.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.5
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Change from Baseline			
		n	13	13	26
		Mean	6.73	-14.42	-3.85
		SD, SE	19.509, 5.411	26.441, 7.333	25.192, 4.940
		Median	0.00	-12.50	0.00
		Q1, Q3	0.00, 25.00	-25.00, 0.00	-12.50, 12.50
		Min, Max	-37.5, 37.5	-62.5, 25.0	-62.5, 37.5
		GEE Estimates			
		LS Mean (SE)	9.44 (3.761)	-6.43 (5.798)	
		95% CI	(2.07, 16.81)	(-17.80, 4.93)	
		LS Mean Difference (SE)		-15.87 (6.872)	
		95% CI		(-29.34, -2.40)	
		p-value		0.0209	
		HedgesG (95% CI)		-0.847 (-1.650, -0.045)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.5
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Baseline			
		n	12	12	24
		Mean	51.04	62.50	56.77
		SD, SE	23.512, 6.787	24.425, 7.051	24.165, 4.933
		Median	56.25	62.50	62.50
		Q1, Q3	31.25, 68.75	50.00, 81.25	37.50, 75.00
		Min, Max	12.5, 87.5	12.5, 100.0	12.5, 100.0
		Observed			
		n	12	12	24
		Mean	53.13	54.17	53.65
		SD, SE	28.765, 8.304	24.618, 7.107	26.189, 5.346
		Median	43.75	62.50	56.25
		Q1, Q3	31.25, 81.25	31.25, 68.75	31.25, 75.00
		Min, Max	12.5, 100.0	12.5, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.5
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Change from Baseline			
		n	12	12	24
		Mean	2.08	-8.33	-3.13
		SD, SE	19.094, 5.512	24.034, 6.938	21.885, 4.467
		Median	6.25	-12.50	0.00
		Q1, Q3	-6.25, 12.50	-18.75, 0.00	-12.50, 12.50
		Min, Max	-37.5, 25.0	-50.0, 50.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	4.60 (4.855)	0.32 (4.289)	
		95% CI	(-4.92, 14.11)	(-8.09, 8.73)	
		LS Mean Difference (SE)		-4.28 (6.676)	
		95% CI		(-17.36, 8.81)	
		p-value		0.5216	
		HedgesG (95% CI)		-0.444 (-1.254, 0.366)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.6
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years		N_1	36	31	67
	Baseline	n	36	31	67
		Mean	59.03	63.71	61.19
		SD, SE	22.082, 3.680	19.988, 3.590	21.112, 2.579
		Median	62.50	62.50	62.50
		Q1, Q3	43.75, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	12.5, 100.0	25.0, 100.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.6
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Baseline			
		n	36	31	67
		Mean	59.03	63.71	61.19
		SD, SE	22.082, 3.680	19.988, 3.590	21.112, 2.579
		Median	62.50	62.50	62.50
		Q1, Q3	43.75, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	12.5, 100.0	25.0, 100.0	12.5, 100.0
		Observed			
		n	36	31	67
		Mean	60.42	56.85	58.77
		SD, SE	20.376, 3.396	25.787, 4.632	22.927, 2.801
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	25.0, 100.0	12.5, 100.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.6
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Change from Baseline			
		n	36	31	67
		Mean	1.39	-6.85	-2.43
		SD, SE	18.366, 3.061	22.785, 4.092	20.785, 2.539
		Median	0.00	-12.50	0.00
		Q1, Q3	-12.50, 12.50	-25.00, 12.50	-12.50, 12.50
		Min, Max	-37.5, 37.5	-62.5, 37.5	-62.5, 37.5
		GEE Estimates			
		LS Mean (SE)	1.50 (3.671)	-5.45 (5.204)	
		95% CI	(-5.69, 8.70)	(-15.65, 4.75)	
		LS Mean Difference (SE)		-6.95 (4.546)	
		95% CI		(-15.86, 1.96)	
		p-value		0.1261	
		HedgesG (95% CI)		-0.391 (-0.876, 0.094)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.6
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Baseline			
		n	36	31	67
		Mean	59.03	63.71	61.19
		SD, SE	22.082, 3.680	19.988, 3.590	21.112, 2.579
		Median	62.50	62.50	62.50
		Q1, Q3	43.75, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	12.5, 100.0	25.0, 100.0	12.5, 100.0
		Observed			
		n	36	31	67
		Mean	57.99	54.84	56.53
		SD, SE	25.557, 4.259	22.050, 3.960	23.872, 2.916
		Median	62.50	50.00	50.00
		Q1, Q3	37.50, 81.25	37.50, 75.00	37.50, 75.00
		Min, Max	12.5, 100.0	25.0, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.6
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Change from Baseline			
		n	36	31	67
		Mean	-1.04	-8.87	-4.66
		SD, SE	22.830, 3.805	23.317, 4.188	23.216, 2.836
		Median	0.00	-12.50	0.00
		Q1, Q3	-12.50, 12.50	-25.00, 12.50	-12.50, 12.50
		Min, Max	-50.0, 50.0	-50.0, 50.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	-0.93 (4.259)	-7.47 (4.002)	
		95% CI	(-9.28, 7.42)	(-15.31, 0.38)	
		LS Mean Difference (SE)		-6.54 (4.966)	
		95% CI		(-16.27, 3.20)	
		p-value		0.1880	
		HedgesG (95% CI)		-0.331 (-0.814, 0.153)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.6
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years		N_1	30	37	67
	Baseline	n	30	37	67
		Mean	64.17	65.54	64.93
		SD, SE	19.066, 3.481	20.709, 3.405	19.853, 2.425
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.6
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Baseline			
		n	30	37	67
		Mean	64.17	65.54	64.93
		SD, SE	19.066, 3.481	20.709, 3.405	19.853, 2.425
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
		Observed			
		n	30	37	67
		Mean	57.92	52.03	54.66
		SD, SE	19.277, 3.519	25.772, 4.237	23.114, 2.824
		Median	62.50	50.00	62.50
		Q1, Q3	50.00, 75.00	25.00, 75.00	37.50, 75.00
		Min, Max	0.0, 87.5	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.6
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Change from Baseline			
		n	30	37	67
		Mean	-6.25	-13.51	-10.26
		SD, SE	16.331, 2.982	23.082, 3.795	20.519, 2.507
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 0.00	-25.00, 0.00	-25.00, 0.00
		Min, Max	-37.5, 25.0	-75.0, 25.0	-75.0, 25.0
		GEE Estimates			
		LS Mean (SE)	-3.48 (4.297)	-9.51 (4.816)	
		95% CI	(-11.90, 4.94)	(-18.95, -0.07)	
		LS Mean Difference (SE)		-6.03 (4.385)	
		95% CI		(-14.63, 2.56)	
		p-value		0.1689	
		HedgesG (95% CI)		-0.348 (-0.833, 0.138)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.6
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Baseline			
		n	29	36	65
		Mean	63.79	64.93	64.42
		SD, SE	19.291, 3.582	20.663, 3.444	19.916, 2.470
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
		Observed			
		n	29	36	65
		Mean	63.36	52.78	57.50
		SD, SE	15.998, 2.971	19.846, 3.308	18.854, 2.339
		Median	62.50	56.25	62.50
		Q1, Q3	50.00, 75.00	37.50, 62.50	50.00, 75.00
		Min, Max	25.0, 100.0	12.5, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.6
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Change from Baseline			
		n	29	36	65
		Mean	-0.43	-12.15	-6.92
		SD, SE	20.724, 3.848	25.615, 4.269	24.108, 2.990
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 0.00
		Min, Max	-37.5, 62.5	-75.0, 50.0	-75.0, 62.5
		GEE Estimates			
		LS Mean (SE)	2.39 (4.437)	-8.11 (4.372)	
		95% CI	(-6.31, 11.09)	(-16.68, 0.46)	
		LS Mean Difference (SE)		-10.50 (4.069)	
		95% CI		(-18.48, -2.53)	
		p-value		0.0098	
		HedgesG (95% CI)		-0.484 (-0.980, 0.012)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.7
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5		N_1	41	39	80
	Baseline	n	41	39	80
		Mean	49.39	50.96	50.16
		SD, SE	16.045, 2.506	13.868, 2.221	14.949, 1.671
		Median	50.00	62.50	50.00
		Q1, Q3	37.50, 62.50	37.50, 62.50	37.50, 62.50
		Min, Max	0.0, 62.5	12.5, 62.5	0.0, 62.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.7
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline			
		n	41	39	80
		Mean	49.39	50.96	50.16
		SD, SE	16.045, 2.506	13.868, 2.221	14.949, 1.671
		Median	50.00	62.50	50.00
		Q1, Q3	37.50, 62.50	37.50, 62.50	37.50, 62.50
		Min, Max	0.0, 62.5	12.5, 62.5	0.0, 62.5
		Observed			
		n	41	39	80
		Mean	53.35	46.79	50.16
		SD, SE	18.962, 2.961	23.424, 3.751	21.374, 2.390
		Median	50.00	50.00	50.00
		Q1, Q3	37.50, 62.50	25.00, 62.50	37.50, 62.50
		Min, Max	0.0, 87.5	0.0, 87.5	0.0, 87.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.7
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline			
		n	41	39	80
		Mean	3.96	-4.17	0.00
		SD, SE	16.403, 2.562	20.546, 3.290	18.868, 2.110
		Median	0.00	-12.50	0.00
		Q1, Q3	0.00, 12.50	-12.50, 12.50	-12.50, 12.50
		Min, Max	-25.0, 37.5	-50.0, 37.5	-50.0, 37.5
		GEE Estimates			
		LS Mean (SE)	1.84 (3.874)	-5.87 (4.701)	
		95% CI	(-5.76, 9.43)	(-15.09, 3.34)	
		LS Mean Difference (SE)		-7.71 (4.000)	
		95% CI		(-15.55, 0.13)	
		p-value		0.0539	
		HedgesG (95% CI)		-0.429 (-0.872, 0.015)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.7
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline			
		n	41	39	80
		Mean	49.39	50.96	50.16
		SD, SE	16.045, 2.506	13.868, 2.221	14.949, 1.671
		Median	50.00	62.50	50.00
		Q1, Q3	37.50, 62.50	37.50, 62.50	37.50, 62.50
		Min, Max	0.0, 62.5	12.5, 62.5	0.0, 62.5
		Observed			
		n	41	39	80
		Mean	54.88	49.36	52.19
		SD, SE	22.686, 3.543	17.897, 2.866	20.552, 2.298
		Median	50.00	50.00	50.00
		Q1, Q3	37.50, 62.50	37.50, 62.50	37.50, 62.50
		Min, Max	12.5, 100.0	12.5, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.7
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline			
		n	41	39	80
		Mean	5.49	-1.60	2.03
		SD, SE	22.887, 3.574	21.685, 3.472	22.453, 2.510
		Median	0.00	0.00	0.00
		Q1, Q3	-12.50, 25.00	-12.50, 12.50	-12.50, 12.50
		Min, Max	-50.0, 62.5	-50.0, 50.0	-50.0, 62.5
		GEE Estimates			
		LS Mean (SE)	3.36 (4.533)	-3.31 (4.049)	
		95% CI	(-5.52, 12.24)	(-11.24, 4.63)	
		LS Mean Difference (SE)		-6.67 (4.205)	
		95% CI		(-14.91, 1.57)	
		p-value		0.1128	
		HedgesG (95% CI)		-0.311 (-0.752, 0.130)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.7
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5		N_1	25	29	54
	Baseline	n	25	29	54
		Mean	81.00	83.19	82.18
		SD, SE	9.629, 1.926	10.175, 1.889	9.894, 1.346
		Median	75.00	75.00	75.00
		Q1, Q3	75.00, 87.50	75.00, 87.50	75.00, 87.50
		Min, Max	75.0, 100.0	75.0, 100.0	75.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.7
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline			
		n	25	29	54
		Mean	81.00	83.19	82.18
		SD, SE	9.629, 1.926	10.175, 1.889	9.894, 1.346
		Median	75.00	75.00	75.00
		Q1, Q3	75.00, 87.50	75.00, 87.50	75.00, 87.50
		Min, Max	75.0, 100.0	75.0, 100.0	75.0, 100.0
		Observed			
		n	25	29	54
		Mean	69.00	64.22	66.44
		SD, SE	17.351, 3.470	25.601, 4.754	22.099, 3.007
		Median	75.00	62.50	68.75
		Q1, Q3	50.00, 75.00	50.00, 87.50	50.00, 75.00
		Min, Max	37.5, 100.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.7
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline			
		n	25	29	54
		Mean	-12.00	-18.97	-15.74
		SD, SE	15.512, 3.102	23.769, 4.414	20.487, 2.788
		Median	-12.50	-25.00	-12.50
		Q1, Q3	-25.00, 0.00	-25.00, 0.00	-25.00, 0.00
		Min, Max	-37.5, 25.0	-75.0, 25.0	-75.0, 25.0
		GEE Estimates			
		LS Mean (SE)	-5.77 (4.159)	-12.79 (4.772)	
		95% CI	(-13.92, 2.38)	(-22.14, -3.44)	
		LS Mean Difference (SE)		-7.02 (5.038)	
		95% CI		(-16.89, 2.86)	
		p-value		0.1635	
		HedgesG (95% CI)		-0.331 (-0.869, 0.208)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.7
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline			
		n	24	28	52
		Mean	81.25	83.04	82.21
		SD, SE	9.752, 1.991	10.327, 1.952	10.008, 1.388
		Median	75.00	75.00	75.00
		Q1, Q3	75.00, 87.50	75.00, 87.50	75.00, 87.50
		Min, Max	75.0, 100.0	75.0, 100.0	75.0, 100.0
		Observed			
		n	24	28	52
		Mean	69.79	59.82	64.42
		SD, SE	16.858, 3.441	23.163, 4.377	20.914, 2.900
		Median	68.75	62.50	62.50
		Q1, Q3	62.50, 81.25	37.50, 81.25	50.00, 81.25
		Min, Max	37.5, 100.0	25.0, 87.5	25.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.7
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline			
		n	24	28	52
		Mean	-11.46	-23.21	-17.79
		SD, SE	14.706, 3.002	22.749, 4.299	20.163, 2.796
		Median	-12.50	-25.00	-12.50
		Q1, Q3	-18.75, 0.00	-43.75, 0.00	-31.25, 0.00
		Min, Max	-37.5, 12.5	-75.0, 12.5	-75.0, 12.5
		GEE Estimates			
		LS Mean (SE)	-4.79 (3.934)	-16.58 (3.937)	
		95% CI	(-12.51, 2.92)	(-24.30, -8.87)	
		LS Mean Difference (SE)		-11.79 (4.892)	
		95% CI		(-21.38, -2.20)	
		p-value		0.0159	
		HedgesG (95% CI)		-0.583 (-1.140, -0.027)	

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Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.8
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	54.39	53.75	54.10
		SD, SE	20.669, 3.398	18.613, 3.398	19.631, 2.398
		Median	62.50	62.50	62.50
		Q1, Q3	37.50, 75.00	37.50, 62.50	37.50, 75.00
		Min, Max	0.0, 87.5	12.5, 87.5	0.0, 87.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.8
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline			
		n	37	30	67
		Mean	54.39	53.75	54.10
		SD, SE	20.669, 3.398	18.613, 3.398	19.631, 2.398
		Median	62.50	62.50	62.50
		Q1, Q3	37.50, 75.00	37.50, 62.50	37.50, 75.00
		Min, Max	0.0, 87.5	12.5, 87.5	0.0, 87.5
		Observed			
		n	37	30	67
		Mean	53.72	37.92	46.64
		SD, SE	17.889, 2.941	18.124, 3.309	19.533, 2.386
		Median	50.00	37.50	50.00
		Q1, Q3	37.50, 62.50	25.00, 50.00	37.50, 62.50
		Min, Max	0.0, 87.5	0.0, 62.5	0.0, 87.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.8
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-0.68	-15.83	-7.46
		SD, SE	18.621, 3.061	18.838, 3.439	20.069, 2.452
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-25.00, -12.50	-25.00, 0.00
		Min, Max	-37.5, 37.5	-50.0, 25.0	-50.0, 37.5
		GEE Estimates			
		LS Mean (SE)	-5.71 (3.388)	-21.88 (4.242)	
		95% CI	(-12.35, 0.93)	(-30.20, -13.57)	
		LS Mean Difference (SE)		-16.18 (3.707)	
		95% CI		(-23.44, -8.91)	
		p-value		<.0001	
		HedgesG (95% CI)		-0.788 (-1.288, -0.289)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.8
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline			
		n	37	30	67
		Mean	54.39	53.75	54.10
		SD, SE	20.669, 3.398	18.613, 3.398	19.631, 2.398
		Median	62.50	62.50	62.50
		Q1, Q3	37.50, 75.00	37.50, 62.50	37.50, 75.00
		Min, Max	0.0, 87.5	12.5, 87.5	0.0, 87.5
		Observed			
		n	37	30	67
		Mean	52.70	45.00	49.25
		SD, SE	20.012, 3.290	15.606, 2.849	18.448, 2.254
		Median	62.50	43.75	50.00
		Q1, Q3	37.50, 62.50	37.50, 62.50	37.50, 62.50
		Min, Max	12.5, 100.0	12.5, 75.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.8
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-1.69	-8.75	-4.85
		SD, SE	24.679, 4.057	23.706, 4.328	24.324, 2.972
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-12.50, 0.00	-12.50, 12.50
		Min, Max	-50.0, 62.5	-50.0, 50.0	-50.0, 62.5
		GEE Estimates			
		LS Mean (SE)	-6.72 (4.036)	-14.80 (3.829)	
		95% CI	(-14.63, 1.19)	(-22.31, -7.30)	
		LS Mean Difference (SE)		-8.08 (3.921)	
		95% CI		(-15.77, -0.40)	
		p-value		0.0393	
		HedgesG (95% CI)		-0.283 (-0.767, 0.200)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.8
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	70.26	73.36	72.01
		SD, SE	17.492, 3.248	17.235, 2.796	17.284, 2.112
		Median	75.00	75.00	75.00
		Q1, Q3	62.50, 75.00	62.50, 87.50	62.50, 87.50
		Min, Max	37.5, 100.0	37.5, 100.0	37.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.8
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline			
		n	29	38	67
		Mean	70.26	73.36	72.01
		SD, SE	17.492, 3.248	17.235, 2.796	17.284, 2.112
		Median	75.00	75.00	75.00
		Q1, Q3	62.50, 75.00	62.50, 87.50	62.50, 87.50
		Min, Max	37.5, 100.0	37.5, 100.0	37.5, 100.0
		Observed			
		n	29	38	67
		Mean	66.38	67.11	66.79
		SD, SE	20.073, 3.728	23.506, 3.813	21.928, 2.679
		Median	62.50	75.00	75.00
		Q1, Q3	50.00, 75.00	50.00, 87.50	50.00, 75.00
		Min, Max	25.0, 100.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.8
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-3.88	-6.25	-5.22
		SD, SE	16.738, 3.108	25.294, 4.103	21.884, 2.674
		Median	0.00	0.00	0.00
		Q1, Q3	-12.50, 0.00	-25.00, 12.50	-12.50, 12.50
		Min, Max	-37.5, 25.0	-75.0, 37.5	-75.0, 37.5
		GEE Estimates			
		LS Mean (SE)	0.61 (4.007)	-0.03 (3.465)	
		95% CI	(-7.24, 8.46)	(-6.82, 6.76)	
		LS Mean Difference (SE)		-0.64 (4.756)	
		95% CI		(-9.96, 8.68)	
		p-value		0.8926	
		HedgesG (95% CI)		-0.105 (-0.588, 0.379)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.8
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline			
		n	28	37	65
		Mean	70.09	72.97	71.73
		SD, SE	17.788, 3.362	17.309, 2.846	17.438, 2.163
		Median	68.75	75.00	75.00
		Q1, Q3	56.25, 81.25	62.50, 87.50	62.50, 87.50
		Min, Max	37.5, 100.0	37.5, 100.0	37.5, 100.0
		Observed			
		n	28	37	65
		Mean	70.54	60.81	65.00
		SD, SE	20.188, 3.815	21.882, 3.597	21.560, 2.674
		Median	75.00	62.50	75.00
		Q1, Q3	50.00, 87.50	50.00, 75.00	50.00, 87.50
		Min, Max	25.0, 100.0	25.0, 87.5	25.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.8
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline			
		n	28	37	65
		Mean	0.45	-12.16	-6.73
		SD, SE	17.507, 3.309	25.257, 4.152	22.972, 2.849
		Median	0.00	-12.50	0.00
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 12.50
		Min, Max	-37.5, 37.5	-75.0, 50.0	-75.0, 50.0
		GEE Estimates			
		LS Mean (SE)	5.02 (4.031)	-5.88 (2.648)	
		95% CI	(-2.88, 12.92)	(-11.07, -0.69)	
		LS Mean Difference (SE)		-10.90 (4.789)	
		95% CI		(-20.29, -1.51)	
		p-value		0.0228	
		HedgesG (95% CI)		-0.551 (-1.051, -0.051)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.9
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50		N_1	42	32	74
	Baseline	n	42	32	74
		Mean	55.95	52.73	54.56
		SD, SE	21.069, 3.251	17.019, 3.009	19.362, 2.251
		Median	62.50	56.25	62.50
		Q1, Q3	50.00, 75.00	37.50, 62.50	37.50, 75.00
		Min, Max	0.0, 100.0	12.5, 75.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.9
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Baseline			
		n	42	32	74
		Mean	55.95	52.73	54.56
		SD, SE	21.069, 3.251	17.019, 3.009	19.362, 2.251
		Median	62.50	56.25	62.50
		Q1, Q3	50.00, 75.00	37.50, 62.50	37.50, 75.00
		Min, Max	0.0, 100.0	12.5, 75.0	0.0, 100.0
		Observed			
		n	42	32	74
		Mean	57.14	41.02	50.17
		SD, SE	18.754, 2.894	22.051, 3.898	21.650, 2.517
		Median	62.50	37.50	50.00
		Q1, Q3	50.00, 75.00	25.00, 50.00	37.50, 62.50
		Min, Max	0.0, 87.5	0.0, 87.5	0.0, 87.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.9
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Change from Baseline			
		n	42	32	74
		Mean	1.19	-11.72	-4.39
		SD, SE	18.273, 2.820	21.284, 3.762	20.527, 2.386
		Median	0.00	-12.50	-6.25
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 12.50
		Min, Max	-37.5, 37.5	-50.0, 37.5	-50.0, 37.5
		GEE Estimates			
		LS Mean (SE)	-0.41 (4.274)	-16.46 (5.268)	
		95% CI	(-8.78, 7.97)	(-26.79, -6.14)	
		LS Mean Difference (SE)		-16.05 (3.982)	
		95% CI		(-23.86, -8.25)	
		p-value		<.0001	
		HedgesG (95% CI)		-0.642 (-1.113, -0.171)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.9
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Baseline			
		n	42	32	74
		Mean	55.95	52.73	54.56
		SD, SE	21.069, 3.251	17.019, 3.009	19.362, 2.251
		Median	62.50	56.25	62.50
		Q1, Q3	50.00, 75.00	37.50, 62.50	37.50, 75.00
		Min, Max	0.0, 100.0	12.5, 75.0	0.0, 100.0
		Observed			
		n	42	32	74
		Mean	55.95	47.27	52.20
		SD, SE	20.887, 3.223	17.313, 3.061	19.776, 2.299
		Median	62.50	50.00	50.00
		Q1, Q3	37.50, 62.50	37.50, 62.50	37.50, 62.50
		Min, Max	12.5, 100.0	12.5, 75.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.9
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Change from Baseline			
		n	42	32	74
		Mean	0.00	-5.47	-2.36
		SD, SE	24.068, 3.714	22.882, 4.045	23.561, 2.739
		Median	0.00	-6.25	0.00
		Q1, Q3	-12.50, 12.50	-12.50, 6.25	-12.50, 12.50
		Min, Max	-50.0, 62.5	-50.0, 50.0	-50.0, 62.5
		GEE Estimates			
		LS Mean (SE)	-1.60 (4.761)	-10.21 (4.490)	
		95% CI	(-10.93, 7.73)	(-19.01, -1.41)	
		LS Mean Difference (SE)		-8.61 (4.018)	
		95% CI		(-16.49, -0.74)	
		p-value		0.0321	
		HedgesG (95% CI)		-0.227 (-0.688, 0.235)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.9
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50		N_1	24	35	59
	Baseline	n	24	35	59
		Mean	70.83	75.71	73.73
		SD, SE	16.757, 3.421	16.864, 2.851	16.850, 2.194
		Median	68.75	75.00	75.00
		Q1, Q3	62.50, 81.25	62.50, 87.50	62.50, 87.50
		Min, Max	37.5, 100.0	37.5, 100.0	37.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.9
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Baseline			
		n	24	35	59
		Mean	70.83	75.71	73.73
		SD, SE	16.757, 3.421	16.864, 2.851	16.850, 2.194
		Median	68.75	75.00	75.00
		Q1, Q3	62.50, 81.25	62.50, 87.50	62.50, 87.50
		Min, Max	37.5, 100.0	37.5, 100.0	37.5, 100.0
		Observed			
		n	24	35	59
		Mean	63.02	66.43	65.04
		SD, SE	21.328, 4.354	23.242, 3.929	22.358, 2.911
		Median	62.50	75.00	62.50
		Q1, Q3	43.75, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	25.0, 100.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.9
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Change from Baseline			
		n	24	35	59
		Mean	-7.81	-9.29	-8.69
		SD, SE	15.557, 3.176	25.063, 4.236	21.558, 2.807
		Median	0.00	0.00	0.00
		Q1, Q3	-18.75, 0.00	-25.00, 12.50	-25.00, 12.50
		Min, Max	-37.5, 25.0	-75.0, 25.0	-75.0, 25.0
		GEE Estimates			
		LS Mean (SE)	-4.81 (3.868)	-2.45 (4.146)	
		95% CI	(-12.39, 2.77)	(-10.58, 5.68)	
		LS Mean Difference (SE)		2.36 (4.913)	
		95% CI		(-7.27, 11.99)	
		p-value		0.6305	
		HedgesG (95% CI)		-0.066 (-0.585, 0.454)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.9
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Baseline			
		n	23	34	57
		Mean	70.65	75.37	73.46
		SD, SE	17.110, 3.568	16.991, 2.914	17.046, 2.258
		Median	62.50	75.00	75.00
		Q1, Q3	62.50, 87.50	62.50, 87.50	62.50, 87.50
		Min, Max	37.5, 100.0	37.5, 100.0	37.5, 100.0
		Observed			
		n	23	34	57
		Mean	68.48	60.29	63.60
		SD, SE	21.608, 4.506	22.077, 3.786	22.069, 2.923
		Median	75.00	62.50	62.50
		Q1, Q3	50.00, 87.50	50.00, 75.00	50.00, 87.50
		Min, Max	25.0, 100.0	25.0, 87.5	25.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.9
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Change from Baseline			
		n	23	34	57
		Mean	-2.17	-15.07	-9.87
		SD, SE	17.128, 3.571	25.521, 4.377	23.234, 3.077
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-37.50, 0.00	-25.00, 0.00
		Min, Max	-37.5, 37.5	-75.0, 50.0	-75.0, 50.0
		GEE Estimates			
		LS Mean (SE)	1.03 (4.187)	-8.11 (3.373)	
		95% CI	(-7.17, 9.24)	(-14.72, -1.50)	
		LS Mean Difference (SE)		-9.15 (5.178)	
		95% CI		(-19.30, 1.00)	
		p-value		0.0773	
		HedgesG (95% CI)		-0.554 (-1.093, -0.016)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.10
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	54.39	52.50	53.54
		SD, SE	20.669, 3.398	17.799, 3.250	19.317, 2.360
		Median	62.50	56.25	62.50
		Q1, Q3	37.50, 75.00	37.50, 62.50	37.50, 62.50
		Min, Max	0.0, 87.5	12.5, 87.5	0.0, 87.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.10
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Baseline			
		n	37	30	67
		Mean	54.39	52.50	53.54
		SD, SE	20.669, 3.398	17.799, 3.250	19.317, 2.360
		Median	62.50	56.25	62.50
		Q1, Q3	37.50, 75.00	37.50, 62.50	37.50, 62.50
		Min, Max	0.0, 87.5	12.5, 87.5	0.0, 87.5
		Observed			
		n	37	30	67
		Mean	53.72	40.83	47.95
		SD, SE	17.889, 2.941	21.002, 3.834	20.249, 2.474
		Median	50.00	37.50	50.00
		Q1, Q3	37.50, 62.50	25.00, 62.50	37.50, 62.50
		Min, Max	0.0, 87.5	0.0, 87.5	0.0, 87.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.10
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-0.68	-11.67	-5.60
		SD, SE	18.621, 3.061	20.483, 3.740	20.095, 2.455
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-25.00, 0.00
		Min, Max	-37.5, 37.5	-50.0, 37.5	-50.0, 37.5
		GEE Estimates			
		LS Mean (SE)	-6.69 (3.484)	-19.62 (4.320)	
		95% CI	(-13.52, 0.14)	(-28.09, -11.16)	
		LS Mean Difference (SE)		-12.93 (4.069)	
		95% CI		(-20.91, -4.96)	
		p-value		0.0015	
		HedgesG (95% CI)		-0.549 (-1.040, -0.059)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.10
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Baseline			
		n	37	30	67
		Mean	54.39	52.50	53.54
		SD, SE	20.669, 3.398	17.799, 3.250	19.317, 2.360
		Median	62.50	56.25	62.50
		Q1, Q3	37.50, 75.00	37.50, 62.50	37.50, 62.50
		Min, Max	0.0, 87.5	12.5, 87.5	0.0, 87.5
		Observed			
		n	37	30	67
		Mean	52.70	46.67	50.00
		SD, SE	20.012, 3.290	15.019, 2.742	18.075, 2.208
		Median	62.50	50.00	50.00
		Q1, Q3	37.50, 62.50	37.50, 62.50	37.50, 62.50
		Min, Max	12.5, 100.0	12.5, 75.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.10
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-1.69	-5.83	-3.54
		SD, SE	24.679, 4.057	22.680, 4.141	23.718, 2.898
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-12.50, 0.00	-12.50, 12.50
		Min, Max	-50.0, 62.5	-50.0, 50.0	-50.0, 62.5
		GEE Estimates			
		LS Mean (SE)	-7.71 (4.080)	-13.79 (3.661)	
		95% CI	(-15.70, 0.29)	(-20.97, -6.62)	
		LS Mean Difference (SE)		-6.08 (3.813)	
		95% CI		(-13.56, 1.39)	
		p-value		0.1105	
		HedgesG (95% CI)		-0.169 (-0.652, 0.313)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.10
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	70.26	74.34	72.57
		SD, SE	17.492, 3.248	16.681, 2.706	17.028, 2.080
		Median	75.00	75.00	75.00
		Q1, Q3	62.50, 75.00	62.50, 87.50	62.50, 87.50
		Min, Max	37.5, 100.0	37.5, 100.0	37.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.10
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Baseline			
		n	29	38	67
		Mean	70.26	74.34	72.57
		SD, SE	17.492, 3.248	16.681, 2.706	17.028, 2.080
		Median	75.00	75.00	75.00
		Q1, Q3	62.50, 75.00	62.50, 87.50	62.50, 87.50
		Min, Max	37.5, 100.0	37.5, 100.0	37.5, 100.0
		Observed			
		n	29	38	67
		Mean	66.38	64.80	65.49
		SD, SE	20.073, 3.728	24.290, 3.940	22.412, 2.738
		Median	62.50	75.00	75.00
		Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	25.0, 100.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.10
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-3.88	-9.54	-7.09
		SD, SE	16.738, 3.108	25.073, 4.067	21.892, 2.675
		Median	0.00	-12.50	0.00
		Q1, Q3	-12.50, 0.00	-25.00, 12.50	-25.00, 12.50
		Min, Max	-37.5, 25.0	-75.0, 25.0	-75.0, 25.0
		GEE Estimates			
		LS Mean (SE)	1.71 (4.107)	-1.92 (3.750)	
		95% CI	(-6.34, 9.76)	(-9.27, 5.43)	
		LS Mean Difference (SE)		-3.63 (4.719)	
		95% CI		(-12.88, 5.62)	
		p-value		0.4417	
		HedgesG (95% CI)		-0.252 (-0.737, 0.233)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.10
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Baseline			
		n	28	37	65
		Mean	70.09	73.99	72.31
		SD, SE	17.788, 3.362	16.765, 2.756	17.186, 2.132
		Median	68.75	75.00	75.00
		Q1, Q3	56.25, 81.25	62.50, 87.50	62.50, 87.50
		Min, Max	37.5, 100.0	37.5, 100.0	37.5, 100.0
		Observed			
		n	28	37	65
		Mean	70.54	59.46	64.23
		SD, SE	20.188, 3.815	23.088, 3.796	22.413, 2.780
		Median	75.00	62.50	75.00
		Q1, Q3	50.00, 87.50	50.00, 75.00	50.00, 87.50
		Min, Max	25.0, 100.0	25.0, 87.5	25.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.10
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Change from Baseline			
		n	28	37	65
		Mean	0.45	-14.53	-8.08
		SD, SE	17.507, 3.309	25.433, 4.181	23.430, 2.906
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-25.00, 0.00
		Min, Max	-37.5, 37.5	-75.0, 50.0	-75.0, 50.0
		GEE Estimates			
		LS Mean (SE)	6.12 (4.126)	-6.79 (2.989)	
		95% CI	(-1.96, 14.21)	(-12.65, -0.94)	
		LS Mean Difference (SE)		-12.92 (4.875)	
		95% CI		(-22.47, -3.36)	
		p-value		0.0081	
		HedgesG (95% CI)		-0.651 (-1.154, -0.147)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.11
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes		N_1	44	47	91
	Baseline	n	44	47	91
		Mean	65.06	68.09	66.62
		SD, SE	17.173, 2.589	19.296, 2.815	18.263, 1.914
		Median	62.50	75.00	62.50
		Q1, Q3	50.00, 75.00	62.50, 75.00	50.00, 75.00
		Min, Max	12.5, 100.0	37.5, 100.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.11
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	44	47	91
		Mean	65.06	68.09	66.62
		SD, SE	17.173, 2.589	19.296, 2.815	18.263, 1.914
		Median	62.50	75.00	62.50
		Q1, Q3	50.00, 75.00	62.50, 75.00	50.00, 75.00
		Min, Max	12.5, 100.0	37.5, 100.0	12.5, 100.0
		Observed			
		n	44	47	91
		Mean	61.65	58.24	59.89
		SD, SE	17.553, 2.646	24.069, 3.511	21.124, 2.214
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	37.50, 75.00	50.00, 75.00
		Min, Max	25.0, 100.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.11
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	44	47	91
		Mean	-3.41	-9.84	-6.73
		SD, SE	17.338, 2.614	24.855, 3.625	21.675, 2.272
		Median	0.00	-12.50	0.00
		Q1, Q3	-12.50, 0.00	-25.00, 12.50	-25.00, 12.50
		Min, Max	-37.5, 37.5	-75.0, 37.5	-75.0, 37.5
		GEE Estimates			
		LS Mean (SE)	-3.26 (4.579)	-7.71 (4.798)	
		95% CI	(-12.23, 5.72)	(-17.11, 1.69)	
		LS Mean Difference (SE)		-4.45 (3.990)	
		95% CI		(-12.27, 3.37)	
		p-value		0.2646	
		HedgesG (95% CI)		-0.293 (-0.706, 0.121)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.11
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	43	46	89
		Mean	64.83	67.66	66.29
		SD, SE	17.307, 2.639	19.289, 2.844	18.310, 1.941
		Median	62.50	68.75	62.50
		Q1, Q3	50.00, 75.00	62.50, 75.00	50.00, 75.00
		Min, Max	12.5, 100.0	37.5, 100.0	12.5, 100.0
		Observed			
		n	43	46	89
		Mean	62.79	55.71	59.13
		SD, SE	18.994, 2.897	21.033, 3.101	20.275, 2.149
		Median	62.50	56.25	62.50
		Q1, Q3	50.00, 75.00	37.50, 75.00	50.00, 75.00
		Min, Max	25.0, 100.0	25.0, 87.5	25.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.11
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	43	46	89
		Mean	-2.03	-11.96	-7.16
		SD, SE	19.274, 2.939	25.814, 3.806	23.301, 2.470
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 0.00
		Min, Max	-37.5, 50.0	-75.0, 50.0	-75.0, 50.0
		GEE Estimates			
		LS Mean (SE)	-1.87 (4.833)	-9.79 (3.877)	
		95% CI	(-11.34, 7.60)	(-17.39, -2.19)	
		LS Mean Difference (SE)		-7.92 (4.071)	
		95% CI		(-15.90, 0.06)	
		p-value		0.0518	
		HedgesG (95% CI)		-0.425 (-0.845, -0.004)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.11
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No		N_1	22	21	43
	Baseline	n	22	21	43
		Mean	53.98	57.14	55.52
		SD, SE	25.409, 5.417	20.756, 4.529	23.033, 3.513
		Median	62.50	62.50	62.50
		Q1, Q3	37.50, 75.00	50.00, 62.50	37.50, 75.00
		Min, Max	0.0, 100.0	12.5, 87.5	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.11
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Baseline			
		n	22	21	43
		Mean	53.98	57.14	55.52
		SD, SE	25.409, 5.417	20.756, 4.529	23.033, 3.513
		Median	62.50	62.50	62.50
		Q1, Q3	37.50, 75.00	50.00, 62.50	37.50, 75.00
		Min, Max	0.0, 100.0	12.5, 87.5	0.0, 100.0
		Observed			
		n	22	21	43
		Mean	54.55	45.24	50.00
		SD, SE	23.320, 4.972	27.522, 6.006	25.588, 3.902
		Median	62.50	37.50	50.00
		Q1, Q3	37.50, 75.00	25.00, 62.50	37.50, 62.50
		Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.11
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Change from Baseline			
		n	22	21	43
		Mean	0.57	-11.90	-5.52
		SD, SE	18.691, 3.985	18.740, 4.089	19.537, 2.979
		Median	0.00	-12.50	0.00
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 12.50
		Min, Max	-37.5, 37.5	-50.0, 25.0	-50.0, 37.5
		GEE Estimates			
		LS Mean (SE)	6.33 (3.343)	-7.76 (4.646)	
		95% CI	(-0.22, 12.88)	(-16.87, 1.35)	
		LS Mean Difference (SE)		-14.09 (4.739)	
		95% CI		(-23.38, -4.80)	
		p-value		0.0029	
		HedgesG (95% CI)		-0.639 (-1.252, -0.026)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.11
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Baseline			
		n	22	21	43
		Mean	53.98	57.14	55.52
		SD, SE	25.409, 5.417	20.756, 4.529	23.033, 3.513
		Median	62.50	62.50	62.50
		Q1, Q3	37.50, 75.00	50.00, 62.50	37.50, 75.00
		Min, Max	0.0, 100.0	12.5, 87.5	0.0, 100.0
		Observed			
		n	22	21	43
		Mean	55.68	49.40	52.62
		SD, SE	26.369, 5.622	19.952, 4.354	23.395, 3.568
		Median	62.50	50.00	50.00
		Q1, Q3	37.50, 62.50	37.50, 62.50	37.50, 62.50
		Min, Max	12.5, 100.0	12.5, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.11
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Change from Baseline			
		n	22	21	43
		Mean	1.70	-7.74	-2.91
		SD, SE	26.247, 5.596	21.461, 4.683	24.220, 3.693
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-12.50, 0.00	-12.50, 12.50
		Min, Max	-50.0, 62.5	-50.0, 50.0	-50.0, 62.5
		GEE Estimates			
		LS Mean (SE)	7.47 (4.407)	-3.59 (3.418)	
		95% CI	(-1.17, 16.11)	(-10.29, 3.11)	
		LS Mean Difference (SE)		-11.06 (5.256)	
		95% CI		(-21.36, -0.76)	
		p-value		0.0353	
		HedgesG (95% CI)		-0.377 (-0.980, 0.227)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.12
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes		N_1	13	17	30
	Baseline	n	13	17	30
		Mean	64.42	66.91	65.83
		SD, SE	14.294, 3.965	17.645, 4.280	16.059, 2.932
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	62.50, 75.00	50.00, 75.00
		Min, Max	50.0, 87.5	37.5, 100.0	37.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.12
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	13	17	30
		Mean	64.42	66.91	65.83
		SD, SE	14.294, 3.965	17.645, 4.280	16.059, 2.932
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	62.50, 75.00	50.00, 75.00
		Min, Max	50.0, 87.5	37.5, 100.0	37.5, 100.0
		Observed			
		n	13	17	30
		Mean	60.58	59.56	60.00
		SD, SE	12.339, 3.422	29.158, 7.072	23.072, 4.212
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	37.50, 75.00	50.00, 75.00
		Min, Max	37.5, 75.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.12
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	13	17	30
		Mean	-3.85	-7.35	-5.83
		SD, SE	18.670, 5.178	25.023, 6.069	22.199, 4.053
		Median	-12.50	0.00	-6.25
		Q1, Q3	-12.50, 0.00	-12.50, 12.50	-12.50, 12.50
		Min, Max	-37.5, 25.0	-75.0, 25.0	-75.0, 25.0
		GEE Estimates			
		LS Mean (SE)	-1.52 (3.374)	-4.70 (6.485)	
		95% CI	(-8.13, 5.09)	(-17.41, 8.01)	
		LS Mean Difference (SE)		-3.18 (6.580)	
		95% CI		(-16.08, 9.72)	
		p-value		0.6288	
		HedgesG (95% CI)		-0.146 (-0.869, 0.577)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.12
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	13	16	29
		Mean	64.42	65.63	65.09
		SD, SE	14.294, 3.965	17.381, 4.345	15.804, 2.935
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	62.50, 75.00	50.00, 75.00
		Min, Max	50.0, 87.5	37.5, 100.0	37.5, 100.0
		Observed			
		n	13	16	29
		Mean	62.50	55.47	58.62
		SD, SE	18.400, 5.103	21.875, 5.469	20.349, 3.779
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	37.50, 75.00	50.00, 75.00
		Min, Max	25.0, 100.0	25.0, 87.5	25.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.12
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	13	16	29
		Mean	-1.92	-10.16	-6.47
		SD, SE	23.300, 6.462	22.921, 5.730	23.054, 4.281
		Median	-12.50	0.00	0.00
		Q1, Q3	-12.50, 0.00	-31.25, 0.00	-12.50, 0.00
		Min, Max	-37.5, 50.0	-50.0, 25.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	0.40 (4.774)	-7.41 (4.659)	
		95% CI	(-8.95, 9.76)	(-16.54, 1.72)	
		LS Mean Difference (SE)		-7.81 (6.163)	
		95% CI		(-19.89, 4.27)	
		p-value		0.2051	
		HedgesG (95% CI)		-0.334 (-1.071, 0.402)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.12
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No		N_1	53	51	104
	Baseline	n	53	51	104
		Mean	60.61	63.97	62.26
		SD, SE	22.117, 3.038	21.161, 2.963	21.614, 2.119
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.12
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Baseline			
		n	53	51	104
		Mean	60.61	63.97	62.26
		SD, SE	22.117, 3.038	21.161, 2.963	21.614, 2.119
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
		Observed			
		n	53	51	104
		Mean	58.96	52.45	55.77
		SD, SE	21.284, 2.924	24.497, 3.430	23.037, 2.259
		Median	62.50	50.00	56.25
		Q1, Q3	37.50, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.12
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Change from Baseline			
		n	53	51	104
		Mean	-1.65	-11.52	-6.49
		SD, SE	17.684, 2.429	22.478, 3.148	20.682, 2.028
		Median	0.00	-12.50	0.00
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-25.00, 6.25
		Min, Max	-37.5, 37.5	-62.5, 37.5	-62.5, 37.5
		GEE Estimates			
		LS Mean (SE)	-0.72 (3.042)	-8.95 (3.608)	
		95% CI	(-6.68, 5.24)	(-16.02, -1.88)	
		LS Mean Difference (SE)		-8.23 (3.519)	
		95% CI		(-15.12, -1.33)	
		p-value		0.0194	
		HedgesG (95% CI)		-0.481 (-0.871, -0.091)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.12
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Baseline			
		n	52	51	103
		Mean	60.34	63.97	62.14
		SD, SE	22.240, 3.084	21.161, 2.963	21.683, 2.136
		Median	62.50	62.50	62.50
		Q1, Q3	50.00, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	12.5, 100.0	0.0, 100.0
		Observed			
		n	52	51	103
		Mean	59.86	53.19	56.55
		SD, SE	22.733, 3.152	20.592, 2.883	21.851, 2.153
		Median	62.50	50.00	62.50
		Q1, Q3	43.75, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	12.5, 100.0	12.5, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.12
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Change from Baseline			
		n	52	51	103
		Mean	-0.48	-10.78	-5.58
		SD, SE	21.574, 2.992	25.127, 3.519	23.854, 2.350
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 12.50
		Min, Max	-50.0, 62.5	-75.0, 50.0	-75.0, 62.5
		GEE Estimates			
		LS Mean (SE)	0.42 (3.439)	-8.21 (3.176)	
		95% CI	(-6.32, 7.16)	(-14.44, -1.99)	
		LS Mean Difference (SE)		-8.63 (3.721)	
		95% CI		(-15.93, -1.34)	
		p-value		0.0203	
		HedgesG (95% CI)		-0.433 (-0.824, -0.042)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.14
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes		N_1	38	32	70
	Baseline	n	38	32	70
		Mean	66.45	66.02	66.25
		SD, SE	16.208, 2.629	22.947, 4.056	19.429, 2.322
		Median	62.50	68.75	62.50
		Q1, Q3	62.50, 75.00	50.00, 81.25	50.00, 75.00
		Min, Max	37.5, 100.0	12.5, 100.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.14
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Baseline			
		n	38	32	70
		Mean	66.45	66.02	66.25
		SD, SE	16.208, 2.629	22.947, 4.056	19.429, 2.322
		Median	62.50	68.75	62.50
		Q1, Q3	62.50, 75.00	50.00, 81.25	50.00, 75.00
		Min, Max	37.5, 100.0	12.5, 100.0	12.5, 100.0
		Observed			
		n	38	32	70
		Mean	61.84	50.00	56.43
		SD, SE	18.368, 2.980	24.180, 4.274	21.884, 2.616
		Median	62.50	50.00	62.50
		Q1, Q3	50.00, 75.00	31.25, 62.50	37.50, 75.00
		Min, Max	25.0, 100.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.14
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Change from Baseline			
		n	38	32	70
		Mean	-4.61	-16.02	-9.82
		SD, SE	17.296, 2.806	20.388, 3.604	19.492, 2.330
		Median	0.00	-12.50	-12.50
		Q1, Q3	-12.50, 0.00	-25.00, 0.00	-25.00, 0.00
		Min, Max	-37.5, 25.0	-62.5, 25.0	-62.5, 25.0
		GEE Estimates			
		LS Mean (SE)	1.98 (3.554)	-9.45 (3.783)	
		95% CI	(-4.99, 8.94)	(-16.86, -2.03)	
		LS Mean Difference (SE)		-11.42 (4.110)	
		95% CI		(-19.48, -3.37)	
		p-value		0.0054	
		HedgesG (95% CI)		-0.593 (-1.073, -0.112)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.14
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Baseline			
		n	37	31	68
		Mean	66.22	65.32	65.81
		SD, SE	16.368, 2.691	22.983, 4.128	19.511, 2.366
		Median	62.50	62.50	62.50
		Q1, Q3	62.50, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	37.5, 100.0	12.5, 100.0	12.5, 100.0
		Observed			
		n	37	31	68
		Mean	64.19	51.61	58.46
		SD, SE	20.233, 3.326	20.852, 3.745	21.319, 2.585
		Median	62.50	50.00	62.50
		Q1, Q3	50.00, 75.00	25.00, 62.50	50.00, 75.00
		Min, Max	25.0, 100.0	25.0, 87.5	25.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.14
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Change from Baseline			
		n	37	31	68
		Mean	-2.03	-13.71	-7.35
		SD, SE	20.940, 3.443	27.263, 4.897	24.552, 2.977
		Median	-12.50	-12.50	-12.50
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-25.00, 0.00
		Min, Max	-37.5, 50.0	-75.0, 50.0	-75.0, 50.0
		GEE Estimates			
		LS Mean (SE)	4.58 (3.821)	-7.10 (3.641)	
		95% CI	(-2.91, 12.07)	(-14.24, 0.03)	
		LS Mean Difference (SE)		-11.68 (4.754)	
		95% CI		(-21.00, -2.36)	
		p-value		0.0140	
		HedgesG (95% CI)		-0.474 (-0.957, 0.010)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.2.24.14
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No		N_1	28	36	64
	Baseline	n	28	36	64
		Mean	54.46	63.54	59.57
		SD, SE	24.347, 4.601	17.772, 2.962	21.216, 2.652
		Median	56.25	62.50	62.50
		Q1, Q3	43.75, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.2.24.14
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Baseline			
		n	28	36	64
		Mean	54.46	63.54	59.57
		SD, SE	24.347, 4.601	17.772, 2.962	21.216, 2.652
		Median	56.25	62.50	62.50
		Q1, Q3	43.75, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0
		Observed			
		n	28	36	64
		Mean	55.80	57.99	57.03
		SD, SE	21.377, 4.040	26.752, 4.459	24.385, 3.048
		Median	62.50	62.50	62.50
		Q1, Q3	37.50, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.2.24.14
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Change from Baseline			
		n	28	36	64
		Mean	1.34	-5.56	-2.54
		SD, SE	18.111, 3.423	24.357, 4.059	21.955, 2.744
		Median	0.00	-6.25	0.00
		Q1, Q3	-12.50, 12.50	-18.75, 12.50	-12.50, 12.50
		Min, Max	-37.5, 37.5	-75.0, 37.5	-75.0, 37.5
		GEE Estimates			
		LS Mean (SE)	-4.43 (5.130)	-8.24 (6.031)	
		95% CI	(-14.48, 5.63)	(-20.06, 3.58)	
		LS Mean Difference (SE)		-3.81 (4.620)	
		95% CI		(-12.87, 5.24)	
		p-value		0.4090	
		HedgesG (95% CI)		-0.307 (-0.803, 0.190)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.14
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Baseline			
		n	28	36	64
		Mean	54.46	63.54	59.57
		SD, SE	24.347, 4.601	17.772, 2.962	21.216, 2.652
		Median	56.25	62.50	62.50
		Q1, Q3	43.75, 75.00	50.00, 75.00	50.00, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0
		Observed			
		n	28	36	64
		Mean	55.36	55.56	55.47
		SD, SE	23.181, 4.381	20.798, 3.466	21.694, 2.712
		Median	62.50	50.00	56.25
		Q1, Q3	37.50, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	12.5, 100.0	12.5, 87.5	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.14
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Change from Baseline			
		n	28	36	64
		Mean	0.89	-7.99	-4.10
		SD, SE	23.056, 4.357	21.785, 3.631	22.609, 2.826
		Median	0.00	0.00	0.00
		Q1, Q3	-12.50, 12.50	-18.75, 12.50	-12.50, 12.50
		Min, Max	-50.0, 62.5	-50.0, 25.0	-50.0, 62.5
		GEE Estimates			
		LS Mean (SE)	-4.87 (5.429)	-10.67 (4.863)	
		95% CI	(-15.51, 5.77)	(-20.20, -1.14)	
		LS Mean Difference (SE)		-5.80 (4.481)	
		95% CI		(-14.58, 2.98)	
		p-value		0.1957	
		HedgesG (95% CI)		-0.386 (-0.885, 0.112)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.15
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High		N_1	29	37	66
	Baseline	n	29	37	66
		Mean	68.53	67.57	67.99
		SD, SE	16.577, 3.078	20.510, 3.372	18.750, 2.308
		Median	62.50	62.50	62.50
		Q1, Q3	62.50, 75.00	62.50, 75.00	62.50, 75.00
		Min, Max	37.5, 100.0	12.5, 100.0	12.5, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.15
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Baseline			
		n	29	37	66
		Mean	68.53	67.57	67.99
		SD, SE	16.577, 3.078	20.510, 3.372	18.750, 2.308
		Median	62.50	62.50	62.50
		Q1, Q3	62.50, 75.00	62.50, 75.00	62.50, 75.00
		Min, Max	37.5, 100.0	12.5, 100.0	12.5, 100.0
		Observed			
		n	29	37	66
		Mean	70.69	60.47	64.96
		SD, SE	17.448, 3.240	26.437, 4.346	23.331, 2.872
		Median	75.00	62.50	75.00
		Q1, Q3	62.50, 75.00	37.50, 75.00	50.00, 75.00
		Min, Max	25.0, 100.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.15
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Change from Baseline			
		n	29	37	66
		Mean	2.16	-7.09	-3.03
		SD, SE	14.966, 2.779	24.745, 4.068	21.378, 2.631
		Median	0.00	-12.50	0.00
		Q1, Q3	-12.50, 12.50	-25.00, 12.50	-12.50, 12.50
		Min, Max	-25.0, 25.0	-75.0, 37.5	-75.0, 37.5
		GEE Estimates			
		LS Mean (SE)	7.13 (3.165)	-3.04 (4.312)	
		95% CI	(0.93, 13.33)	(-11.49, 5.42)	
		LS Mean Difference (SE)		-10.17 (4.700)	
		95% CI		(-19.38, -0.95)	
		p-value		0.0305	
		HedgesG (95% CI)		-0.428 (-0.919, 0.064)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.15
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Baseline			
		n	28	36	64
		Mean	68.30	67.01	67.58
		SD, SE	16.833, 3.181	20.518, 3.420	18.861, 2.358
		Median	62.50	62.50	62.50
		Q1, Q3	62.50, 75.00	62.50, 75.00	62.50, 75.00
		Min, Max	37.5, 100.0	12.5, 100.0	12.5, 100.0
		Observed			
		n	28	36	64
		Mean	70.09	56.60	62.50
		SD, SE	20.508, 3.876	20.591, 3.432	21.478, 2.685
		Median	75.00	62.50	62.50
		Q1, Q3	56.25, 87.50	37.50, 75.00	50.00, 75.00
		Min, Max	25.0, 100.0	25.0, 87.5	25.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.15
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Change from Baseline			
		n	28	36	64
		Mean	1.79	-10.42	-5.08
		SD, SE	19.159, 3.621	24.731, 4.122	23.115, 2.889
		Median	0.00	-12.50	0.00
		Q1, Q3	-12.50, 12.50	-25.00, 0.00	-12.50, 12.50
		Min, Max	-37.5, 50.0	-75.0, 50.0	-75.0, 50.0
		GEE Estimates			
		LS Mean (SE)	6.67 (3.442)	-6.31 (3.590)	
		95% CI	(-0.08, 13.42)	(-13.35, 0.72)	
		LS Mean Difference (SE)		-12.98 (4.662)	
		95% CI		(-22.12, -3.84)	
		p-value		0.0054	
		HedgesG (95% CI)		-0.528 (-1.030, -0.026)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.15
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low		N_1	36	30	66
	Baseline	n	36	30	66
		Mean	55.56	61.25	58.14
		SD, SE	22.449, 3.742	20.062, 3.663	21.427, 2.637
		Median	62.50	62.50	62.50
		Q1, Q3	43.75, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.15
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Baseline			
		n	36	30	66
		Mean	55.56	61.25	58.14
		SD, SE	22.449, 3.742	20.062, 3.663	21.427, 2.637
		Median	62.50	62.50	62.50
		Q1, Q3	43.75, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0
		Observed			
		n	36	30	66
		Mean	49.65	46.67	48.30
		SD, SE	16.498, 2.750	23.428, 4.277	19.841, 2.442
		Median	50.00	50.00	50.00
		Q1, Q3	37.50, 62.50	25.00, 62.50	37.50, 62.50
		Min, Max	0.0, 75.0	0.0, 100.0	0.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.15
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Change from Baseline			
		n	36	30	66
		Mean	-5.90	-14.58	-9.85
		SD, SE	19.246, 3.208	20.783, 3.794	20.276, 2.496
		Median	0.00	-12.50	-12.50
		Q1, Q3	-25.00, 0.00	-25.00, 0.00	-25.00, 0.00
		Min, Max	-37.5, 37.5	-62.5, 25.0	-62.5, 37.5
		GEE Estimates			
		LS Mean (SE)	-7.88 (3.248)	-13.50 (3.559)	
		95% CI	(-14.24, -1.51)	(-20.47, -6.52)	
		LS Mean Difference (SE)		-5.62 (4.100)	
		95% CI		(-13.66, 2.42)	
		p-value		0.1704	
		HedgesG (95% CI)		-0.423 (-0.913, 0.067)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.15
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Baseline			
		n	36	30	66
		Mean	55.56	61.25	58.14
		SD, SE	22.449, 3.742	20.062, 3.663	21.427, 2.637
		Median	62.50	62.50	62.50
		Q1, Q3	43.75, 75.00	37.50, 75.00	37.50, 75.00
		Min, Max	0.0, 100.0	25.0, 100.0	0.0, 100.0
		Observed			
		n	36	30	66
		Mean	51.74	50.83	51.33
		SD, SE	18.697, 3.116	21.002, 3.834	19.627, 2.416
		Median	50.00	50.00	50.00
		Q1, Q3	37.50, 62.50	37.50, 62.50	37.50, 62.50
		Min, Max	12.5, 87.5	12.5, 87.5	12.5, 87.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.2.2.2.24.15
Subgroup Analysis: Change from baseline to week 24 in the Stiffness score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Change from Baseline			
		n	36	30	66
		Mean	-3.82	-10.42	-6.82
		SD, SE	22.917, 3.819	24.802, 4.528	23.837, 2.934
		Median	0.00	-12.50	-12.50
		Q1, Q3	-18.75, 12.50	-25.00, 0.00	-25.00, 0.00
		Min, Max	-50.0, 62.5	-50.0, 50.0	-50.0, 62.5
		GEE Estimates			
		LS Mean (SE)	-5.79 (3.500)	-9.33 (3.920)	
		95% CI	(-12.65, 1.07)	(-17.01, -1.65)	
		LS Mean Difference (SE)		-3.54 (4.534)	
		95% CI		(-12.42, 5.35)	
		p-value		0.4352	
		HedgesG (95% CI)		-0.270 (-0.757, 0.217)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Stiffness as the dependent variable, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Stiffness as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_stiff_SUB.sas

Table 2.10.999.1.24.1
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
BPI Worst Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<= 6.0	N	17	27
	Responder - n(%)	4 (23.53%)	2 (7.41%)
	Difference in responder (KRN23 vs Placebo) - %	16.1%	
	Logistic Regression[1]		
	Responder - %	23.5%	7.4%
	95% C.I.	8.8%, 49.4%	1.8%, 26.1%
	Odds ratio (KRN23 vs Placebo)	3.846	
	95% C.I. of odds ratio	0.587, 25.181	
	P-value	0.1554	
	RR[3] (95% CI), P-value	3.176 (0.651, 15.502), 0.1857	
	ARR[3] (95% CI), P-value	3.846 (0.620, 23.853), 0.1480	
	ARD[4]		
	Difference (95% C.I.)	0.161 (-0.063, 0.386)	
	P-value	0.1857	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.1
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
BPI Worst Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
> 6.0	N	51	39
	Responder - n(%)	17 (33.33%)	8 (20.51%)
	Difference in responder (KRN23 vs Placebo) - %	12.8%	
	Logistic Regression[1]		
	Responder - %	33.3%	20.5%
	95% C.I.	21.7%, 47.4%	10.5%, 36.2%
	Odds ratio (KRN23 vs Placebo)	1.937	
	95% C.I. of odds ratio	0.724, 5.186	
	P-value	0.1854	
	RR[3] (95% CI), P-value	1.625 (0.783, 3.371), 0.2366	
	ARR[3] (95% CI), P-value	1.937 (0.734, 5.117), 0.1819	
	ARD[4]		
	Difference (95% C.I.)	0.128 (-0.053, 0.309)	
	P-value	0.2366	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.2
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
BPI Average Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<= 6.0	N	48	49
	Responder - n(%)	14 (29.17%)	9 (18.37%)
	Difference in responder (KRN23 vs Placebo) - %	10.8%	
	Logistic Regression[1]		
	Responder - %	29.2%	18.4%
	95% C.I.	18.0%, 43.6%	9.8%, 31.9%
	Odds ratio (KRN23 vs Placebo)	1.830	
	95% C.I. of odds ratio	0.696, 4.810	
	P-value	0.2175	
	RR[3] (95% CI), P-value	1.588 (0.760, 3.317), 0.2399	
	ARR[3] (95% CI), P-value	1.830 (0.705, 4.750), 0.2145	
	ARD[4]		
	Difference (95% C.I.)	0.108 (-0.060, 0.276)	
	P-value	0.2399	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.2
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
BPI Average Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
> 6.0	N	20	17
	Responder - n(%)	7 (35.00%)	1 (5.88%)
	Difference in responder (KRN23 vs Placebo) - %	29.1%	
	Logistic Regression[1]		
	Responder - %	35.0%	5.9%
	95% C.I.	17.2%, 58.2%	0.8%, 33.6%
	Odds ratio (KRN23 vs Placebo)	8.615	
	95% C.I. of odds ratio	0.865, 85.833	
	P-value	0.0655	
	RR[3] (95% CI), P-value	5.950 (0.811, 43.660), 0.0481	
	ARR[3] (95% CI), P-value	8.615 (0.936, 79.277), 0.0572	
	ARD[4]		
	Difference (95% C.I.)	0.291 (0.054, 0.528)	
	P-value	0.0481	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.3
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Region

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
North America/EU	N	58	58
	Responder - n(%)	19 (32.76%)	9 (15.52%)
	Difference in responder (KRN23 vs Placebo) - %	17.2%	
	Logistic Regression[1]		
	Responder - %	32.8%	15.5%
	95% C.I.	21.9%, 45.9%	8.2%, 27.4%
	Odds ratio (KRN23 vs Placebo)	2.652	
	95% C.I. of odds ratio	1.070, 6.572	
	P-value	0.0353	
	RR[3] (95% CI), P-value	2.111 (1.043, 4.271), 0.0497	
	ARR[3] (95% CI), P-value	2.652 (1.081, 6.509), 0.0332	
	ARD[4]		
	Difference (95% C.I.)	0.172 (0.020, 0.325)	
	P-value	0.0497	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.3
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Region

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Asia	N	10	8
	Responder - n(%)	2 (20.00%)	1 (12.50%)
	Difference in responder (KRN23 vs Placebo) - %	7.5%	
	Logistic Regression[1]		
	Responder - %	20.0%	12.5%
	95% C.I.	4.5%, 57.2%	1.5%, 57.9%
	Odds ratio (KRN23 vs Placebo)	1.750	
	95% C.I. of odds ratio	0.104, 29.320	
	P-value	0.6794	
	RR[3] (95% CI), P-value	1.600 (0.175, 14.631), 1.0000	
	ARR[3] (95% CI), P-value	1.750 (0.129, 23.703), 0.6738	
	ARD[4]		
	Difference (95% C.I.)	0.075 (-0.263, 0.413)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.4
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Gender

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Male	N	24	23
	Responder - n(%)	5 (20.83%)	3 (13.04%)
	Difference in responder (KRN23 vs Placebo) - %	7.8%	
	Logistic Regression[1]		
	Responder - %	20.8%	13.0%
	95% C.I.	8.7%, 42.0%	4.1%, 34.3%
	Odds ratio (KRN23 vs Placebo)	1.754	
	95% C.I. of odds ratio	0.352, 8.744	
	P-value	0.4845	
	RR[3] (95% CI), P-value	1.597 (0.430, 5.932), 0.7008	
	ARR[3] (95% CI), P-value	1.754 (0.368, 8.374), 0.4809	
	ARD[4]		
	Difference (95% C.I.)	0.078 (-0.135, 0.291)	
	P-value	0.7008	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.4
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Gender

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Female	N	44	43
	Responder - n(%)	16 (36.36%)	7 (16.28%)
	Difference in responder (KRN23 vs Placebo) - %	20.1%	
	Logistic Regression[1]		
	Responder - %	36.4%	16.3%
	95% C.I.	23.5%, 51.6%	7.9%, 30.7%
	Odds ratio (KRN23 vs Placebo)	2.939	
	95% C.I. of odds ratio	1.048, 8.239	
	P-value	0.0406	
	RR[3] (95% CI), P-value	2.234 (1.021, 4.885), 0.0509	
	ARR[3] (95% CI), P-value	2.939 (1.064, 8.119), 0.0376	
	ARD[4]		
	Difference (95% C.I.)	0.201 (0.021, 0.381)	
	P-value	0.0509	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.5
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Age

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<=41	N	31	36
	Responder - n(%)	10 (32.26%)	6 (16.67%)
	Difference in responder (KRN23 vs Placebo) - %	15.6%	
	Logistic Regression[1]		
	Responder - %	32.3%	16.7%
	95% C.I.	18.1%, 50.6%	7.6%, 32.8%
	Odds ratio (KRN23 vs Placebo)	2.381	
	95% C.I. of odds ratio	0.733, 7.729	
	P-value	0.1460	
	RR[3] (95% CI), P-value	1.935 (0.794, 4.718), 0.1602	
	ARR[3] (95% CI), P-value	2.381 (0.750, 7.562), 0.1412	
	ARD[4]		
	Difference (95% C.I.)	0.156 (-0.049, 0.361)	
	P-value	0.1602	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.5
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Age

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
>41	N	37	30
	Responder - n(%)	11 (29.73%)	4 (13.33%)
	Difference in responder (KRN23 vs Placebo) - %	16.4%	
	Logistic Regression[1]		
	Responder - %	29.7%	13.3%
	95% C.I.	17.1%, 46.5%	5.0%, 31.0%
	Odds ratio (KRN23 vs Placebo)	2.750	
	95% C.I. of odds ratio	0.756, 10.000	
	P-value	0.1224	
	RR[3] (95% CI), P-value	2.230 (0.790, 6.297), 0.1451	
	ARR[3] (95% CI), P-value	2.750 (0.775, 9.762), 0.1176	
	ARD[4]		
	Difference (95% C.I.)	0.164 (-0.027, 0.355)	
	P-value	0.1451	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.6
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Race

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
White	N	55	53
	Responder - n(%)	18 (32.73%)	8 (15.09%)
	Difference in responder (KRN23 vs Placebo) - %	17.6%	
	Logistic Regression[1]		
	Responder - %	32.7%	15.1%
	95% C.I.	21.6%, 46.2%	7.7%, 27.6%
	Odds ratio (KRN23 vs Placebo)	2.736	
	95% C.I. of odds ratio	1.058, 7.079	
	P-value	0.0381	
	RR[3] (95% CI), P-value	2.168 (1.032, 4.556), 0.0427	
	ARR[3] (95% CI), P-value	2.736 (1.069, 7.002), 0.0357	
	ARD[4]		
	Difference (95% C.I.)	0.176 (0.019, 0.333)	
	P-value	0.0427	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.6
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Race

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Non-White	N	13	13
	Responder - n(%)	3 (23.08%)	2 (15.38%)
	Difference in responder (KRN23 vs Placebo) - %	7.7%	
	Logistic Regression[1]		
	Responder - %	23.1%	15.4%
	95% C.I.	7.2%, 53.9%	3.6%, 47.0%
	Odds ratio (KRN23 vs Placebo)	1.650	
	95% C.I. of odds ratio	0.204, 13.324	
	P-value	0.6252	
	RR[3] (95% CI), P-value	1.500 (0.298, 7.546), 1.0000	
	ARR[3] (95% CI), P-value	1.650 (0.227, 11.991), 0.6208	
	ARD[4]		
	Difference (95% C.I.)	0.077 (-0.225, 0.378)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.7
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Stiffness

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<=62.5	N	39	41
	Responder - n(%)	6 (15.38%)	4 (9.76%)
	Difference in responder (KRN23 vs Placebo) - %	5.6%	
	Logistic Regression[1]		
	Responder - %	15.4%	9.8%
	95% C.I.	7.0%, 30.6%	3.7%, 23.6%
	Odds ratio (KRN23 vs Placebo)	1.682	
	95% C.I. of odds ratio	0.427, 6.623	
	P-value	0.4525	
	RR[3] (95% CI), P-value	1.577 (0.481, 5.167), 0.5133	
	ARR[3] (95% CI), P-value	1.682 (0.436, 6.483), 0.4502	
	ARD[4]		
	Difference (95% C.I.)	0.056 (-0.089, 0.201)	
	P-value	0.5133	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.7
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Stiffness

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
>62.5	N	29	25
	Responder - n(%)	15 (51.72%)	6 (24.00%)
	Difference in responder (KRN23 vs Placebo) - %	27.7%	
	Logistic Regression[1]		
	Responder - %	51.7%	24.0%
	95% C.I.	33.7%, 69.3%	11.0%, 44.7%
	Odds ratio (KRN23 vs Placebo)	3.393	
	95% C.I. of odds ratio	1.022, 11.260	
	P-value	0.0461	
	RR[3] (95% CI), P-value	2.155 (0.987, 4.707), 0.0516	
	ARR[3] (95% CI), P-value	3.393 (1.051, 10.951), 0.0410	
	ARD[4]		
	Difference (95% C.I.)	0.277 (0.030, 0.524)	
	P-value	0.0516	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.8
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Physical Function

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<=47.8	N	30	37
	Responder - n(%)	7 (23.33%)	8 (21.62%)
	Difference in responder (KRN23 vs Placebo) - %	1.7%	
	Logistic Regression[1]		
	Responder - %	23.3%	21.6%
	95% C.I.	11.4%, 41.9%	11.1%, 38.0%
	Odds ratio (KRN23 vs Placebo)	1.103	
	95% C.I. of odds ratio	0.341, 3.571	
	P-value	0.8678	
	RR[3] (95% CI), P-value	1.079 (0.442, 2.635), 1.0000	
	ARR[3] (95% CI), P-value	1.103 (0.348, 3.493), 0.8673	
	ARD[4]		
	Difference (95% C.I.)	0.017 (-0.184, 0.218)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.8
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Physical Function

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
>47.8	N	38	29
	Responder - n(%)	14 (36.84%)	2 (6.90%)
	Difference in responder (KRN23 vs Placebo) - %	29.9%	
	Logistic Regression[1]		
	Responder - %	36.8%	6.9%
	95% C.I.	23.0%, 53.3%	1.7%, 24.2%
	Odds ratio (KRN23 vs Placebo)	7.875	
	95% C.I. of odds ratio	1.574, 39.409	
	P-value	0.0128	
	RR[3] (95% CI), P-value	5.342 (1.317, 21.675), 0.0079	
	ARR[3] (95% CI), P-value	7.875 (1.622, 38.245), 0.0105	
	ARD[4]		
	Difference (95% C.I.)	0.299 (0.120, 0.478)	
	P-value	0.0079	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.9
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<=50.0	N	32	42
	Responder - n(%)	6 (18.75%)	7 (16.67%)
	Difference in responder (KRN23 vs Placebo) - %	2.1%	
	Logistic Regression[1]		
	Responder - %	18.8%	16.7%
	95% C.I.	8.6%, 36.3%	8.1%, 31.3%
	Odds ratio (KRN23 vs Placebo)	1.154	
	95% C.I. of odds ratio	0.340, 3.921	
	P-value	0.8163	
	RR[3] (95% CI), P-value	1.125 (0.419, 3.024), 1.0000	
	ARR[3] (95% CI), P-value	1.154 (0.347, 3.841), 0.8156	
	ARD[4]		
	Difference (95% C.I.)	0.021 (-0.155, 0.197)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.9
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
>50.0	N	35	24
	Responder - n(%)	14 (40.00%)	3 (12.50%)
	Difference in responder (KRN23 vs Placebo) - %	27.5%	
	Logistic Regression[1]		
	Responder - %	40.0%	12.5%
	95% C.I.	25.0%, 57.1%	4.0%, 33.0%
	Odds ratio (KRN23 vs Placebo)	4.667	
	95% C.I. of odds ratio	1.133, 19.229	
	P-value	0.0335	
	RR[3] (95% CI), P-value	3.200 (1.030, 9.942), 0.0388	
	ARR[3] (95% CI), P-value	4.666 (1.167, 18.655), 0.0294	
	ARD[4]		
	Difference (95% C.I.)	0.275 (0.066, 0.484)	
	P-value	0.0388	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.10
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Total Score

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<=49.5	N	30	37
	Responder - n(%)	6 (20.00%)	8 (21.62%)
	Difference in responder (KRN23 vs Placebo) - %	-1.6%	
	Logistic Regression[1]		
	Responder - %	20.0%	21.6%
	95% C.I.	9.1%, 38.3%	11.1%, 38.0%
	Odds ratio (KRN23 vs Placebo)	0.906	
	95% C.I. of odds ratio	0.270, 3.043	
	P-value	0.8716	
	RR[3] (95% CI), P-value	0.925 (0.360, 2.374), 1.0000	
	ARR[3] (95% CI), P-value	0.906 (0.276, 2.975), 0.8711	
	ARD[4]		
	Difference (95% C.I.)	-0.016 (-0.211, 0.179)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.10
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Total Score

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
>49.5	N	38	29
	Responder - n(%)	15 (39.47%)	2 (6.90%)
	Difference in responder (KRN23 vs Placebo) - %	32.6%	
	Logistic Regression[1]		
	Responder - %	39.5%	6.9%
	95% C.I.	25.2%, 55.9%	1.7%, 24.2%
	Odds ratio (KRN23 vs Placebo)	8.804	
	95% C.I. of odds ratio	1.766, 43.899	
	P-value	0.0087	
	RR[3] (95% CI), P-value	5.724 (1.420, 23.072), 0.0038	
	ARR[3] (95% CI), P-value	8.804 (1.819, 42.605), 0.0069	
	ARD[4]		
	Difference (95% C.I.)	0.326 (0.145, 0.506)	
	P-value	0.0038	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.11
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
6MWT

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Low	N	37	29
	Responder - n(%)	12 (32.43%)	1 (3.45%)
	Difference in responder (KRN23 vs Placebo) - %	29.0%	
	Logistic Regression[1]		
	Responder - %	32.4%	3.4%
	95% C.I.	19.2%, 49.2%	0.5%, 21.4%
	Odds ratio (KRN23 vs Placebo)	13.440	
	95% C.I. of odds ratio	1.564, 115.465	
	P-value	0.0187	
	RR[3] (95% CI), P-value	9.405 (1.297, 68.205), 0.0040	
	ARR[3] (95% CI), P-value	13.434 (1.629, 110.765), 0.0158	
	ARD[4]		
	Difference (95% C.I.)	0.290 (0.125, 0.455)	
	P-value	0.0040	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.11
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
6MWT

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
High	N	30	36
	Responder - n(%)	8 (26.67%)	9 (25.00%)
	Difference in responder (KRN23 vs Placebo) - %	1.7%	
	Logistic Regression[1]		
	Responder - %	26.7%	25.0%
	95% C.I.	13.7%, 45.3%	13.4%, 41.8%
	Odds ratio (KRN23 vs Placebo)	1.091	
	95% C.I. of odds ratio	0.353, 3.369	
	P-value	0.8780	
	RR[3] (95% CI), P-value	1.067 (0.470, 2.422), 1.0000	
	ARR[3] (95% CI), P-value	1.091 (0.361, 3.298), 0.8775	
	ARD[4]		
	Difference (95% C.I.)	0.017 (-0.196, 0.229)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.12
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Pain Medication use at BL

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Yes	N	47	44
	Responder - n(%)	16 (34.04%)	6 (13.64%)
	Difference in responder (KRN23 vs Placebo) - %	20.4%	
	Logistic Regression[1]		
	Responder - %	34.0%	13.6%
	95% C.I.	21.9%, 48.8%	6.2%, 27.4%
	Odds ratio (KRN23 vs Placebo)	3.269	
	95% C.I. of odds ratio	1.126, 9.490	
	P-value	0.0298	
	RR[3] (95% CI), P-value	2.496 (1.074, 5.802), 0.0285	
	ARR[3] (95% CI), P-value	3.269 (1.142, 9.354), 0.0272	
	ARD[4]		
	Difference (95% C.I.)	0.204 (0.035, 0.373)	
	P-value	0.0285	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.12
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Pain Medication use at BL

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
No	N	21	22
	Responder - n(%)	5 (23.81%)	4 (18.18%)
	Difference in responder (KRN23 vs Placebo) - %	5.6%	
	Logistic Regression[1]		
	Responder - %	23.8%	18.2%
	95% C.I.	10.0%, 46.8%	6.8%, 40.4%
	Odds ratio (KRN23 vs Placebo)	1.406	
	95% C.I. of odds ratio	0.307, 6.443	
	P-value	0.6534	
	RR[3] (95% CI), P-value	1.310 (0.406, 4.223), 0.7205	
	ARR[3] (95% CI), P-value	1.406 (0.321, 6.160), 0.6510	
	ARD[4]		
	Difference (95% C.I.)	0.056 (-0.187, 0.300)	
	P-value	0.7205	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.13
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Opioid Pain Medication use at BL

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Yes	N	17	13
	Responder - n(%)	5 (29.41%)	2 (15.38%)
	Difference in responder (KRN23 vs Placebo) - %	14.0%	
	Logistic Regression[1]		
	Responder - %	29.4%	15.4%
	95% C.I.	12.3%, 55.4%	3.6%, 46.8%
	Odds ratio (KRN23 vs Placebo)	2.292	
	95% C.I. of odds ratio	0.338, 15.558	
	P-value	0.3827	
	RR[3] (95% CI), P-value	1.912 (0.439, 8.334), 0.4268	
	ARR[3] (95% CI), P-value	2.292 (0.367, 14.323), 0.3751	
	ARD[4]		
	Difference (95% C.I.)	0.140 (-0.152, 0.432)	
	P-value	0.4268	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.13
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Opioid Pain Medication use at BL

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
No	N	51	53
	Responder - n(%)	16 (31.37%)	8 (15.09%)
	Difference in responder (KRN23 vs Placebo) - %	16.3%	
	Logistic Regression[1]		
	Responder - %	31.4%	15.1%
	95% C.I.	20.1%, 45.4%	7.7%, 27.6%
	Odds ratio (KRN23 vs Placebo)	2.571	
	95% C.I. of odds ratio	0.976, 6.771	
	P-value	0.0558	
	RR[3] (95% CI), P-value	2.078 (0.975, 4.429), 0.0633	
	ARR[3] (95% CI), P-value	2.571 (0.988, 6.694), 0.0530	
	ARD[4]		
	Difference (95% C.I.)	0.163 (0.003, 0.322)	
	P-value	0.0633	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.14
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Active fractures and pseudofractures at BL

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Yes	N	32	38
	Responder - n(%)	12 (37.50%)	6 (15.79%)
	Difference in responder (KRN23 vs Placebo) - %	21.7%	
	Logistic Regression[1]		
	Responder - %	37.5%	15.8%
	95% C.I.	22.5%, 55.4%	7.2%, 31.3%
	Odds ratio (KRN23 vs Placebo)	3.200	
	95% C.I. of odds ratio	1.015, 10.091	
	P-value	0.0472	
	RR[3] (95% CI), P-value	2.375 (1.005, 5.611), 0.0549	
	ARR[3] (95% CI), P-value	3.200 (1.036, 9.887), 0.0433	
	ARD[4]		
	Difference (95% C.I.)	0.217 (0.013, 0.421)	
	P-value	0.0549	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.10.999.1.24.14
Subgroup Analysis: WOMAC Stiffness responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Active fractures and pseudofractures at BL

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
No	N	36	28
	Responder - n(%)	9 (25.00%)	4 (14.29%)
	Difference in responder (KRN23 vs Placebo) - %	10.7%	
	Logistic Regression[1]		
	Responder - %	25.0%	14.3%
	95% C.I.	13.4%, 41.8%	5.4%, 32.9%
	Odds ratio (KRN23 vs Placebo)	2.000	
	95% C.I. of odds ratio	0.531, 7.530	
	P-value	0.3000	
	RR[3] (95% CI), P-value	1.750 (0.601, 5.098), 0.3587	
	ARR[3] (95% CI), P-value	2.000 (0.545, 7.337), 0.2959	
	ARD[4]		
	Difference (95% C.I.)	0.107 (-0.085, 0.299)	
	P-value	0.3587	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent_SUB.sas

Table 2.2.2.3.24.1
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6		N_1	27	17	44
	Baseline	n	27	17	44
		Mean	37.04	34.83	36.18
		SD, SE	19.484, 3.750	16.918, 4.103	18.364, 2.768
		Median	41.18	36.76	37.50
		Q1, Q3	17.65, 54.41	25.00, 47.06	21.32, 50.74
		Min, Max	5.9, 66.2	7.4, 61.8	5.9, 66.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.1
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Baseline			
		n	27	17	44
		Mean	37.04	34.83	36.18
		SD, SE	19.484, 3.750	16.918, 4.103	18.364, 2.768
		Median	41.18	36.76	37.50
		Q1, Q3	17.65, 54.41	25.00, 47.06	21.32, 50.74
		Min, Max	5.9, 66.2	7.4, 61.8	5.9, 66.2
		Observed			
		n	27	17	44
		Mean	32.19	30.28	31.45
		SD, SE	17.616, 3.390	14.029, 3.403	16.179, 2.439
		Median	32.35	29.41	31.62
		Q1, Q3	14.71, 47.06	22.06, 36.76	15.44, 44.85
		Min, Max	2.9, 64.7	7.4, 58.8	2.9, 64.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.1
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Change from Baseline			
		n	27	17	44
		Mean	-4.85	-4.55	-4.73
		SD, SE	11.161, 2.148	9.446, 2.291	10.418, 1.571
		Median	-1.47	-1.47	-1.47
		Q1, Q3	-10.29, 2.94	-11.76, 1.47	-10.29, 2.94
		Min, Max	-41.2, 11.8	-23.5, 10.3	-41.2, 11.8
		GEE Estimates			
		LS Mean (SE)	-6.83 (3.158)	-7.34 (2.745)	
		95% CI	(-13.02, -0.64)	(-12.72, -1.96)	
		LS Mean Difference (SE)		-0.51 (2.593)	
		95% CI		(-5.59, 4.58)	
		p-value		0.8455	
		HedgesG (95% CI)		0.027 (-0.580, 0.634)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.1
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Baseline			
		n	27	17	44
		Mean	37.04	34.83	36.18
		SD, SE	19.484, 3.750	16.918, 4.103	18.364, 2.768
		Median	41.18	36.76	37.50
		Q1, Q3	17.65, 54.41	25.00, 47.06	21.32, 50.74
		Min, Max	5.9, 66.2	7.4, 61.8	5.9, 66.2
		Observed			
		n	27	17	44
		Mean	35.02	32.18	33.92
		SD, SE	18.318, 3.525	17.173, 4.165	17.736, 2.674
		Median	36.76	29.41	31.62
		Q1, Q3	22.06, 48.53	22.06, 41.18	22.06, 46.32
		Min, Max	1.5, 72.1	5.9, 64.7	1.5, 72.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.1
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Change from Baseline			
		n	27	17	44
		Mean	-2.02	-2.65	-2.26
		SD, SE	12.605, 2.426	11.177, 2.711	11.944, 1.801
		Median	-2.94	-4.41	-2.94
		Q1, Q3	-10.29, 5.88	-11.76, 4.41	-10.29, 4.41
		Min, Max	-26.5, 30.9	-20.6, 19.1	-26.5, 30.9
		GEE Estimates			
		LS Mean (SE)	-4.00 (3.275)	-5.43 (4.035)	
		95% CI	(-10.42, 2.42)	(-13.34, 2.47)	
		LS Mean Difference (SE)		-1.43 (3.295)	
		95% CI		(-7.89, 5.02)	
		p-value		0.6633	
		HedgesG (95% CI)		-0.050 (-0.657, 0.556)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.1
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6		N_1	39	51	90
	Baseline	n	39	51	90
		Mean	48.64	56.11	52.88
		SD, SE	19.071, 3.054	17.631, 2.469	18.541, 1.954
		Median	50.00	57.35	54.41
		Q1, Q3	35.29, 61.76	42.65, 67.65	39.71, 66.18
		Min, Max	0.0, 97.1	11.8, 91.2	0.0, 97.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.1
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Baseline			
		n	39	51	90
		Mean	48.64	56.11	52.88
		SD, SE	19.071, 3.054	17.631, 2.469	18.541, 1.954
		Median	50.00	57.35	54.41
		Q1, Q3	35.29, 61.76	42.65, 67.65	39.71, 66.18
		Min, Max	0.0, 97.1	11.8, 91.2	0.0, 97.1
		Observed			
		n	39	51	90
		Mean	46.23	47.55	46.98
		SD, SE	22.074, 3.535	20.340, 2.848	20.998, 2.213
		Median	39.71	50.00	44.85
		Q1, Q3	32.35, 58.82	35.29, 63.24	32.35, 58.82
		Min, Max	8.8, 100.0	4.4, 82.4	4.4, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.1
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Change from Baseline			
		n	39	51	90
		Mean	-2.41	-8.56	-5.90
		SD, SE	15.805, 2.531	11.841, 1.658	13.957, 1.471
		Median	-2.94	-7.35	-5.88
		Q1, Q3	-11.76, 10.29	-13.24, 1.47	-11.76, 2.94
		Min, Max	-36.8, 26.5	-42.6, 10.3	-42.6, 26.5
		GEE Estimates			
		LS Mean (SE)	3.20 (3.174)	-2.19 (2.282)	
		95% CI	(-3.02, 9.42)	(-6.66, 2.28)	
		LS Mean Difference (SE)		-5.38 (3.024)	
		95% CI		(-11.31, 0.54)	
		p-value		0.0750	
		HedgesG (95% CI)		-0.440 (-0.862, -0.018)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.1
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Baseline			
		n	38	49	87
		Mean	48.30	55.70	52.47
		SD, SE	19.203, 3.115	17.214, 2.459	18.377, 1.970
		Median	47.79	57.35	54.41
		Q1, Q3	35.29, 61.76	44.12, 67.65	39.71, 66.18
		Min, Max	0.0, 97.1	11.8, 91.2	0.0, 97.1
		Observed			
		n	38	49	87
		Mean	48.07	47.33	47.65
		SD, SE	24.242, 3.933	18.885, 2.698	21.261, 2.279
		Median	41.91	48.53	45.59
		Q1, Q3	32.35, 63.24	33.82, 61.76	32.35, 63.24
		Min, Max	5.9, 98.5	7.4, 83.8	5.9, 98.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.1
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Change from Baseline			
		n	38	49	87
		Mean	-0.23	-8.37	-4.82
		SD, SE	16.177, 2.624	16.361, 2.337	16.687, 1.789
		Median	0.74	-7.35	-4.41
		Q1, Q3	-10.29, 10.29	-16.18, 0.00	-14.71, 2.94
		Min, Max	-29.4, 41.2	-47.1, 55.9	-47.1, 55.9
		GEE Estimates			
		LS Mean (SE)	5.41 (3.165)	-1.99 (2.924)	
		95% CI	(-0.80, 11.61)	(-7.72, 3.74)	
		LS Mean Difference (SE)		-7.40 (3.296)	
		95% CI		(-13.86, -0.94)	
		p-value		0.0247	
		HedgesG (95% CI)		-0.490 (-0.920, -0.060)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.2
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6		N_1	49	48	97
	Baseline	n	49	48	97
		Mean	39.29	44.69	41.96
		SD, SE	18.319, 2.617	16.994, 2.453	17.792, 1.806
		Median	42.65	45.59	44.12
		Q1, Q3	25.00, 54.41	36.03, 57.35	29.41, 55.88
		Min, Max	0.0, 69.1	7.4, 76.5	0.0, 76.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.2
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Baseline			
		n	49	48	97
		Mean	39.29	44.69	41.96
		SD, SE	18.319, 2.617	16.994, 2.453	17.792, 1.806
		Median	42.65	45.59	44.12
		Q1, Q3	25.00, 54.41	36.03, 57.35	29.41, 55.88
		Min, Max	0.0, 69.1	7.4, 76.5	0.0, 76.5
		Observed			
		n	49	48	97
		Mean	36.22	38.94	37.57
		SD, SE	19.532, 2.790	18.495, 2.670	18.976, 1.927
		Median	35.29	37.50	36.76
		Q1, Q3	23.53, 45.59	26.47, 54.41	26.47, 48.53
		Min, Max	2.9, 91.2	5.9, 77.9	2.9, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.2
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Change from Baseline			
		n	49	48	97
		Mean	-3.06	-5.75	-4.39
		SD, SE	12.625, 1.804	11.110, 1.604	11.914, 1.210
		Median	-1.47	-2.94	-2.94
		Q1, Q3	-10.29, 4.41	-11.76, 1.47	-10.29, 2.94
		Min, Max	-41.2, 23.5	-42.6, 10.3	-42.6, 23.5
		GEE Estimates			
		LS Mean (SE)	-0.06 (2.759)	-1.79 (2.233)	
		95% CI	(-5.47, 5.35)	(-6.17, 2.58)	
		LS Mean Difference (SE)		-1.74 (2.419)	
		95% CI		(-6.48, 3.01)	
		p-value		0.4730	
		HedgesG (95% CI)		-0.222 (-0.621, 0.178)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.2
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Baseline			
		n	49	48	97
		Mean	39.29	44.69	41.96
		SD, SE	18.319, 2.617	16.994, 2.453	17.792, 1.806
		Median	42.65	45.59	44.12
		Q1, Q3	25.00, 54.41	36.03, 57.35	29.41, 55.88
		Min, Max	0.0, 69.1	7.4, 76.5	0.0, 76.5
		Observed			
		n	49	48	97
		Mean	38.36	39.92	39.13
		SD, SE	20.199, 2.886	17.892, 2.582	19.009, 1.930
		Median	36.76	38.24	36.76
		Q1, Q3	25.00, 48.53	28.68, 54.41	27.94, 51.47
		Min, Max	1.5, 95.6	5.9, 76.6	1.5, 95.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.2
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Change from Baseline			
		n	49	48	97
		Mean	-0.93	-4.77	-2.83
		SD, SE	13.187, 1.884	14.948, 2.158	14.144, 1.436
		Median	-1.47	-5.15	-2.94
		Q1, Q3	-7.35, 5.88	-13.24, 0.78	-10.29, 4.41
		Min, Max	-29.4, 30.9	-33.8, 55.9	-33.8, 55.9
		GEE Estimates			
		LS Mean (SE)	2.07 (2.794)	-0.81 (2.723)	
		95% CI	(-3.40, 7.55)	(-6.15, 4.52)	
		LS Mean Difference (SE)		-2.88 (2.654)	
		95% CI		(-8.09, 2.32)	
		p-value		0.2772	
		HedgesG (95% CI)		-0.267 (-0.667, 0.132)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.2
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6		N_1	17	20	37
	Baseline	n	17	20	37
		Mean	57.18	65.44	61.65
		SD, SE	18.861, 4.574	18.127, 4.053	18.680, 3.071
		Median	60.29	67.65	61.76
		Q1, Q3	50.00, 67.65	59.56, 76.47	54.41, 70.59
		Min, Max	8.8, 97.1	26.5, 91.2	8.8, 97.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.2
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Baseline			
		n	17	20	37
		Mean	57.18	65.44	61.65
		SD, SE	18.861, 4.574	18.127, 4.053	18.680, 3.071
		Median	60.29	67.65	61.76
		Q1, Q3	50.00, 67.65	59.56, 76.47	54.41, 70.59
		Min, Max	8.8, 97.1	26.5, 91.2	8.8, 97.1
		Observed			
		n	17	20	37
		Mean	52.77	53.53	53.18
		SD, SE	22.308, 5.410	21.222, 4.745	21.425, 3.522
		Median	50.00	55.15	54.41
		Q1, Q3	36.76, 63.24	41.18, 69.85	38.24, 66.18
		Min, Max	22.1, 100.0	4.4, 82.4	4.4, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.2
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Change from Baseline			
		n	17	20	37
		Mean	-4.41	-11.91	-8.47
		SD, SE	17.943, 4.352	11.014, 2.463	14.882, 2.447
		Median	-2.94	-10.29	-7.35
		Q1, Q3	-16.18, 7.35	-17.65, -4.41	-16.18, 1.47
		Min, Max	-36.8, 26.5	-38.2, 2.9	-38.2, 26.5
		GEE Estimates			
		LS Mean (SE)	-3.17 (4.497)	-9.74 (1.716)	
		95% CI	(-11.98, 5.64)	(-13.11, -6.38)	
		LS Mean Difference (SE)		-6.57 (5.051)	
		95% CI		(-16.47, 3.33)	
		p-value		0.1932	
		HedgesG (95% CI)		-0.489 (-1.145, 0.167)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.2
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Baseline			
		n	16	18	34
		Mean	56.89	65.36	61.38
		SD, SE	19.441, 4.860	17.380, 4.096	18.596, 3.189
		Median	59.56	67.65	61.76
		Q1, Q3	50.00, 69.12	60.29, 76.47	54.41, 70.59
		Min, Max	8.8, 97.1	26.5, 91.2	8.8, 97.1
		Observed			
		n	16	18	34
		Mean	55.79	52.78	54.20
		SD, SE	25.694, 6.423	21.037, 4.959	23.030, 3.950
		Median	54.41	52.94	53.68
		Q1, Q3	36.76, 75.00	42.65, 70.59	41.18, 71.88
		Min, Max	11.8, 98.5	7.4, 83.8	7.4, 98.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.2
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Change from Baseline			
		n	16	18	34
		Mean	-1.10	-12.58	-7.18
		SD, SE	19.178, 4.794	15.261, 3.597	17.915, 3.072
		Median	0.74	-8.09	-7.35
		Q1, Q3	-17.65, 9.56	-16.18, -2.94	-16.18, 2.94
		Min, Max	-27.9, 41.2	-47.1, 5.9	-47.1, 41.2
		GEE Estimates			
		LS Mean (SE)	0.37 (4.961)	-10.03 (1.993)	
		95% CI	(-9.35, 10.09)	(-13.94, -6.12)	
		LS Mean Difference (SE)		-10.40 (5.731)	
		95% CI		(-21.63, 0.83)	
		p-value		0.0696	
		HedgesG (95% CI)		-0.631 (-1.321, 0.058)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.3
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU		N_1	58	58	116
	Baseline	n	58	58	116
		Mean	46.15	51.99	49.07
		SD, SE	18.646, 2.448	18.038, 2.368	18.499, 1.718
		Median	46.32	52.94	50.00
		Q1, Q3	33.82, 60.29	38.24, 66.18	36.76, 61.76
		Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.3
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Baseline			
		n	58	58	116
		Mean	46.15	51.99	49.07
		SD, SE	18.646, 2.448	18.038, 2.368	18.499, 1.718
		Median	46.32	52.94	50.00
		Q1, Q3	33.82, 60.29	38.24, 66.18	36.76, 61.76
		Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
		Observed			
		n	58	58	116
		Mean	42.04	43.71	42.88
		SD, SE	20.064, 2.635	19.681, 2.584	19.805, 1.839
		Median	39.71	42.65	40.44
		Q1, Q3	29.41, 51.47	29.41, 58.82	29.41, 55.88
		Min, Max	8.8, 100.0	4.4, 82.4	4.4, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.3
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Change from Baseline			
		n	58	58	116
		Mean	-4.11	-8.28	-6.19
		SD, SE	14.355, 1.885	11.825, 1.553	13.261, 1.231
		Median	-2.94	-7.35	-5.15
		Q1, Q3	-11.76, 4.41	-14.71, 1.47	-12.50, 2.94
		Min, Max	-41.2, 26.5	-42.6, 10.3	-42.6, 26.5
		GEE Estimates			
		LS Mean (SE)	-4.61 (1.847)	-7.70 (1.519)	
		95% CI	(-8.23, -0.99)	(-10.68, -4.72)	
		LS Mean Difference (SE)		-3.09 (2.436)	
		95% CI		(-7.86, 1.69)	
		p-value		0.2053	
		HedgesG (95% CI)		-0.313 (-0.679, 0.054)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.3
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Baseline			
		n	57	56	113
		Mean	45.87	51.49	48.65
		SD, SE	18.694, 2.476	17.592, 2.351	18.294, 1.721
		Median	45.59	52.94	50.00
		Q1, Q3	33.82, 60.29	37.50, 65.44	36.76, 61.76
		Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
		Observed			
		n	57	56	113
		Mean	44.43	42.65	43.55
		SD, SE	21.026, 2.785	18.698, 2.499	19.837, 1.866
		Median	39.71	41.18	41.18
		Q1, Q3	29.41, 57.35	29.41, 58.09	29.41, 57.35
		Min, Max	5.9, 98.5	7.4, 76.6	5.9, 98.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.3
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Change from Baseline			
		n	57	56	113
		Mean	-1.44	-8.84	-5.11
		SD, SE	15.083, 1.998	13.294, 1.776	14.640, 1.377
		Median	-1.47	-7.35	-4.41
		Q1, Q3	-10.29, 7.35	-14.71, 0.05	-14.71, 2.94
		Min, Max	-29.4, 41.2	-47.1, 17.6	-47.1, 41.2
		GEE Estimates			
		LS Mean (SE)	-1.90 (1.945)	-8.25 (1.647)	
		95% CI	(-5.72, 1.91)	(-11.48, -5.02)	
		LS Mean Difference (SE)		-6.34 (2.563)	
		95% CI		(-11.37, -1.32)	
		p-value		0.0133	
		HedgesG (95% CI)		-0.512 (-0.886, -0.137)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.3
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia		N_1	8	10	18
	Baseline	n	8	10	18
		Mean	27.57	43.82	36.60
		SD, SE	22.670, 8.015	27.449, 8.680	26.068, 6.144
		Median	19.85	46.32	36.76
		Q1, Q3	8.82, 44.12	13.24, 61.76	11.76, 60.29
		Min, Max	5.9, 69.1	7.4, 91.2	5.9, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.3
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Baseline			
		n	8	10	18
		Mean	27.57	43.82	36.60
		SD, SE	22.670, 8.015	27.449, 8.680	26.068, 6.144
		Median	19.85	46.32	36.76
		Q1, Q3	8.82, 44.12	13.24, 61.76	11.76, 60.29
		Min, Max	5.9, 69.1	7.4, 91.2	5.9, 91.2
		Observed			
		n	8	10	18
		Mean	29.23	40.44	35.46
		SD, SE	28.358, 10.026	24.649, 7.795	26.185, 6.172
		Median	24.26	44.85	32.35
		Q1, Q3	9.56, 36.03	14.71, 58.82	13.24, 50.00
		Min, Max	2.9, 91.2	7.4, 80.9	2.9, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.3
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Change from Baseline			
		n	8	10	18
		Mean	1.65	-3.38	-1.14
		SD, SE	10.989, 3.885	7.206, 2.279	9.157, 2.158
		Median	-0.74	-2.21	-1.47
		Q1, Q3	-7.35, 8.82	-10.29, 0.00	-10.29, 2.94
		Min, Max	-10.3, 22.1	-11.8, 10.3	-11.8, 22.1
		GEE Estimates			
		LS Mean (SE)	1.38 (4.870)	-1.25 (2.591)	
		95% CI	(-8.17, 10.92)	(-6.32, 3.83)	
		LS Mean Difference (SE)		-2.62 (5.496)	
		95% CI		(-13.40, 8.15)	
		p-value		0.6331	
		HedgesG (95% CI)		-0.499 (-1.443, 0.445)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.3
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Baseline			
		n	8	10	18
		Mean	27.57	43.82	36.60
		SD, SE	22.670, 8.015	27.449, 8.680	26.068, 6.144
		Median	19.85	46.32	36.76
		Q1, Q3	8.82, 44.12	13.24, 61.76	11.76, 60.29
		Min, Max	5.9, 69.1	7.4, 91.2	5.9, 91.2
		Observed			
		n	8	10	18
		Mean	29.96	47.79	39.87
		SD, SE	31.462, 11.123	24.226, 7.661	28.309, 6.673
		Median	27.21	50.00	46.32
		Q1, Q3	3.68, 40.44	44.12, 61.76	8.82, 57.35
		Min, Max	1.5, 95.6	5.9, 83.8	1.5, 95.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.3
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Change from Baseline			
		n	8	10	18
		Mean	2.39	3.97	3.27
		SD, SE	12.074, 4.269	21.469, 6.789	17.455, 4.114
		Median	1.47	-3.68	-2.21
		Q1, Q3	-7.35, 7.35	-7.35, 16.18	-7.35, 10.29
		Min, Max	-10.3, 26.5	-16.2, 55.9	-16.2, 55.9
		GEE Estimates			
		LS Mean (SE)	2.11 (5.193)	6.11 (5.908)	
		95% CI	(-8.06, 12.29)	(-5.47, 17.69)	
		LS Mean Difference (SE)		3.99 (7.992)	
		95% CI		(-11.67, 19.66)	
		p-value		0.6172	
		HedgesG (95% CI)		0.079 (-0.851, 1.009)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.4
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male		N_1	23	24	47
	Baseline	n	23	24	47
		Mean	40.92	46.67	43.86
		SD, SE	17.313, 3.610	19.553, 3.991	18.519, 2.701
		Median	42.65	47.06	44.12
		Q1, Q3	25.00, 57.35	34.56, 58.82	29.41, 57.35
		Min, Max	8.8, 69.1	7.4, 89.7	7.4, 89.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.4
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Baseline			
		n	23	24	47
		Mean	40.92	46.67	43.86
		SD, SE	17.313, 3.610	19.553, 3.991	18.519, 2.701
		Median	42.65	47.06	44.12
		Q1, Q3	25.00, 57.35	34.56, 58.82	29.41, 57.35
		Min, Max	8.8, 69.1	7.4, 89.7	7.4, 89.7
		Observed			
		n	23	24	47
		Mean	41.43	40.26	40.83
		SD, SE	25.381, 5.292	17.507, 3.574	21.487, 3.134
		Median	35.29	35.29	35.29
		Q1, Q3	16.18, 52.94	27.94, 55.15	26.47, 54.41
		Min, Max	2.9, 91.2	11.8, 76.5	2.9, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.4
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Change from Baseline			
		n	23	24	47
		Mean	0.51	-6.41	-3.02
		SD, SE	15.132, 3.155	11.419, 2.331	13.673, 1.994
		Median	2.94	-5.88	-4.41
		Q1, Q3	-10.29, 11.76	-11.03, 1.47	-10.29, 4.41
		Min, Max	-35.3, 26.5	-42.6, 10.3	-42.6, 26.5
		GEE Estimates			
		LS Mean (SE)	2.61 (3.930)	-3.90 (2.959)	
		95% CI	(-5.10, 10.31)	(-9.70, 1.90)	
		LS Mean Difference (SE)		-6.50 (3.901)	
		95% CI		(-14.15, 1.14)	
		p-value		0.0956	
		HedgesG (95% CI)		-0.498 (-1.079, 0.082)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.4
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Baseline			
		n	23	23	46
		Mean	40.92	44.80	42.86
		SD, SE	17.313, 3.610	17.660, 3.682	17.403, 2.566
		Median	42.65	47.06	43.38
		Q1, Q3	25.00, 57.35	33.82, 57.35	29.41, 57.35
		Min, Max	8.8, 69.1	7.4, 76.5	7.4, 76.5
		Observed			
		n	23	23	46
		Mean	43.86	39.63	41.75
		SD, SE	25.570, 5.332	17.245, 3.596	21.671, 3.195
		Median	39.71	36.76	38.24
		Q1, Q3	27.94, 69.12	23.53, 57.35	25.00, 57.35
		Min, Max	1.5, 95.6	11.8, 71.9	1.5, 95.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.4
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Change from Baseline			
		n	23	23	46
		Mean	2.94	-5.16	-1.11
		SD, SE	16.346, 3.408	12.871, 2.684	15.113, 2.228
		Median	5.88	-7.35	-5.15
		Q1, Q3	-10.29, 14.71	-14.71, 4.41	-11.76, 10.29
		Min, Max	-29.4, 30.9	-27.9, 19.1	-29.4, 30.9
		GEE Estimates			
		LS Mean (SE)	5.04 (4.157)	-2.93 (3.242)	
		95% CI	(-3.11, 13.18)	(-9.28, 3.43)	
		LS Mean Difference (SE)		-7.96 (4.170)	
		95% CI		(-16.14, 0.21)	
		p-value		0.0562	
		HedgesG (95% CI)		-0.530 (-1.118, 0.058)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.4
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female		N_1	43	44	87
	Baseline	n	43	44	87
		Mean	45.49	53.04	49.31
		SD, SE	21.232, 3.238	19.572, 2.951	20.643, 2.213
		Median	50.00	54.41	51.47
		Q1, Q3	32.35, 61.76	41.18, 66.91	35.29, 64.71
		Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.4
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Baseline			
		n	43	44	87
		Mean	45.49	53.04	49.31
		SD, SE	21.232, 3.238	19.572, 2.951	20.643, 2.213
		Median	50.00	54.41	51.47
		Q1, Q3	32.35, 61.76	41.18, 66.91	35.29, 64.71
		Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
		Observed			
		n	43	44	87
		Mean	39.98	44.85	42.44
		SD, SE	19.226, 2.932	21.707, 3.272	20.546, 2.203
		Median	39.71	44.85	41.18
		Q1, Q3	26.47, 50.00	29.41, 58.82	27.94, 58.82
		Min, Max	5.9, 100.0	4.4, 82.4	4.4, 100.0

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.4
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Change from Baseline			
		n	43	44	87
		Mean	-5.51	-8.19	-6.86
		SD, SE	13.134, 2.003	11.406, 1.720	12.293, 1.318
		Median	-2.94	-7.35	-4.41
		Q1, Q3	-11.76, 2.94	-14.71, 1.47	-13.24, 2.94
		Min, Max	-41.2, 13.2	-38.2, 10.3	-41.2, 13.2
		GEE Estimates			
		LS Mean (SE)	-2.70 (2.839)	-4.01 (2.135)	
		95% CI	(-8.26, 2.87)	(-8.20, 0.18)	
		LS Mean Difference (SE)		-1.31 (2.703)	
		95% CI		(-6.61, 3.99)	
		p-value		0.6271	
		HedgesG (95% CI)		-0.214 (-0.635, 0.208)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.4
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Baseline			
		n	42	43	85
		Mean	45.10	53.28	49.24
		SD, SE	21.335, 3.292	19.737, 3.010	20.830, 2.259
		Median	48.53	54.41	51.47
		Q1, Q3	32.35, 61.76	39.71, 67.65	35.29, 64.71
		Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
		Observed			
		n	42	43	85
		Mean	41.98	45.46	43.74
		SD, SE	21.366, 3.297	20.519, 3.129	20.890, 2.266
		Median	39.71	47.06	42.65
		Q1, Q3	27.94, 54.41	29.41, 63.24	29.41, 55.88
		Min, Max	1.5, 98.5	5.9, 83.8	1.5, 98.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.4
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Change from Baseline			
		n	42	43	85
		Mean	-3.12	-7.82	-5.50
		SD, SE	13.471, 2.079	16.554, 2.524	15.205, 1.649
		Median	-2.21	-5.88	-2.94
		Q1, Q3	-13.24, 4.41	-14.71, 0.00	-14.71, 1.47
		Min, Max	-27.9, 41.2	-47.1, 55.9	-47.1, 55.9
		GEE Estimates			
		LS Mean (SE)	-0.27 (2.800)	-3.53 (3.022)	
		95% CI	(-5.76, 5.22)	(-9.45, 2.40)	
		LS Mean Difference (SE)		-3.26 (3.004)	
		95% CI		(-9.15, 2.63)	
		p-value		0.2780	
		HedgesG (95% CI)		-0.305 (-0.733, 0.123)	

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The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.5
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White		N_1	53	55	108
	Baseline	n	53	55	108
		Mean	46.00	51.67	48.89
		SD, SE	19.110, 2.625	17.671, 2.383	18.525, 1.783
		Median	45.59	54.41	50.00
		Q1, Q3	33.82, 60.29	38.24, 66.18	36.03, 62.50
		Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.5
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Baseline			
		n	53	55	108
		Mean	46.00	51.67	48.89
		SD, SE	19.110, 2.625	17.671, 2.383	18.525, 1.783
		Median	45.59	54.41	50.00
		Q1, Q3	33.82, 60.29	38.24, 66.18	36.03, 62.50
		Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
		Observed			
		n	53	55	108
		Mean	40.76	43.56	42.18
		SD, SE	19.796, 2.719	19.560, 2.637	19.634, 1.889
		Median	38.24	42.65	39.71
		Q1, Q3	27.94, 51.47	29.41, 58.82	29.41, 55.88
		Min, Max	8.8, 100.0	4.4, 82.4	4.4, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.5
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Change from Baseline			
		n	53	55	108
		Mean	-5.24	-8.12	-6.71
		SD, SE	14.148, 1.943	12.123, 1.635	13.173, 1.268
		Median	-4.41	-5.88	-5.88
		Q1, Q3	-11.76, 4.41	-14.71, 1.47	-13.97, 2.94
		Min, Max	-41.2, 23.5	-42.6, 10.3	-42.6, 23.5
		GEE Estimates			
		LS Mean (SE)	-5.84 (1.879)	-7.55 (1.599)	
		95% CI	(-9.52, -2.16)	(-10.69, -4.42)	
		LS Mean Difference (SE)		-1.71 (2.500)	
		95% CI		(-6.61, 3.19)	
		p-value		0.4931	
		HedgesG (95% CI)		-0.215 (-0.593, 0.163)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.5
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Baseline			
		n	53	54	107
		Mean	46.00	51.84	48.95
		SD, SE	19.110, 2.625	17.793, 2.421	18.602, 1.798
		Median	45.59	54.41	50.00
		Q1, Q3	33.82, 60.29	38.24, 66.18	35.29, 63.24
		Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
		Observed			
		n	53	54	107
		Mean	44.17	42.92	43.54
		SD, SE	20.665, 2.839	18.957, 2.580	19.737, 1.908
		Median	39.71	41.18	41.18
		Q1, Q3	29.41, 57.35	29.41, 60.29	29.41, 58.82
		Min, Max	5.9, 98.5	7.4, 76.6	5.9, 98.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.5
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Change from Baseline			
		n	53	54	107
		Mean	-1.83	-8.92	-5.41
		SD, SE	15.110, 2.076	13.534, 1.842	14.706, 1.422
		Median	-2.94	-7.35	-4.41
		Q1, Q3	-10.29, 7.35	-14.71, 0.09	-14.71, 4.41
		Min, Max	-29.4, 41.2	-47.1, 17.6	-47.1, 41.2
		GEE Estimates			
		LS Mean (SE)	-2.43 (1.998)	-8.25 (1.716)	
		95% CI	(-6.34, 1.49)	(-11.61, -4.88)	
		LS Mean Difference (SE)		-5.82 (2.641)	
		95% CI		(-10.99, -0.64)	
		p-value		0.0276	
		HedgesG (95% CI)		-0.486 (-0.871, -0.102)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.5
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White		N_1	13	13	26
	Baseline	n	13	13	26
		Mean	35.29	47.06	41.18
		SD, SE	21.705, 6.020	27.096, 7.515	24.790, 4.862
		Median	36.76	47.06	40.44
		Q1, Q3	17.65, 50.00	35.29, 61.76	17.65, 60.29
		Min, Max	5.9, 69.1	7.4, 91.2	5.9, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.5
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Baseline			
		n	13	13	26
		Mean	35.29	47.06	41.18
		SD, SE	21.705, 6.020	27.096, 7.515	24.790, 4.862
		Median	36.76	47.06	40.44
		Q1, Q3	17.65, 50.00	35.29, 61.76	17.65, 60.29
		Min, Max	5.9, 69.1	7.4, 91.2	5.9, 91.2
		Observed			
		n	13	13	26
		Mean	39.37	41.86	40.61
		SD, SE	27.884, 7.734	24.064, 6.674	25.550, 5.011
		Median	39.71	44.12	39.71
		Q1, Q3	16.18, 47.06	26.47, 58.82	16.18, 58.82
		Min, Max	2.9, 91.2	7.4, 80.9	2.9, 91.2

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.5
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Change from Baseline			
		n	13	13	26
		Mean	4.07	-5.20	-0.57
		SD, SE	11.218, 3.111	7.170, 1.989	10.366, 2.033
		Median	1.47	-10.29	-1.47
		Q1, Q3	-2.94, 10.29	-10.29, 0.00	-10.29, 2.94
		Min, Max	-10.3, 26.5	-13.2, 10.3	-13.2, 26.5
		GEE Estimates			
		LS Mean (SE)	4.36 (3.585)	-3.99 (2.323)	
		95% CI	(-2.67, 11.39)	(-8.54, 0.56)	
		LS Mean Difference (SE)		-8.35 (4.388)	
		95% CI		(-16.95, 0.25)	
		p-value		0.0571	
		HedgesG (95% CI)		-0.917 (-1.725, -0.109)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.5
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Baseline			
		n	12	12	24
		Mean	33.09	43.50	38.30
		SD, SE	21.093, 6.089	24.937, 7.199	23.205, 4.737
		Median	33.09	42.65	37.50
		Q1, Q3	14.71, 47.79	24.26, 61.03	15.44, 57.35
		Min, Max	5.9, 69.1	7.4, 91.2	5.9, 91.2
		Observed			
		n	12	12	24
		Mean	35.91	45.71	40.81
		SD, SE	30.569, 8.824	22.587, 6.520	26.758, 5.462
		Median	32.35	48.53	42.65
		Q1, Q3	12.50, 49.26	35.29, 59.56	20.59, 54.41
		Min, Max	1.5, 95.6	5.9, 83.8	1.5, 95.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.5
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Change from Baseline			
		n	12	12	24
		Mean	2.82	2.21	2.51
		SD, SE	12.720, 3.672	19.854, 5.731	16.309, 3.329
		Median	0.00	-5.15	-2.21
		Q1, Q3	-7.35, 7.35	-7.35, 7.35	-7.35, 7.35
		Min, Max	-10.3, 26.5	-16.2, 55.9	-16.2, 55.9
		GEE Estimates			
		LS Mean (SE)	2.89 (3.952)	2.88 (5.363)	
		95% CI	(-4.86, 10.64)	(-7.63, 13.40)	
		LS Mean Difference (SE)		-0.01 (6.757)	
		95% CI		(-13.25, 13.24)	
		p-value		0.9991	
		HedgesG (95% CI)		-0.034 (-0.834, 0.766)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.6
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years		N_1	36	31	67
	Baseline	n	36	31	67
		Mean	39.30	48.75	43.67
		SD, SE	20.867, 3.478	15.081, 2.709	18.890, 2.308
		Median	38.97	50.00	42.65
		Q1, Q3	23.53, 58.82	36.76, 61.76	29.41, 60.29
		Min, Max	0.0, 72.1	19.1, 76.5	0.0, 76.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.6
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Baseline			
		n	36	31	67
		Mean	39.30	48.75	43.67
		SD, SE	20.867, 3.478	15.081, 2.709	18.890, 2.308
		Median	38.97	50.00	42.65
		Q1, Q3	23.53, 58.82	36.76, 61.76	29.41, 60.29
		Min, Max	0.0, 72.1	19.1, 76.5	0.0, 76.5
		Observed			
		n	36	31	67
		Mean	35.42	40.84	37.93
		SD, SE	21.332, 3.555	18.010, 3.235	19.905, 2.432
		Median	32.35	42.65	35.29
		Q1, Q3	22.79, 45.59	26.47, 54.41	23.53, 50.00
		Min, Max	2.9, 91.2	4.4, 73.5	2.9, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.6
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Change from Baseline			
		n	36	31	67
		Mean	-3.88	-7.91	-5.74
		SD, SE	16.033, 2.672	10.804, 1.941	13.909, 1.699
		Median	-2.94	-7.35	-5.88
		Q1, Q3	-11.76, 6.62	-13.24, 0.53	-11.76, 2.94
		Min, Max	-41.2, 26.5	-32.4, 10.3	-41.2, 26.5
		GEE Estimates			
		LS Mean (SE)	-0.90 (3.764)	-3.34 (2.964)	
		95% CI	(-8.28, 6.47)	(-9.14, 2.47)	
		LS Mean Difference (SE)		-2.43 (3.497)	
		95% CI		(-9.29, 4.42)	
		p-value		0.4868	
		HedgesG (95% CI)		-0.283 (-0.765, 0.200)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.6
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Baseline			
		n	36	30	66
		Mean	39.30	48.95	43.69
		SD, SE	20.867, 3.478	15.295, 2.793	19.035, 2.343
		Median	38.97	50.00	43.38
		Q1, Q3	23.53, 58.82	36.76, 61.76	29.41, 60.29
		Min, Max	0.0, 72.1	19.1, 76.5	0.0, 76.5
		Observed			
		n	36	30	66
		Mean	36.64	42.99	39.53
		SD, SE	22.910, 3.818	19.157, 3.498	21.366, 2.630
		Median	36.03	45.59	37.50
		Q1, Q3	19.85, 44.12	27.94, 60.29	23.53, 54.41
		Min, Max	1.5, 95.6	7.4, 73.5	1.5, 95.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.6
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Change from Baseline			
		n	36	30	66
		Mean	-2.66	-5.96	-4.16
		SD, SE	14.922, 2.487	13.509, 2.466	14.285, 1.758
		Median	-4.41	-6.62	-4.41
		Q1, Q3	-10.29, 8.82	-14.71, 2.94	-13.24, 4.41
		Min, Max	-29.4, 26.5	-47.1, 19.1	-47.1, 26.5
		GEE Estimates			
		LS Mean (SE)	0.32 (3.747)	-1.21 (3.184)	
		95% CI	(-7.02, 7.67)	(-7.45, 5.03)	
		LS Mean Difference (SE)		-1.53 (3.520)	
		95% CI		(-8.43, 5.37)	
		p-value		0.6635	
		HedgesG (95% CI)		-0.225 (-0.711, 0.261)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.6
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years		N_1	30	37	67
	Baseline	n	30	37	67
		Mean	49.41	52.50	51.12
		SD, SE	17.544, 3.203	22.874, 3.760	20.568, 2.513
		Median	51.47	57.35	54.41
		Q1, Q3	41.18, 61.76	38.24, 67.65	39.71, 63.24
		Min, Max	8.8, 97.1	7.4, 91.2	7.4, 97.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.6
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Baseline			
		n	30	37	67
		Mean	49.41	52.50	51.12
		SD, SE	17.544, 3.203	22.874, 3.760	20.568, 2.513
		Median	51.47	57.35	54.41
		Q1, Q3	41.18, 61.76	38.24, 67.65	39.71, 63.24
		Min, Max	8.8, 97.1	7.4, 91.2	7.4, 97.1
		Observed			
		n	30	37	67
		Mean	46.57	45.23	45.83
		SD, SE	20.143, 3.678	22.101, 3.633	21.099, 2.578
		Median	45.59	42.65	44.12
		Q1, Q3	35.29, 58.82	32.35, 58.82	33.82, 58.82
		Min, Max	8.8, 100.0	5.9, 82.4	5.9, 100.0

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Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.6
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Change from Baseline			
		n	30	37	67
		Mean	-2.84	-7.27	-5.29
		SD, SE	11.462, 2.093	11.942, 1.963	11.851, 1.448
		Median	-1.47	-5.88	-2.94
		Q1, Q3	-5.88, 4.41	-11.76, 1.47	-10.29, 2.94
		Min, Max	-35.3, 17.6	-42.6, 10.3	-42.6, 17.6
		GEE Estimates			
		LS Mean (SE)	-0.11 (3.141)	-3.99 (2.278)	
		95% CI	(-6.26, 6.05)	(-8.45, 0.48)	
		LS Mean Difference (SE)		-3.88 (2.927)	
		95% CI		(-9.61, 1.86)	
		p-value		0.1853	
		HedgesG (95% CI)		-0.368 (-0.853, 0.118)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.6
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Baseline			
		n	29	36	65
		Mean	48.99	51.47	50.36
		SD, SE	17.696, 3.286	22.305, 3.718	20.264, 2.513
		Median	51.47	55.88	52.94
		Q1, Q3	41.18, 58.82	37.50, 66.91	39.71, 63.24
		Min, Max	8.8, 97.1	7.4, 91.2	7.4, 97.1
		Observed			
		n	29	36	65
		Mean	50.10	43.80	46.61
		SD, SE	20.592, 3.824	20.058, 3.343	20.384, 2.528
		Median	48.53	41.91	44.12
		Q1, Q3	35.29, 63.24	29.41, 59.56	29.41, 63.24
		Min, Max	16.2, 98.5	5.9, 83.8	5.9, 98.5

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structure.
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Table 2.2.2.3.24.6
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Change from Baseline			
		n	29	36	65
		Mean	1.12	-7.67	-3.75
		SD, SE	14.444, 2.682	16.835, 2.806	16.299, 2.022
		Median	1.47	-5.88	-1.47
		Q1, Q3	-5.88, 5.88	-14.71, 0.00	-13.24, 2.94
		Min, Max	-27.9, 41.2	-39.7, 55.9	-39.7, 55.9
		GEE Estimates			
		LS Mean (SE)	3.89 (3.287)	-4.58 (3.278)	
		95% CI	(-2.56, 10.33)	(-11.01, 1.84)	
		LS Mean Difference (SE)		-8.47 (3.462)	
		95% CI		(-15.26, -1.69)	
		p-value		0.0144	
		HedgesG (95% CI)		-0.541 (-1.038, -0.043)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.7
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5		N_1	41	39	80
	Baseline	n	41	39	80
		Mean	39.67	42.33	40.97
		SD, SE	20.884, 3.262	17.986, 2.880	19.448, 2.174
		Median	41.18	44.12	42.65
		Q1, Q3	23.53, 52.94	29.41, 57.35	26.47, 54.88
		Min, Max	0.0, 97.1	7.4, 76.5	0.0, 97.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.7
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline			
		n	41	39	80
		Mean	39.67	42.33	40.97
		SD, SE	20.884, 3.262	17.986, 2.880	19.448, 2.174
		Median	41.18	44.12	42.65
		Q1, Q3	23.53, 52.94	29.41, 57.35	26.47, 54.88
		Min, Max	0.0, 97.1	7.4, 76.5	0.0, 97.1
		Observed			
		n	41	39	80
		Mean	36.26	37.90	37.06
		SD, SE	20.302, 3.171	20.442, 3.273	20.258, 2.265
		Median	35.29	36.76	36.03
		Q1, Q3	23.53, 45.59	22.06, 55.88	22.06, 47.06
		Min, Max	2.9, 100.0	4.4, 77.9	2.9, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.7
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline			
		n	41	39	80
		Mean	-3.41	-4.44	-3.91
		SD, SE	12.173, 1.901	11.622, 1.861	11.843, 1.324
		Median	-2.94	0.00	-1.47
		Q1, Q3	-10.29, 2.94	-10.29, 2.94	-10.29, 2.94
		Min, Max	-35.3, 23.5	-42.6, 10.3	-42.6, 23.5
		GEE Estimates			
		LS Mean (SE)	-1.29 (2.598)	-2.03 (2.296)	
		95% CI	(-6.38, 3.80)	(-6.53, 2.47)	
		LS Mean Difference (SE)		-0.74 (2.641)	
		95% CI		(-5.92, 4.43)	
		p-value		0.7785	
		HedgesG (95% CI)		-0.084 (-0.523, 0.354)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.7
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline			
		n	41	38	79
		Mean	39.67	42.32	40.95
		SD, SE	20.884, 3.262	18.227, 2.957	19.571, 2.202
		Median	41.18	44.12	42.65
		Q1, Q3	23.53, 52.94	29.41, 57.35	26.47, 55.36
		Min, Max	0.0, 97.1	7.4, 76.5	0.0, 97.1
		Observed			
		n	41	38	79
		Mean	37.91	39.01	38.44
		SD, SE	23.059, 3.601	19.236, 3.120	21.178, 2.383
		Median	35.29	36.03	35.29
		Q1, Q3	22.06, 47.06	23.53, 54.41	23.53, 51.47
		Min, Max	1.5, 98.5	5.9, 76.6	1.5, 98.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
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Table 2.2.2.3.24.7
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline			
		n	41	38	79
		Mean	-1.76	-3.31	-2.51
		SD, SE	15.326, 2.394	15.838, 2.569	15.494, 1.743
		Median	-2.94	-2.94	-2.94
		Q1, Q3	-10.29, 5.88	-11.76, 1.47	-11.76, 4.41
		Min, Max	-29.4, 41.2	-47.1, 55.9	-47.1, 55.9
		GEE Estimates			
		LS Mean (SE)	0.36 (2.877)	-0.85 (3.112)	
		95% CI	(-5.28, 6.00)	(-6.95, 5.25)	
		LS Mean Difference (SE)		-1.21 (3.236)	
		95% CI		(-7.55, 5.13)	
		p-value		0.7083	
		HedgesG (95% CI)		-0.098 (-0.539, 0.344)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.7
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5		N_1	25	29	54
	Baseline	n	25	29	54
		Mean	50.82	62.17	56.92
		SD, SE	16.409, 3.282	15.877, 2.948	16.962, 2.308
		Median	57.35	61.76	60.29
		Q1, Q3	42.65, 61.76	51.47, 70.59	44.12, 67.65
		Min, Max	8.8, 72.1	36.8, 91.2	8.8, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.7
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline			
		n	25	29	54
		Mean	50.82	62.17	56.92
		SD, SE	16.409, 3.282	15.877, 2.948	16.962, 2.308
		Median	57.35	61.76	60.29
		Q1, Q3	42.65, 61.76	51.47, 70.59	44.12, 67.65
		Min, Max	8.8, 72.1	36.8, 91.2	8.8, 91.2
		Observed			
		n	25	29	54
		Mean	47.41	50.41	49.02
		SD, SE	21.710, 4.342	18.083, 3.358	19.709, 2.682
		Median	48.53	51.47	49.26
		Q1, Q3	32.35, 63.24	38.24, 63.24	35.29, 63.24
		Min, Max	8.8, 91.2	7.4, 82.4	7.4, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.7
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline			
		n	25	29	54
		Mean	-3.41	-11.76	-7.90
		SD, SE	16.953, 3.391	9.667, 1.795	14.042, 1.911
		Median	1.47	-10.29	-6.62
		Q1, Q3	-8.82, 5.88	-17.65, -5.88	-14.71, 1.47
		Min, Max	-41.2, 26.5	-38.2, 2.9	-41.2, 26.5
		GEE Estimates			
		LS Mean (SE)	1.59 (3.663)	-4.80 (3.167)	
		95% CI	(-5.59, 8.77)	(-11.01, 1.41)	
		LS Mean Difference (SE)		-6.39 (4.089)	
		95% CI		(-14.40, 1.63)	
		p-value		0.1183	
		HedgesG (95% CI)		-0.597 (-1.144, -0.051)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.7
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline			
		n	24	28	52
		Mean	50.37	61.19	56.19
		SD, SE	16.600, 3.388	15.243, 2.881	16.641, 2.308
		Median	56.62	61.76	60.29
		Q1, Q3	41.18, 62.50	49.26, 69.85	44.12, 67.65
		Min, Max	8.8, 72.1	36.8, 91.2	8.8, 91.2
		Observed			
		n	24	28	52
		Mean	50.74	49.43	50.03
		SD, SE	20.210, 4.125	18.555, 3.507	19.155, 2.656
		Median	51.47	48.53	48.53
		Q1, Q3	37.50, 63.24	36.91, 64.71	37.50, 63.24
		Min, Max	16.2, 95.6	10.3, 83.8	10.3, 95.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.7
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline			
		n	24	28	52
		Mean	0.37	-11.76	-6.16
		SD, SE	13.831, 2.823	13.372, 2.527	14.772, 2.048
		Median	3.68	-8.82	-5.88
		Q1, Q3	-8.09, 7.35	-16.91, -0.74	-16.18, 4.41
		Min, Max	-27.9, 26.5	-39.7, 8.8	-39.7, 26.5
		GEE Estimates			
		LS Mean (SE)	5.48 (3.246)	-4.89 (3.261)	
		95% CI	(-0.88, 11.84)	(-11.28, 1.50)	
		LS Mean Difference (SE)		-10.37 (3.765)	
		95% CI		(-17.75, -2.99)	
		p-value		0.0059	
		HedgesG (95% CI)		-0.862 (-1.432, -0.292)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.8
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	29.77	32.79	31.12
		SD, SE	13.578, 2.232	11.638, 2.125	12.742, 1.557
		Median	32.35	36.76	35.29
		Q1, Q3	22.06, 42.65	26.47, 42.65	23.53, 42.65
		Min, Max	0.0, 47.1	7.4, 47.1	0.0, 47.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.8
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline			
		n	37	30	67
		Mean	29.77	32.79	31.12
		SD, SE	13.578, 2.232	11.638, 2.125	12.742, 1.557
		Median	32.35	36.76	35.29
		Q1, Q3	22.06, 42.65	26.47, 42.65	23.53, 42.65
		Min, Max	0.0, 47.1	7.4, 47.1	0.0, 47.1
		Observed			
		n	37	30	67
		Mean	28.50	26.96	27.81
		SD, SE	13.670, 2.247	12.378, 2.260	13.033, 1.592
		Median	32.35	29.41	29.41
		Q1, Q3	14.71, 39.71	19.12, 36.76	14.71, 38.24
		Min, Max	2.9, 52.9	4.4, 45.6	2.9, 52.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.8
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-1.27	-5.83	-3.31
		SD, SE	10.463, 1.720	10.236, 1.869	10.534, 1.287
		Median	-1.47	-5.88	-1.47
		Q1, Q3	-5.88, 4.41	-11.76, 1.47	-10.29, 2.94
		Min, Max	-35.3, 23.5	-29.4, 10.3	-35.3, 23.5
		GEE Estimates			
		LS Mean (SE)	0.05 (2.732)	-3.51 (2.556)	
		95% CI	(-5.30, 5.41)	(-8.52, 1.50)	
		LS Mean Difference (SE)		-3.56 (2.445)	
		95% CI		(-8.36, 1.23)	
		p-value		0.1448	
		HedgesG (95% CI)		-0.429 (-0.916, 0.058)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
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Table 2.2.2.3.24.8
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline			
		n	37	29	66
		Mean	29.77	32.45	30.95
		SD, SE	13.578, 2.232	11.692, 2.171	12.759, 1.571
		Median	32.35	36.76	34.56
		Q1, Q3	22.06, 42.65	26.47, 39.71	23.53, 42.65
		Min, Max	0.0, 47.1	7.4, 47.1	0.0, 47.1
		Observed			
		n	37	29	66
		Mean	29.05	30.48	29.68
		SD, SE	14.813, 2.435	14.711, 2.732	14.672, 1.806
		Median	29.41	29.41	29.41
		Q1, Q3	19.12, 38.24	22.06, 39.71	20.59, 38.24
		Min, Max	1.5, 72.1	5.9, 67.6	1.5, 72.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.8
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline			
		n	37	29	66
		Mean	-0.72	-1.98	-1.27
		SD, SE	12.884, 2.118	15.589, 2.895	14.037, 1.728
		Median	-2.94	-4.41	-2.94
		Q1, Q3	-7.35, 5.88	-11.76, 2.94	-10.29, 4.41
		Min, Max	-29.4, 30.9	-29.4, 55.9	-29.4, 55.9
		GEE Estimates			
		LS Mean (SE)	0.61 (2.912)	0.39 (3.706)	
		95% CI	(-5.10, 6.32)	(-6.87, 7.65)	
		LS Mean Difference (SE)		-0.22 (3.120)	
		95% CI		(-6.33, 5.90)	
		p-value		0.9441	
		HedgesG (95% CI)		-0.087 (-0.573, 0.399)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.8
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	61.92	65.00	63.67
		SD, SE	9.262, 1.720	11.123, 1.804	10.399, 1.270
		Median	61.76	63.24	61.76
		Q1, Q3	57.35, 66.18	57.35, 70.59	57.35, 67.65
		Min, Max	50.0, 97.1	48.5, 91.2	48.5, 97.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.8
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline			
		n	29	38	67
		Mean	61.92	65.00	63.67
		SD, SE	9.262, 1.720	11.123, 1.804	10.399, 1.270
		Median	61.76	63.24	61.76
		Q1, Q3	57.35, 66.18	57.35, 70.59	57.35, 67.65
		Min, Max	50.0, 97.1	48.5, 91.2	48.5, 97.1
		Observed			
		n	29	38	67
		Mean	55.78	56.08	55.95
		SD, SE	19.730, 3.664	15.583, 2.528	17.358, 2.121
		Median	51.47	55.88	55.88
		Q1, Q3	44.12, 64.71	48.53, 66.18	44.12, 66.18
		Min, Max	23.5, 100.0	14.7, 82.4	14.7, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.8
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-6.14	-8.93	-7.72
		SD, SE	17.423, 3.235	12.130, 1.968	14.601, 1.784
		Median	-5.88	-8.82	-7.35
		Q1, Q3	-17.65, 5.88	-13.24, 1.47	-16.18, 2.94
		Min, Max	-41.2, 26.5	-42.6, 10.3	-42.6, 26.5
		GEE Estimates			
		LS Mean (SE)	-1.97 (3.794)	-4.42 (2.398)	
		95% CI	(-9.41, 5.46)	(-9.12, 0.28)	
		LS Mean Difference (SE)		-2.45 (3.837)	
		95% CI		(-9.97, 5.07)	
		p-value		0.5235	
		HedgesG (95% CI)		-0.185 (-0.670, 0.299)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.8
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline			
		n	28	37	65
		Mean	61.92	64.33	63.30
		SD, SE	9.432, 1.782	10.476, 1.722	10.036, 1.245
		Median	61.03	61.76	61.76
		Q1, Q3	56.62, 66.18	57.35, 69.12	57.35, 67.65
		Min, Max	50.0, 97.1	48.5, 91.2	48.5, 97.1
		Observed			
		n	28	37	65
		Mean	60.61	53.58	56.61
		SD, SE	18.642, 3.523	16.663, 2.739	17.751, 2.202
		Median	58.09	54.41	55.88
		Q1, Q3	44.85, 71.32	44.12, 64.71	44.12, 69.12
		Min, Max	32.4, 98.5	7.4, 83.8	7.4, 98.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.8
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline			
		n	28	37	65
		Mean	-1.31	-10.75	-6.69
		SD, SE	17.086, 3.229	14.146, 2.326	16.059, 1.992
		Median	0.00	-7.35	-5.88
		Q1, Q3	-16.18, 7.35	-17.65, -1.47	-16.18, 2.94
		Min, Max	-27.9, 41.2	-47.1, 9.3	-47.1, 41.2
		GEE Estimates			
		LS Mean (SE)	3.03 (3.717)	-6.37 (2.460)	
		95% CI	(-4.25, 10.32)	(-11.19, -1.55)	
		LS Mean Difference (SE)		-9.41 (3.872)	
		95% CI		(-17.00, -1.82)	
		p-value		0.0151	
		HedgesG (95% CI)		-0.593 (-1.095, -0.092)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.9
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50		N_1	42	32	74
	Baseline	n	42	32	74
		Mean	34.49	37.91	35.97
		SD, SE	16.949, 2.615	16.447, 2.907	16.707, 1.942
		Median	35.29	37.50	36.76
		Q1, Q3	23.53, 45.59	26.47, 49.26	25.00, 47.06
		Min, Max	0.0, 66.2	7.4, 64.7	0.0, 66.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.9
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Baseline			
		n	42	32	74
		Mean	34.49	37.91	35.97
		SD, SE	16.949, 2.615	16.447, 2.907	16.707, 1.942
		Median	35.29	37.50	36.76
		Q1, Q3	23.53, 45.59	26.47, 49.26	25.00, 47.06
		Min, Max	0.0, 66.2	7.4, 64.7	0.0, 66.2
		Observed			
		n	42	32	74
		Mean	34.14	32.12	33.27
		SD, SE	18.979, 2.929	16.402, 2.899	17.820, 2.072
		Median	33.82	32.35	32.35
		Q1, Q3	16.18, 47.06	20.59, 41.18	16.18, 45.59
		Min, Max	2.9, 80.9	4.4, 64.7	2.9, 80.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.9
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Change from Baseline			
		n	42	32	74
		Mean	-0.35	-5.79	-2.70
		SD, SE	10.519, 1.623	11.770, 2.081	11.329, 1.317
		Median	-0.74	-5.88	-1.47
		Q1, Q3	-5.88, 5.88	-11.76, 2.94	-8.82, 4.41
		Min, Max	-35.3, 23.5	-42.6, 10.3	-42.6, 23.5
		GEE Estimates			
		LS Mean (SE)	2.08 (3.146)	-3.34 (2.580)	
		95% CI	(-4.08, 8.25)	(-8.39, 1.72)	
		LS Mean Difference (SE)		-5.42 (2.744)	
		95% CI		(-10.80, -0.04)	
		p-value		0.0482	
		HedgesG (95% CI)		-0.479 (-0.946, -0.013)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.9
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Baseline			
		n	42	32	74
		Mean	34.49	37.91	35.97
		SD, SE	16.949, 2.615	16.447, 2.907	16.707, 1.942
		Median	35.29	37.50	36.76
		Q1, Q3	23.53, 45.59	26.47, 49.26	25.00, 47.06
		Min, Max	0.0, 66.2	7.4, 64.7	0.0, 66.2
		Observed			
		n	42	32	74
		Mean	36.06	34.65	35.45
		SD, SE	21.242, 3.278	15.799, 2.793	18.972, 2.205
		Median	33.82	30.15	32.35
		Q1, Q3	22.06, 47.06	22.79, 47.79	22.06, 47.06
		Min, Max	1.5, 92.6	5.9, 67.6	1.5, 92.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.9
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Change from Baseline			
		n	42	32	74
		Mean	1.58	-3.26	-0.52
		SD, SE	13.831, 2.134	15.553, 2.749	14.697, 1.708
		Median	0.00	-5.15	-2.94
		Q1, Q3	-5.88, 10.29	-12.50, 1.47	-8.82, 5.88
		Min, Max	-29.4, 41.2	-32.4, 55.9	-32.4, 55.9
		GEE Estimates			
		LS Mean (SE)	4.01 (3.435)	-0.81 (3.471)	
		95% CI	(-2.72, 10.74)	(-7.61, 5.99)	
		LS Mean Difference (SE)		-4.82 (3.147)	
		95% CI		(-10.99, 1.35)	
		p-value		0.1258	
		HedgesG (95% CI)		-0.324 (-0.786, 0.139)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.9
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50		N_1	24	35	59
	Baseline	n	24	35	59
		Mean	60.36	62.44	61.59
		SD, SE	12.926, 2.639	14.789, 2.500	13.983, 1.820
		Median	61.76	61.76	61.76
		Q1, Q3	53.68, 66.91	51.47, 75.00	51.47, 69.12
		Min, Max	29.4, 97.1	36.8, 91.2	29.4, 97.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.9
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Baseline			
		n	24	35	59
		Mean	60.36	62.44	61.59
		SD, SE	12.926, 2.639	14.789, 2.500	13.983, 1.820
		Median	61.76	61.76	61.76
		Q1, Q3	53.68, 66.91	51.47, 75.00	51.47, 69.12
		Min, Max	29.4, 97.1	36.8, 91.2	29.4, 97.1
		Observed			
		n	24	35	59
		Mean	51.59	53.03	52.44
		SD, SE	21.169, 4.321	18.656, 3.153	19.551, 2.545
		Median	46.32	54.41	51.47
		Q1, Q3	34.56, 61.03	42.65, 67.65	36.76, 66.18
		Min, Max	23.5, 100.0	7.4, 82.4	7.4, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.9
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Change from Baseline			
		n	24	35	59
		Mean	-8.76	-9.41	-9.15
		SD, SE	17.703, 3.614	10.931, 1.848	13.943, 1.815
		Median	-9.56	-8.82	-8.82
		Q1, Q3	-21.32, 2.94	-17.65, 0.00	-19.12, 1.47
		Min, Max	-41.2, 26.5	-38.2, 4.4	-41.2, 26.5
		GEE Estimates			
		LS Mean (SE)	-5.12 (4.099)	-4.93 (2.937)	
		95% CI	(-13.15, 2.92)	(-10.69, 0.83)	
		LS Mean Difference (SE)		0.19 (4.003)	
		95% CI		(-7.66, 8.03)	
		p-value		0.9628	
		HedgesG (95% CI)		-0.045 (-0.564, 0.475)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.9
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Baseline			
		n	23	33	56
		Mean	60.29	62.21	61.42
		SD, SE	13.213, 2.755	14.031, 2.442	13.612, 1.819
		Median	61.76	61.76	61.76
		Q1, Q3	51.47, 67.65	54.41, 70.59	52.94, 69.12
		Min, Max	29.4, 97.1	36.8, 91.2	29.4, 97.1
		Observed			
		n	23	33	56
		Mean	54.67	51.30	52.68
		SD, SE	20.791, 4.335	19.393, 3.376	19.863, 2.654
		Median	48.53	52.94	52.21
		Q1, Q3	39.71, 67.65	40.00, 67.65	39.71, 67.65
		Min, Max	19.1, 98.5	7.4, 83.8	7.4, 98.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.9
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Change from Baseline			
		n	23	33	56
		Mean	-5.63	-10.91	-8.74
		SD, SE	15.447, 3.221	14.299, 2.489	14.876, 1.988
		Median	-7.35	-7.35	-7.35
		Q1, Q3	-16.18, 5.88	-17.65, 0.00	-16.91, 2.11
		Min, Max	-27.9, 26.5	-47.1, 8.8	-47.1, 26.5
		GEE Estimates			
		LS Mean (SE)	-1.71 (3.749)	-6.33 (3.114)	
		95% CI	(-9.06, 5.64)	(-12.44, -0.23)	
		LS Mean Difference (SE)		-4.62 (3.899)	
		95% CI		(-12.26, 3.02)	
		p-value		0.2357	
		HedgesG (95% CI)		-0.346 (-0.883, 0.190)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.10
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	29.77	33.41	31.40
		SD, SE	13.578, 2.232	12.470, 2.277	13.123, 1.603
		Median	32.35	36.76	35.29
		Q1, Q3	22.06, 42.65	26.47, 42.65	23.53, 42.65
		Min, Max	0.0, 47.1	7.4, 55.4	0.0, 55.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.10
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Baseline			
		n	37	30	67
		Mean	29.77	33.41	31.40
		SD, SE	13.578, 2.232	12.470, 2.277	13.123, 1.603
		Median	32.35	36.76	35.29
		Q1, Q3	22.06, 42.65	26.47, 42.65	23.53, 42.65
		Min, Max	0.0, 47.1	7.4, 55.4	0.0, 55.4
		Observed			
		n	37	30	67
		Mean	28.50	28.73	28.60
		SD, SE	13.670, 2.247	14.866, 2.714	14.108, 1.724
		Median	32.35	29.41	29.41
		Q1, Q3	14.71, 39.71	19.12, 36.76	14.71, 39.71
		Min, Max	2.9, 52.9	4.4, 58.8	2.9, 58.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.10
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-1.27	-4.69	-2.80
		SD, SE	10.463, 1.720	10.524, 1.921	10.550, 1.289
		Median	-1.47	-4.41	-1.47
		Q1, Q3	-5.88, 4.41	-10.29, 2.94	-8.82, 4.41
		Min, Max	-35.3, 23.5	-29.4, 10.3	-35.3, 23.5
		GEE Estimates			
		LS Mean (SE)	0.10 (2.660)	-2.32 (2.602)	
		95% CI	(-5.11, 5.32)	(-7.42, 2.78)	
		LS Mean Difference (SE)		-2.42 (2.546)	
		95% CI		(-7.41, 2.57)	
		p-value		0.3415	
		HedgesG (95% CI)		-0.317 (-0.802, 0.167)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.10
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Baseline			
		n	37	29	66
		Mean	29.77	33.10	31.23
		SD, SE	13.578, 2.232	12.566, 2.333	13.149, 1.618
		Median	32.35	36.76	34.56
		Q1, Q3	22.06, 42.65	26.47, 39.71	23.53, 42.65
		Min, Max	0.0, 47.1	7.4, 55.4	0.0, 55.4
		Observed			
		n	37	29	66
		Mean	29.05	31.69	30.21
		SD, SE	14.813, 2.435	16.069, 2.984	15.314, 1.885
		Median	29.41	29.41	29.41
		Q1, Q3	19.12, 38.24	22.06, 41.18	20.59, 39.71
		Min, Max	1.5, 72.1	5.9, 67.6	1.5, 72.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.10
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Change from Baseline			
		n	37	29	66
		Mean	-0.72	-1.40	-1.02
		SD, SE	12.884, 2.118	15.384, 2.857	13.928, 1.714
		Median	-2.94	-2.94	-2.94
		Q1, Q3	-7.35, 5.88	-11.76, 2.94	-10.29, 4.41
		Min, Max	-29.4, 30.9	-29.4, 55.9	-29.4, 55.9
		GEE Estimates			
		LS Mean (SE)	0.66 (2.830)	1.01 (3.704)	
		95% CI	(-4.89, 6.21)	(-6.25, 8.27)	
		LS Mean Difference (SE)		0.35 (3.166)	
		95% CI		(-5.86, 6.55)	
		p-value		0.9124	
		HedgesG (95% CI)		-0.048 (-0.534, 0.439)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.10
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	61.92	64.51	63.39
		SD, SE	9.262, 1.720	11.825, 1.918	10.792, 1.318
		Median	61.76	63.24	61.76
		Q1, Q3	57.35, 66.18	57.35, 70.59	57.35, 67.65
		Min, Max	50.0, 97.1	44.1, 91.2	44.1, 97.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.10
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Baseline			
		n	29	38	67
		Mean	61.92	64.51	63.39
		SD, SE	9.262, 1.720	11.825, 1.918	10.792, 1.318
		Median	61.76	63.24	61.76
		Q1, Q3	57.35, 66.18	57.35, 70.59	57.35, 67.65
		Min, Max	50.0, 97.1	44.1, 91.2	44.1, 97.1
		Observed			
		n	29	38	67
		Mean	55.78	54.68	55.16
		SD, SE	19.730, 3.664	16.386, 2.658	17.775, 2.172
		Median	51.47	55.15	54.41
		Q1, Q3	44.12, 64.71	44.12, 66.18	44.12, 66.18
		Min, Max	23.5, 100.0	14.7, 82.4	14.7, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.10
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-6.14	-9.83	-8.23
		SD, SE	17.423, 3.235	11.610, 1.883	14.413, 1.761
		Median	-5.88	-9.56	-7.35
		Q1, Q3	-17.65, 5.88	-14.71, 0.00	-17.65, 1.47
		Min, Max	-41.2, 26.5	-42.6, 4.4	-42.6, 26.5
		GEE Estimates			
		LS Mean (SE)	-1.47 (3.745)	-5.12 (2.307)	
		95% CI	(-8.81, 5.87)	(-9.64, -0.59)	
		LS Mean Difference (SE)		-3.64 (3.736)	
		95% CI		(-10.96, 3.68)	
		p-value		0.3298	
		HedgesG (95% CI)		-0.250 (-0.735, 0.235)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.10
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Baseline			
		n	28	37	65
		Mean	61.92	63.83	63.01
		SD, SE	9.432, 1.782	11.207, 1.843	10.445, 1.296
		Median	61.03	61.76	61.76
		Q1, Q3	56.62, 66.18	57.35, 69.12	57.35, 67.65
		Min, Max	50.0, 97.1	44.1, 91.2	44.1, 97.1
		Observed			
		n	28	37	65
		Mean	60.61	52.63	56.07
		SD, SE	18.642, 3.523	16.980, 2.792	18.018, 2.235
		Median	58.09	52.94	55.88
		Q1, Q3	44.85, 71.32	42.65, 64.71	42.65, 69.12
		Min, Max	32.4, 98.5	7.4, 83.8	7.4, 98.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.10
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Change from Baseline			
		n	28	37	65
		Mean	-1.31	-11.20	-6.94
		SD, SE	17.086, 3.229	14.016, 2.304	16.063, 1.992
		Median	0.00	-7.35	-5.88
		Q1, Q3	-16.18, 7.35	-17.65, -1.47	-16.18, 2.94
		Min, Max	-27.9, 41.2	-47.1, 8.8	-47.1, 41.2
		GEE Estimates			
		LS Mean (SE)	3.53 (3.682)	-6.59 (2.414)	
		95% CI	(-3.68, 10.75)	(-11.32, -1.86)	
		LS Mean Difference (SE)		-10.12 (3.830)	
		95% CI		(-17.63, -2.62)	
		p-value		0.0082	
		HedgesG (95% CI)		-0.624 (-1.127, -0.122)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.11
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes		N_1	44	47	91
	Baseline	n	44	47	91
		Mean	47.03	54.71	51.00
		SD, SE	17.717, 2.671	18.148, 2.647	18.254, 1.914
		Median	50.74	57.35	54.41
		Q1, Q3	35.29, 61.76	42.65, 67.65	39.71, 64.71
		Min, Max	0.0, 72.1	7.4, 91.2	0.0, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.11
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	44	47	91
		Mean	47.03	54.71	51.00
		SD, SE	17.717, 2.671	18.148, 2.647	18.254, 1.914
		Median	50.74	57.35	54.41
		Q1, Q3	35.29, 61.76	42.65, 67.65	39.71, 64.71
		Min, Max	0.0, 72.1	7.4, 91.2	0.0, 91.2
		Observed			
		n	44	47	91
		Mean	43.42	47.25	45.39
		SD, SE	17.227, 2.597	19.550, 2.852	18.462, 1.935
		Median	40.44	50.00	44.12
		Q1, Q3	32.35, 52.21	32.35, 58.82	32.35, 58.82
		Min, Max	11.8, 86.8	5.9, 82.4	5.9, 86.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.11
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	44	47	91
		Mean	-3.61	-7.47	-5.60
		SD, SE	13.917, 2.098	11.815, 1.723	12.948, 1.357
		Median	-2.94	-5.88	-4.41
		Q1, Q3	-11.03, 4.41	-13.24, 1.47	-11.76, 2.94
		Min, Max	-41.2, 26.5	-42.6, 10.3	-42.6, 26.5
		GEE Estimates			
		LS Mean (SE)	-5.06 (2.278)	-6.96 (1.545)	
		95% CI	(-9.53, -0.60)	(-9.99, -3.93)	
		LS Mean Difference (SE)		-1.89 (2.704)	
		95% CI		(-7.19, 3.41)	
		p-value		0.4838	
		HedgesG (95% CI)		-0.294 (-0.707, 0.120)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.11
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	43	46	89
		Mean	46.68	53.95	50.44
		SD, SE	17.778, 2.711	17.575, 2.591	17.948, 1.903
		Median	50.00	56.36	54.41
		Q1, Q3	35.29, 61.76	42.65, 67.65	39.71, 63.24
		Min, Max	0.0, 72.1	7.4, 91.2	0.0, 91.2
		Observed			
		n	43	46	89
		Mean	45.31	45.43	45.38
		SD, SE	17.828, 2.719	17.887, 2.637	17.757, 1.882
		Median	42.65	44.85	44.12
		Q1, Q3	32.35, 58.82	29.41, 60.29	30.88, 60.29
		Min, Max	11.8, 86.8	10.3, 76.6	10.3, 86.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.11
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	43	46	89
		Mean	-1.37	-8.52	-5.06
		SD, SE	13.894, 2.119	13.018, 1.919	13.846, 1.468
		Median	0.00	-6.62	-2.94
		Q1, Q3	-10.29, 7.35	-14.71, 0.09	-14.71, 2.94
		Min, Max	-27.9, 30.9	-39.7, 17.6	-39.7, 30.9
		GEE Estimates			
		LS Mean (SE)	-2.78 (2.306)	-8.16 (1.496)	
		95% CI	(-7.30, 1.74)	(-11.09, -5.23)	
		LS Mean Difference (SE)		-5.38 (2.706)	
		95% CI		(-10.68, -0.07)	
		p-value		0.0469	
		HedgesG (95% CI)		-0.521 (-0.944, -0.099)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.11
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No		N_1	22	21	43
	Baseline	n	22	21	43
		Mean	37.63	42.02	39.77
		SD, SE	22.938, 4.890	20.502, 4.474	21.637, 3.300
		Median	38.97	38.24	38.24
		Q1, Q3	22.06, 50.00	26.47, 54.41	25.00, 54.41
		Min, Max	5.9, 97.1	7.4, 91.2	5.9, 97.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.11
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Baseline			
		n	22	21	43
		Mean	37.63	42.02	39.77
		SD, SE	22.938, 4.890	20.502, 4.474	21.637, 3.300
		Median	38.97	38.24	38.24
		Q1, Q3	22.06, 50.00	26.47, 54.41	25.00, 54.41
		Min, Max	5.9, 97.1	7.4, 91.2	5.9, 97.1
		Observed			
		n	22	21	43
		Mean	34.63	34.24	34.44
		SD, SE	27.459, 5.854	19.499, 4.255	23.624, 3.603
		Median	32.35	32.35	32.35
		Q1, Q3	13.24, 47.06	22.06, 44.12	14.71, 45.59
		Min, Max	2.9, 100.0	4.4, 80.9	2.9, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.11
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Change from Baseline			
		n	22	21	43
		Mean	-3.01	-7.77	-5.34
		SD, SE	14.625, 3.118	10.534, 2.299	12.868, 1.962
		Median	-0.74	-10.29	-2.94
		Q1, Q3	-10.29, 7.35	-11.76, 0.00	-11.76, 2.94
		Min, Max	-36.8, 22.1	-32.4, 10.3	-36.8, 22.1
		GEE Estimates			
		LS Mean (SE)	-0.02 (3.238)	-4.95 (2.176)	
		95% CI	(-6.37, 6.32)	(-9.22, -0.68)	
		LS Mean Difference (SE)		-4.93 (3.805)	
		95% CI		(-12.38, 2.53)	
		p-value		0.1954	
		HedgesG (95% CI)		-0.357 (-0.960, 0.246)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.11
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Baseline			
		n	22	20	42
		Mean	37.63	41.99	39.71
		SD, SE	22.938, 4.890	21.034, 4.703	21.894, 3.378
		Median	38.97	37.50	37.50
		Q1, Q3	22.06, 50.00	26.47, 55.88	25.00, 54.41
		Min, Max	5.9, 97.1	7.4, 91.2	5.9, 97.1
		Observed			
		n	22	20	42
		Mean	37.43	38.82	38.10
		SD, SE	30.000, 6.396	22.629, 5.060	26.434, 4.079
		Median	32.35	36.03	32.35
		Q1, Q3	16.18, 48.53	22.06, 54.41	19.12, 50.00
		Min, Max	1.5, 98.5	5.9, 83.8	1.5, 98.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.11
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Change from Baseline			
		n	22	20	42
		Mean	-0.20	-3.16	-1.61
		SD, SE	16.528, 3.524	19.511, 4.363	17.849, 2.754
		Median	-1.47	-5.88	-4.41
		Q1, Q3	-10.29, 10.29	-9.56, 1.47	-10.29, 4.41
		Min, Max	-29.4, 41.2	-47.1, 55.9	-47.1, 55.9
		GEE Estimates			
		LS Mean (SE)	2.78 (3.604)	-0.15 (3.865)	
		95% CI	(-4.28, 9.85)	(-7.73, 7.42)	
		LS Mean Difference (SE)		-2.94 (5.081)	
		95% CI		(-12.90, 7.02)	
		p-value		0.5632	
		HedgesG (95% CI)		-0.157 (-0.764, 0.449)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.12
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes		N_1	13	17	30
	Baseline	n	13	17	30
		Mean	41.06	57.87	50.59
		SD, SE	19.979, 5.541	22.181, 5.380	22.547, 4.117
		Median	42.65	64.71	50.74
		Q1, Q3	23.53, 58.82	36.76, 75.00	29.41, 67.65
		Min, Max	8.8, 67.6	19.1, 91.2	8.8, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.12
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	13	17	30
		Mean	41.06	57.87	50.59
		SD, SE	19.979, 5.541	22.181, 5.380	22.547, 4.117
		Median	42.65	64.71	50.74
		Q1, Q3	23.53, 58.82	36.76, 75.00	29.41, 67.65
		Min, Max	8.8, 67.6	19.1, 91.2	8.8, 91.2
		Observed			
		n	13	17	30
		Mean	40.27	50.78	46.23
		SD, SE	18.675, 5.179	23.148, 5.614	21.633, 3.950
		Median	38.24	44.12	40.44
		Q1, Q3	25.00, 51.47	36.76, 73.53	29.41, 66.18
		Min, Max	13.2, 76.5	7.4, 82.4	7.4, 82.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.12
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	13	17	30
		Mean	-0.79	-7.09	-4.36
		SD, SE	17.072, 4.735	13.278, 3.221	15.099, 2.757
		Median	0.00	-5.88	-0.74
		Q1, Q3	-4.41, 8.82	-13.24, 2.94	-13.24, 4.41
		Min, Max	-41.2, 23.5	-38.2, 10.3	-41.2, 23.5
		GEE Estimates			
		LS Mean (SE)	-3.21 (4.478)	-4.92 (3.143)	
		95% CI	(-11.99, 5.57)	(-11.08, 1.24)	
		LS Mean Difference (SE)		-1.71 (5.788)	
		95% CI		(-13.06, 9.63)	
		p-value		0.7673	
		HedgesG (95% CI)		-0.394 (-1.123, 0.335)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.12
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	13	16	29
		Mean	41.06	55.88	49.24
		SD, SE	19.979, 5.541	21.284, 5.321	21.680, 4.026
		Median	42.65	63.24	50.00
		Q1, Q3	23.53, 58.82	36.76, 72.79	29.41, 66.18
		Min, Max	8.8, 67.6	19.1, 91.2	8.8, 91.2
		Observed			
		n	13	16	29
		Mean	43.55	48.19	46.11
		SD, SE	18.703, 5.187	18.959, 4.740	18.654, 3.464
		Median	39.71	50.00	44.12
		Q1, Q3	29.41, 58.82	29.41, 66.91	29.41, 64.71
		Min, Max	19.1, 73.5	22.1, 76.6	19.1, 76.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.12
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	13	16	29
		Mean	2.49	-7.70	-3.13
		SD, SE	13.550, 3.758	14.020, 3.505	14.511, 2.695
		Median	7.35	-3.68	0.00
		Q1, Q3	-4.41, 10.29	-13.24, 1.52	-8.82, 7.35
		Min, Max	-26.5, 22.1	-39.7, 8.8	-39.7, 22.1
		GEE Estimates			
		LS Mean (SE)	0.07 (3.663)	-5.95 (2.702)	
		95% CI	(-7.11, 7.25)	(-11.25, -0.65)	
		LS Mean Difference (SE)		-6.02 (4.668)	
		95% CI		(-15.17, 3.13)	
		p-value		0.1973	
		HedgesG (95% CI)		-0.692 (-1.445, 0.062)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.12
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No		N_1	53	51	104
	Baseline	n	53	51	104
		Mean	44.59	48.43	46.47
		SD, SE	20.058, 2.755	18.379, 2.574	19.256, 1.888
		Median	44.12	50.00	47.06
		Q1, Q3	32.35, 60.29	36.76, 60.29	35.29, 60.29
		Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.12
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Baseline			
		n	53	51	104
		Mean	44.59	48.43	46.47
		SD, SE	20.058, 2.755	18.379, 2.574	19.256, 1.888
		Median	44.12	50.00	47.06
		Q1, Q3	32.35, 60.29	36.76, 60.29	35.29, 60.29
		Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
		Observed			
		n	53	51	104
		Mean	40.54	40.72	40.63
		SD, SE	22.163, 3.044	18.855, 2.640	20.508, 2.011
		Median	38.24	42.65	39.71
		Q1, Q3	27.94, 50.00	26.47, 55.88	26.47, 54.41
		Min, Max	2.9, 100.0	4.4, 80.9	2.9, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.12
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Change from Baseline			
		n	53	51	104
		Mean	-4.05	-7.72	-5.85
		SD, SE	13.313, 1.829	10.786, 1.510	12.221, 1.198
		Median	-2.94	-7.35	-5.88
		Q1, Q3	-10.29, 4.41	-11.76, 1.47	-11.76, 2.94
		Min, Max	-36.8, 26.5	-42.6, 10.3	-42.6, 26.5
		GEE Estimates			
		LS Mean (SE)	-0.54 (2.558)	-3.97 (1.905)	
		95% CI	(-5.55, 4.48)	(-7.70, -0.23)	
		LS Mean Difference (SE)		-3.43 (2.380)	
		95% CI		(-8.09, 1.23)	
		p-value		0.1496	
		HedgesG (95% CI)		-0.297 (-0.683, 0.090)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.12
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Baseline			
		n	52	50	102
		Mean	44.26	48.55	46.36
		SD, SE	20.107, 2.788	18.546, 2.623	19.382, 1.919
		Median	44.12	50.74	47.06
		Q1, Q3	32.35, 58.82	36.76, 60.29	35.29, 60.29
		Min, Max	0.0, 97.1	7.4, 91.2	0.0, 97.1
		Observed			
		n	52	50	102
		Mean	42.42	41.91	42.17
		SD, SE	23.822, 3.304	19.622, 2.775	21.758, 2.154
		Median	39.71	41.91	41.18
		Q1, Q3	27.94, 55.15	29.41, 57.35	27.94, 55.88
		Min, Max	1.5, 98.5	5.9, 83.8	1.5, 98.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.12
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Change from Baseline			
		n	52	50	102
		Mean	-1.84	-6.64	-4.19
		SD, SE	14.994, 2.079	15.842, 2.240	15.527, 1.537
		Median	-2.21	-7.35	-4.41
		Q1, Q3	-10.29, 5.88	-14.71, 0.00	-13.24, 2.94
		Min, Max	-29.4, 41.2	-47.1, 55.9	-47.1, 55.9
		GEE Estimates			
		LS Mean (SE)	1.71 (2.688)	-2.80 (2.555)	
		95% CI	(-3.56, 6.98)	(-7.81, 2.21)	
		LS Mean Difference (SE)		-4.51 (2.870)	
		95% CI		(-10.14, 1.11)	
		p-value		0.1157	
		HedgesG (95% CI)		-0.306 (-0.697, 0.084)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.14
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes		N_1	38	32	70
	Baseline	n	38	32	70
		Mean	46.32	50.92	48.42
		SD, SE	17.948, 2.912	20.066, 3.547	18.946, 2.264
		Median	45.59	50.74	48.53
		Q1, Q3	35.29, 61.76	39.71, 61.03	36.76, 61.76
		Min, Max	8.8, 72.1	11.8, 91.2	8.8, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.14
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Baseline			
		n	38	32	70
		Mean	46.32	50.92	48.42
		SD, SE	17.948, 2.912	20.066, 3.547	18.946, 2.264
		Median	45.59	50.74	48.53
		Q1, Q3	35.29, 61.76	39.71, 61.03	36.76, 61.76
		Min, Max	8.8, 72.1	11.8, 91.2	8.8, 91.2
		Observed			
		n	38	32	70
		Mean	42.14	40.90	41.58
		SD, SE	20.240, 3.283	18.071, 3.194	19.151, 2.289
		Median	38.97	39.71	39.71
		Q1, Q3	32.35, 52.94	29.41, 51.47	29.41, 52.94
		Min, Max	8.8, 91.2	11.8, 82.4	8.8, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.14
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Change from Baseline			
		n	38	32	70
		Mean	-4.18	-10.02	-6.85
		SD, SE	15.991, 2.594	10.796, 1.909	14.074, 1.682
		Median	-2.21	-10.29	-6.62
		Q1, Q3	-11.76, 5.88	-14.71, -2.21	-11.76, 2.94
		Min, Max	-41.2, 23.5	-42.6, 10.3	-42.6, 23.5
		GEE Estimates			
		LS Mean (SE)	1.41 (3.247)	-3.24 (2.260)	
		95% CI	(-4.96, 7.77)	(-7.67, 1.19)	
		LS Mean Difference (SE)		-4.65 (3.060)	
		95% CI		(-10.64, 1.35)	
		p-value		0.1290	
		HedgesG (95% CI)		-0.410 (-0.886, 0.065)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.14
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Baseline			
		n	37	30	67
		Mean	45.91	49.90	47.70
		SD, SE	18.008, 2.961	19.367, 3.536	18.593, 2.272
		Median	45.59	50.74	47.06
		Q1, Q3	35.29, 61.76	36.76, 60.29	35.29, 61.76
		Min, Max	8.8, 72.1	11.8, 91.2	8.8, 91.2
		Observed			
		n	37	30	67
		Mean	44.79	40.44	42.84
		SD, SE	19.487, 3.204	18.221, 3.327	18.915, 2.311
		Median	39.71	38.24	39.71
		Q1, Q3	32.35, 55.88	29.41, 52.94	29.41, 55.88
		Min, Max	11.8, 95.6	7.4, 83.8	7.4, 95.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.14
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-1.11	-9.47	-4.85
		SD, SE	15.355, 2.524	18.612, 3.398	17.272, 2.110
		Median	1.47	-9.56	-5.88
		Q1, Q3	-10.29, 8.82	-16.18, 0.00	-16.18, 5.88
		Min, Max	-27.9, 30.9	-47.1, 55.9	-47.1, 55.9
		GEE Estimates			
		LS Mean (SE)	4.48 (3.068)	-2.76 (2.995)	
		95% CI	(-1.54, 10.49)	(-8.63, 3.11)	
		LS Mean Difference (SE)		-7.24 (3.411)	
		95% CI		(-13.93, -0.56)	
		p-value		0.0338	
		HedgesG (95% CI)		-0.482 (-0.970, 0.007)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.14
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No		N_1	28	36	64
	Baseline	n	28	36	64
		Mean	40.60	50.68	46.27
		SD, SE	22.271, 4.209	19.577, 3.263	21.235, 2.654
		Median	42.65	56.36	47.79
		Q1, Q3	27.21, 57.35	36.76, 66.91	31.62, 63.24
		Min, Max	0.0, 97.1	7.4, 77.9	0.0, 97.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.14
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Baseline			
		n	28	36	64
		Mean	40.60	50.68	46.27
		SD, SE	22.271, 4.209	19.577, 3.263	21.235, 2.654
		Median	42.65	56.36	47.79
		Q1, Q3	27.21, 57.35	36.76, 66.91	31.62, 63.24
		Min, Max	0.0, 97.1	7.4, 77.9	0.0, 97.1
		Observed			
		n	28	36	64
		Mean	38.24	45.30	42.21
		SD, SE	23.034, 4.353	22.160, 3.693	22.643, 2.830
		Median	36.03	52.94	44.12
		Q1, Q3	19.85, 50.00	28.68, 63.97	26.47, 58.82
		Min, Max	2.9, 100.0	4.4, 77.9	2.9, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.14
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Change from Baseline			
		n	28	36	64
		Mean	-2.36	-5.38	-4.06
		SD, SE	11.073, 2.093	11.544, 1.924	11.351, 1.419
		Median	-2.21	-0.74	-1.47
		Q1, Q3	-9.56, 5.15	-11.76, 2.94	-10.29, 2.94
		Min, Max	-23.5, 26.5	-38.2, 10.3	-38.2, 26.5
		GEE Estimates			
		LS Mean (SE)	-1.61 (2.860)	-4.03 (2.390)	
		95% CI	(-7.21, 4.00)	(-8.71, 0.66)	
		LS Mean Difference (SE)		-2.42 (2.943)	
		95% CI		(-8.19, 3.35)	
		p-value		0.4107	
		HedgesG (95% CI)		-0.258 (-0.754, 0.237)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.14
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Baseline			
		n	28	36	64
		Mean	40.60	50.68	46.27
		SD, SE	22.271, 4.209	19.577, 3.263	21.235, 2.654
		Median	42.65	56.36	47.79
		Q1, Q3	27.21, 57.35	36.76, 66.91	31.62, 63.24
		Min, Max	0.0, 97.1	7.4, 77.9	0.0, 97.1
		Observed			
		n	28	36	64
		Mean	39.81	45.93	43.25
		SD, SE	26.588, 5.025	20.433, 3.406	23.330, 2.916
		Median	36.03	47.79	41.91
		Q1, Q3	19.12, 53.68	28.68, 63.97	25.00, 62.50
		Min, Max	1.5, 98.5	5.9, 76.6	1.5, 98.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.14
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-0.79	-4.75	-3.02
		SD, SE	14.108, 2.666	11.772, 1.962	12.893, 1.612
		Median	-2.94	-2.94	-2.94
		Q1, Q3	-10.29, 5.15	-11.03, 1.52	-10.29, 2.94
		Min, Max	-29.4, 41.2	-37.9, 19.1	-37.9, 41.2
		GEE Estimates			
		LS Mean (SE)	-0.03 (3.197)	-3.40 (2.675)	
		95% CI	(-6.30, 6.24)	(-8.65, 1.84)	
		LS Mean Difference (SE)		-3.37 (3.365)	
		95% CI		(-9.97, 3.22)	
		p-value		0.3161	
		HedgesG (95% CI)		-0.300 (-0.797, 0.196)	

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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.15
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High		N_1	29	37	66
	Baseline	n	29	37	66
		Mean	52.08	57.51	55.12
		SD, SE	16.250, 3.018	19.026, 3.128	17.934, 2.207
		Median	57.35	60.29	58.09
		Q1, Q3	44.12, 64.71	47.06, 69.12	44.12, 67.65
		Min, Max	8.8, 72.1	11.8, 91.2	8.8, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.15
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Baseline			
		n	29	37	66
		Mean	52.08	57.51	55.12
		SD, SE	16.250, 3.018	19.026, 3.128	17.934, 2.207
		Median	57.35	60.29	58.09
		Q1, Q3	44.12, 64.71	47.06, 69.12	44.12, 67.65
		Min, Max	8.8, 72.1	11.8, 91.2	8.8, 91.2
		Observed			
		n	29	37	66
		Mean	50.10	49.96	50.02
		SD, SE	18.713, 3.475	20.099, 3.304	19.355, 2.382
		Median	47.06	52.94	47.79
		Q1, Q3	36.76, 63.24	36.76, 66.18	36.76, 64.71
		Min, Max	22.1, 91.2	5.9, 82.4	5.9, 91.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.15
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Change from Baseline			
		n	29	37	66
		Mean	-1.98	-7.55	-5.10
		SD, SE	15.913, 2.955	12.246, 2.013	14.139, 1.740
		Median	-1.47	-7.35	-5.15
		Q1, Q3	-8.82, 8.82	-11.76, 1.47	-11.76, 2.94
		Min, Max	-36.8, 26.5	-42.6, 10.3	-42.6, 26.5
		GEE Estimates			
		LS Mean (SE)	1.29 (3.156)	-3.37 (1.948)	
		95% CI	(-4.90, 7.47)	(-7.19, 0.45)	
		LS Mean Difference (SE)		-4.66 (3.509)	
		95% CI		(-11.53, 2.22)	
		p-value		0.1846	
		HedgesG (95% CI)		-0.388 (-0.879, 0.102)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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structure.
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Table 2.2.2.3.24.15
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Baseline			
		n	28	36	64
		Mean	51.73	56.62	54.48
		SD, SE	16.440, 3.107	18.490, 3.082	17.656, 2.207
		Median	57.35	59.56	57.35
		Q1, Q3	43.38, 64.71	45.59, 68.38	44.12, 67.65
		Min, Max	8.8, 72.1	11.8, 91.2	8.8, 91.2
		Observed			
		n	28	36	64
		Mean	51.26	50.86	51.04
		SD, SE	19.786, 3.739	17.344, 2.891	18.301, 2.288
		Median	46.32	52.21	48.53
		Q1, Q3	37.50, 65.44	37.50, 66.18	37.50, 66.18
		Min, Max	11.8, 95.6	17.6, 83.8	11.8, 95.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
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Table 2.2.2.3.24.15
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-0.47	-5.75	-3.44
		SD, SE	15.003, 2.835	16.651, 2.775	16.046, 2.006
		Median	1.47	-5.88	-2.94
		Q1, Q3	-8.09, 8.82	-13.97, 2.85	-13.24, 5.15
		Min, Max	-27.9, 26.5	-39.7, 55.9	-39.7, 55.9
		GEE Estimates			
		LS Mean (SE)	2.81 (3.013)	-1.78 (2.264)	
		95% CI	(-3.10, 8.71)	(-6.22, 2.65)	
		LS Mean Difference (SE)		-4.59 (3.438)	
		95% CI		(-11.33, 2.15)	
		p-value		0.1819	
		HedgesG (95% CI)		-0.322 (-0.819, 0.175)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.15
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low		N_1	36	30	66
	Baseline	n	36	30	66
		Mean	35.83	42.35	38.79
		SD, SE	17.994, 2.999	17.653, 3.223	18.003, 2.216
		Median	37.50	41.18	39.71
		Q1, Q3	23.53, 50.74	29.41, 57.35	26.47, 54.41
		Min, Max	0.0, 66.2	7.4, 76.5	0.0, 76.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
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Table 2.2.2.3.24.15
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Baseline			
		n	36	30	66
		Mean	35.83	42.35	38.79
		SD, SE	17.994, 2.999	17.653, 3.223	18.003, 2.216
		Median	37.50	41.18	39.71
		Q1, Q3	23.53, 50.74	29.41, 57.35	26.47, 54.41
		Min, Max	0.0, 66.2	7.4, 76.5	0.0, 76.5
		Observed			
		n	36	30	66
		Mean	31.09	34.51	32.64
		SD, SE	17.337, 2.889	17.595, 3.212	17.404, 2.142
		Median	32.35	34.56	32.35
		Q1, Q3	14.71, 44.12	20.59, 50.00	16.18, 45.59
		Min, Max	2.9, 76.5	4.4, 67.6	2.9, 76.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.15
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Change from Baseline			
		n	36	30	66
		Mean	-4.74	-7.84	-6.15
		SD, SE	12.617, 2.103	10.465, 1.911	11.705, 1.441
		Median	-2.94	-6.62	-4.41
		Q1, Q3	-11.03, 3.68	-13.24, 0.00	-11.76, 1.47
		Min, Max	-41.2, 17.6	-32.4, 10.3	-41.2, 17.6
		GEE Estimates			
		LS Mean (SE)	-9.29 (2.124)	-11.14 (2.169)	
		95% CI	(-13.45, -5.12)	(-15.39, -6.89)	
		LS Mean Difference (SE)		-1.85 (2.803)	
		95% CI		(-7.35, 3.64)	
		p-value		0.5087	
		HedgesG (95% CI)		-0.258 (-0.745, 0.228)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
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Table 2.2.2.3.24.15
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Baseline			
		n	36	29	65
		Mean	35.83	42.34	38.73
		SD, SE	17.994, 2.999	17.965, 3.336	18.137, 2.250
		Median	37.50	39.71	39.71
		Q1, Q3	23.53, 50.74	29.41, 57.35	26.47, 54.41
		Min, Max	0.0, 66.2	7.4, 76.5	0.0, 76.5
		Observed			
		n	36	29	65
		Mean	34.40	33.47	33.98
		SD, SE	20.655, 3.442	17.815, 3.308	19.297, 2.394
		Median	30.88	29.41	29.41
		Q1, Q3	19.85, 44.85	22.06, 44.12	22.06, 44.12
		Min, Max	1.5, 92.6	5.9, 73.5	1.5, 92.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.2.2.3.24.15
Subgroup Analysis: Change from baseline to week 24 in the Physical Function score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Change from Baseline			
		n	36	29	65
		Mean	-1.43	-8.87	-4.75
		SD, SE	14.896, 2.483	13.538, 2.514	14.678, 1.821
		Median	-2.94	-7.35	-4.41
		Q1, Q3	-10.29, 5.88	-16.18, 0.00	-13.24, 1.47
		Min, Max	-29.4, 41.2	-47.1, 17.6	-47.1, 41.2
		GEE Estimates			
		LS Mean (SE)	-5.98 (2.351)	-12.00 (2.636)	
		95% CI	(-10.59, -1.37)	(-17.16, -6.83)	
		LS Mean Difference (SE)		-6.02 (3.393)	
		95% CI		(-12.67, 0.63)	
		p-value		0.0761	
		HedgesG (95% CI)		-0.506 (-1.003, -0.009)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Physical Function as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Physical Function as a covariate, with compound symmetry covariance
structure.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t_womac_pf_SUB.sas

Table 2.10.999.2.24.1
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
BPI Worst Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<= 6.0	N	17	27
	Responder - n(%)	1 (5.88%)	4 (14.81%)
	Difference in responder (KRN23 vs Placebo) - %	-8.9%	
	Logistic Regression[1]		
	Responder - %	5.9%	14.8%
	95% C.I.	0.8%, 33.3%	5.5%, 34.2%
	Odds ratio (KRN23 vs Placebo)	0.359	
	95% C.I. of odds ratio	0.034, 3.768	
	P-value	0.3845	
	RR[3] (95% CI), P-value	0.397 (0.048, 3.261), 0.6337	
	ARR[3] (95% CI), P-value	0.359 (0.037, 3.522), 0.3795	
	ARD[4]		
	Difference (95% C.I.)	-0.089 (-0.264, 0.085)	
	P-value	0.6337	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.1
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
BPI Worst Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
> 6.0	N	51	39
	Responder - n(%)	13 (25.49%)	7 (17.95%)
	Difference in responder (KRN23 vs Placebo) - %	7.5%	
	Logistic Regression[1]		
	Responder - %	25.5%	17.9%
	95% C.I.	15.3%, 39.3%	8.7%, 33.4%
	Odds ratio (KRN23 vs Placebo)	1.564	
	95% C.I. of odds ratio	0.549, 4.454	
	P-value	0.3981	
	RR[3] (95% CI), P-value	1.420 (0.626, 3.221), 0.4511	
	ARR[3] (95% CI), P-value	1.564 (0.557, 4.390), 0.3959	
	ARD[4]		
	Difference (95% C.I.)	0.075 (-0.094, 0.245)	
	P-value	0.4511	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.2
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
BPI Average Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<= 6.0	N	48	49
	Responder - n(%)	8 (16.67%)	6 (12.24%)
	Difference in responder (KRN23 vs Placebo) - %	4.4%	
	Logistic Regression[1]		
	Responder - %	16.7%	12.2%
	95% C.I.	8.5%, 30.1%	5.5%, 24.9%
	Odds ratio (KRN23 vs Placebo)	1.433	
	95% C.I. of odds ratio	0.450, 4.561	
	P-value	0.5384	
	RR[3] (95% CI), P-value	1.361 (0.510, 3.630), 0.5759	
	ARR[3] (95% CI), P-value	1.433 (0.457, 4.494), 0.5369	
	ARD[4]		
	Difference (95% C.I.)	0.044 (-0.096, 0.184)	
	P-value	0.5759	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.3
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Region

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
North America/EU	N	58	58
	Responder - n(%)	13 (22.41%)	11 (18.97%)
	Difference in responder (KRN23 vs Placebo) - %	3.4%	
	Logistic Regression[1]		
	Responder - %	22.4%	19.0%
	95% C.I.	13.4%, 35.0%	10.8%, 31.2%
	Odds ratio (KRN23 vs Placebo)	1.234	
	95% C.I. of odds ratio	0.497, 3.069	
	P-value	0.6478	
	RR[3] (95% CI), P-value	1.182 (0.578, 2.418), 0.8191	
	ARR[3] (95% CI), P-value	1.234 (0.501, 3.039), 0.6470	
	ARD[4]		
	Difference (95% C.I.)	0.034 (-0.113, 0.182)	
	P-value	0.8191	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.3
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Region

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Asia	N	10	8
	Responder - n(%)	1 (10.00%)	0 (0.00%)
	Difference in responder (KRN23 vs Placebo) - %	10.0%	
	Logistic Regression[1]		
	Responder - %	10.0%	0.0%
	95% C.I.	1.2%, 50.9%	0.0%, 100.0%
	Odds ratio (KRN23 vs Placebo)	>999.999	
	95% C.I. of odds ratio	<0.001, >999.999	
	P-value	0.9811	
	RR[3] (95% CI), P-value		
	ARR[3] (95% CI), P-value	45561.1 (0.000, 235E195), 0.9622	
	ARD[4]		
	Difference (95% C.I.)	0.100 (-0.086, 0.286)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.4
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Gender

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Male	N	24	23
	Responder - n(%)	4 (16.67%)	2 (8.70%)
	Difference in responder (KRN23 vs Placebo) - %	8.0%	
	Logistic Regression[1]		
	Responder - %	16.7%	8.7%
	95% C.I.	6.2%, 37.6%	2.1%, 29.7%
	Odds ratio (KRN23 vs Placebo)	2.100	
	95% C.I. of odds ratio	0.329, 13.413	
	P-value	0.4246	
	RR[3] (95% CI), P-value	1.917 (0.388, 9.476), 0.6662	
	ARR[3] (95% CI), P-value	2.100 (0.346, 12.761), 0.4203	
	ARD[4]		
	Difference (95% C.I.)	0.080 (-0.109, 0.268)	
	P-value	0.6662	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.4
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Gender

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Female	N	44	43
	Responder - n(%)	10 (22.73%)	9 (20.93%)
	Difference in responder (KRN23 vs Placebo) - %	1.8%	
	Logistic Regression[1]		
	Responder - %	22.7%	20.9%
	95% C.I.	12.6%, 37.6%	11.2%, 35.8%
	Odds ratio (KRN23 vs Placebo)	1.111	
	95% C.I. of odds ratio	0.395, 3.122	
	P-value	0.8398	
	RR[3] (95% CI), P-value	1.086 (0.490, 2.408), 1.0000	
	ARR[3] (95% CI), P-value	1.111 (0.401, 3.076), 0.8393	
	ARD[4]		
	Difference (95% C.I.)	0.018 (-0.156, 0.192)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.5
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Age

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<=41	N	31	36
	Responder - n(%)	6 (19.35%)	7 (19.44%)
	Difference in responder (KRN23 vs Placebo) - %	-0.1%	
	Logistic Regression[1]		
	Responder - %	19.4%	19.4%
	95% C.I.	8.8%, 37.3%	9.4%, 35.9%
	Odds ratio (KRN23 vs Placebo)	0.994	
	95% C.I. of odds ratio	0.288, 3.428	
	P-value	0.9926	
	RR[3] (95% CI), P-value	0.995 (0.374, 2.649), 1.0000	
	ARR[3] (95% CI), P-value	0.994 (0.295, 3.350), 0.9926	
	ARD[4]		
	Difference (95% C.I.)	-0.001 (-0.191, 0.189)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.5
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Age

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
>41	N	37	30
	Responder - n(%)	8 (21.62%)	4 (13.33%)
	Difference in responder (KRN23 vs Placebo) - %	8.3%	
	Logistic Regression[1]		
	Responder - %	21.6%	13.3%
	95% C.I.	11.1%, 38.0%	5.0%, 31.0%
	Odds ratio (KRN23 vs Placebo)	1.793	
	95% C.I. of odds ratio	0.471, 6.825	
	P-value	0.3862	
	RR[3] (95% CI), P-value	1.622 (0.540, 4.869), 0.5252	
	ARR[3] (95% CI), P-value	1.793 (0.483, 6.657), 0.3829	
	ARD[4]		
	Difference (95% C.I.)	0.083 (-0.097, 0.263)	
	P-value	0.5252	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.6
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Race

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
White	N	55	53
	Responder - n(%)	13 (23.64%)	11 (20.75%)
	Difference in responder (KRN23 vs Placebo) - %	2.9%	
	Logistic Regression[1]		
	Responder - %	23.6%	20.8%
	95% C.I.	14.2%, 36.7%	11.8%, 33.9%
	Odds ratio (KRN23 vs Placebo)	1.182	
	95% C.I. of odds ratio	0.471, 2.966	
	P-value	0.7196	
	RR[3] (95% CI), P-value	1.139 (0.561, 2.314), 0.8183	
	ARR[3] (95% CI), P-value	1.182 (0.476, 2.935), 0.7189	
	ARD[4]		
	Difference (95% C.I.)	0.029 (-0.128, 0.185)	
	P-value	0.8183	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.6
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Race

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Non-White	N	13	13
	Responder - n(%)	1 (7.69%)	0 (0.00%)
	Difference in responder (KRN23 vs Placebo) - %	7.7%	
	Logistic Regression[1]		
	Responder - %	7.7%	0.0%
	95% C.I.	1.0%, 41.7%	0.0%, 100.0%
	Odds ratio (KRN23 vs Placebo)	>999.999	
	95% C.I. of odds ratio	<0.001, >999.999	
	P-value	0.9764	
	RR[3] (95% CI), P-value		
	ARR[3] (95% CI), P-value	48834.9 (0.000, 26E184), 0.9594	
	ARD[4]		
	Difference (95% C.I.)	0.077 (-0.068, 0.222)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.7
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Stiffness

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<=62.5	N	39	41
	Responder - n(%)	4 (10.26%)	7 (17.07%)
	Difference in responder (KRN23 vs Placebo) - %	-6.8%	
	Logistic Regression[1]		
	Responder - %	10.3%	17.1%
	95% C.I.	3.8%, 24.6%	8.3%, 32.0%
	Odds ratio (KRN23 vs Placebo)	0.555	
	95% C.I. of odds ratio	0.146, 2.113	
	P-value	0.3834	
	RR[3] (95% CI), P-value	0.601 (0.191, 1.893), 0.5196	
	ARR[3] (95% CI), P-value	0.555 (0.149, 2.070), 0.3807	
	ARD[4]		
	Difference (95% C.I.)	-0.068 (-0.218, 0.081)	
	P-value	0.5196	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.7
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Stiffness

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
>62.5	N	29	25
	Responder - n(%)	10 (34.48%)	4 (16.00%)
	Difference in responder (KRN23 vs Placebo) - %	18.5%	
	Logistic Regression[1]		
	Responder - %	34.5%	16.0%
	95% C.I.	19.4%, 53.5%	6.0%, 36.3%
	Odds ratio (KRN23 vs Placebo)	2.763	
	95% C.I. of odds ratio	0.719, 10.621	
	P-value	0.1359	
	RR[3] (95% CI), P-value	2.155 (0.770, 6.029), 0.2123	
	ARR[3] (95% CI), P-value	2.763 (0.742, 10.294), 0.1298	
	ARD[4]		
	Difference (95% C.I.)	0.185 (-0.040, 0.410)	
	P-value	0.2123	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.8
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Physical Function

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<=47.8	N	30	37
	Responder - n(%)	2 (6.67%)	3 (8.11%)
	Difference in responder (KRN23 vs Placebo) - %	-1.4%	
	Logistic Regression[1]		
	Responder - %	6.7%	8.1%
	95% C.I.	1.6%, 23.6%	2.6%, 22.7%
	Odds ratio (KRN23 vs Placebo)	0.810	
	95% C.I. of odds ratio	0.122, 5.375	
	P-value	0.8243	
	RR[3] (95% CI), P-value	0.822 (0.147, 4.606), 1.0000	
	ARR[3] (95% CI), P-value	0.810 (0.126, 5.189), 0.8236	
	ARD[4]		
	Difference (95% C.I.)	-0.014 (-0.140, 0.111)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.8
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Physical Function

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
>47.8	N	38	29
	Responder - n(%)	12 (31.58%)	8 (27.59%)
	Difference in responder (KRN23 vs Placebo) - %	4.0%	
	Logistic Regression[1]		
	Responder - %	31.6%	27.6%
	95% C.I.	18.7%, 48.1%	14.2%, 46.6%
	Odds ratio (KRN23 vs Placebo)	1.212	
	95% C.I. of odds ratio	0.410, 3.581	
	P-value	0.7247	
	RR[3] (95% CI), P-value	1.145 (0.539, 2.430), 0.7921	
	ARR[3] (95% CI), P-value	1.212 (0.418, 3.509), 0.7236	
	ARD[4]		
	Difference (95% C.I.)	0.040 (-0.180, 0.260)	
	P-value	0.7921	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.9
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<=50.0	N	32	42
	Responder - n(%)	3 (9.38%)	3 (7.14%)
	Difference in responder (KRN23 vs Placebo) - %	2.2%	
	Logistic Regression[1]		
	Responder - %	9.4%	7.1%
	95% C.I.	3.0%, 25.7%	2.3%, 20.3%
	Odds ratio (KRN23 vs Placebo)	1.345	
	95% C.I. of odds ratio	0.246, 7.358	
	P-value	0.7292	
	RR[3] (95% CI), P-value	1.313 (0.283, 6.078), 1.0000	
	ARR[3] (95% CI), P-value	1.345 (0.253, 7.150), 0.7282	
	ARD[4]		
	Difference (95% C.I.)	0.022 (-0.105, 0.150)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.9
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
>50.0	N	35	24
	Responder - n(%)	11 (31.43%)	8 (33.33%)
	Difference in responder (KRN23 vs Placebo) - %	-1.9%	
	Logistic Regression[1]		
	Responder - %	31.4%	33.3%
	95% C.I.	18.1%, 48.7%	17.4%, 54.3%
	Odds ratio (KRN23 vs Placebo)	0.917	
	95% C.I. of odds ratio	0.295, 2.846	
	P-value	0.8783	
	RR[3] (95% CI), P-value	0.943 (0.446, 1.992), 1.0000	
	ARR[3] (95% CI), P-value	0.917 (0.302, 2.778), 0.8778	
	ARD[4]		
	Difference (95% C.I.)	-0.019 (-0.262, 0.224)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.10
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Total Score

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
<=49.5	N	30	37
	Responder - n(%)	1 (3.33%)	3 (8.11%)
	Difference in responder (KRN23 vs Placebo) - %	-4.8%	
	Logistic Regression[1]		
	Responder - %	3.3%	8.1%
	95% C.I.	0.5%, 20.8%	2.6%, 22.7%
	Odds ratio (KRN23 vs Placebo)	0.391	
	95% C.I. of odds ratio	0.037, 4.142	
	P-value	0.4296	
	RR[3] (95% CI), P-value	0.411 (0.045, 3.753), 0.6220	
	ARR[3] (95% CI), P-value	0.391 (0.039, 3.964), 0.4267	
	ARD[4]		
	Difference (95% C.I.)	-0.048 (-0.157, 0.061)	
	P-value	0.6220	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.10
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
WOMAC Total Score

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
>49.5	N	38	29
	Responder - n(%)	13 (34.21%)	8 (27.59%)
	Difference in responder (KRN23 vs Placebo) - %	6.6%	
	Logistic Regression[1]		
	Responder - %	34.2%	27.6%
	95% C.I.	20.8%, 50.7%	14.2%, 46.6%
	Odds ratio (KRN23 vs Placebo)	1.365	
	95% C.I. of odds ratio	0.466, 3.998	
	P-value	0.5651	
	RR[3] (95% CI), P-value	1.240 (0.594, 2.590), 0.6052	
	ARR[3] (95% CI), P-value	1.365 (0.475, 3.919), 0.5631	
	ARD[4]		
	Difference (95% C.I.)	0.066 (-0.156, 0.288)	
	P-value	0.6052	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.11
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
6MWT

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Low	N	37	29
	Responder - n(%)	6 (16.22%)	6 (20.69%)
	Difference in responder (KRN23 vs Placebo) - %	-4.5%	
	Logistic Regression[1]		
	Responder - %	16.2%	20.7%
	95% C.I.	7.4%, 32.1%	9.5%, 39.5%
	Odds ratio (KRN23 vs Placebo)	0.742	
	95% C.I. of odds ratio	0.207, 2.662	
	P-value	0.6423	
	RR[3] (95% CI), P-value	0.784 (0.282, 2.178), 0.7516	
	ARR[3] (95% CI), P-value	0.742 (0.212, 2.599), 0.6407	
	ARD[4]		
	Difference (95% C.I.)	-0.045 (-0.234, 0.145)	
	P-value	0.7516	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.11
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
6MWT

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
High	N	30	36
	Responder - n(%)	8 (26.67%)	5 (13.89%)
	Difference in responder (KRN23 vs Placebo) - %	12.8%	
	Logistic Regression[1]		
	Responder - %	26.7%	13.9%
	95% C.I.	13.7%, 45.3%	5.8%, 29.7%
	Odds ratio (KRN23 vs Placebo)	2.255	
	95% C.I. of odds ratio	0.635, 8.010	
	P-value	0.2048	
	RR[3] (95% CI), P-value	1.920 (0.702, 5.255), 0.2266	
	ARR[3] (95% CI), P-value	2.255 (0.650, 7.820), 0.2002	
	ARD[4]		
	Difference (95% C.I.)	0.128 (-0.067, 0.322)	
	P-value	0.2266	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.12
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Pain Medication use at BL

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Yes	N	47	44
	Responder - n(%)	11 (23.40%)	8 (18.18%)
	Difference in responder (KRN23 vs Placebo) - %	5.2%	
	Logistic Regression[1]		
	Responder - %	23.4%	18.2%
	95% C.I.	13.4%, 37.7%	9.3%, 32.6%
	Odds ratio (KRN23 vs Placebo)	1.375	
	95% C.I. of odds ratio	0.488, 3.872	
	P-value	0.5426	
	RR[3] (95% CI), P-value	1.287 (0.571, 2.901), 0.6115	
	ARR[3] (95% CI), P-value	1.375 (0.495, 3.818), 0.5411	
	ARD[4]		
	Difference (95% C.I.)	0.052 (-0.114, 0.218)	
	P-value	0.6115	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.12
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Pain Medication use at BL

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
No	N	21	22
	Responder - n(%)	3 (14.29%)	3 (13.64%)
	Difference in responder (KRN23 vs Placebo) - %	0.6%	
	Logistic Regression[1]		
	Responder - %	14.3%	13.6%
	95% C.I.	4.5%, 37.0%	4.3%, 35.6%
	Odds ratio (KRN23 vs Placebo)	1.056	
	95% C.I. of odds ratio	0.178, 6.245	
	P-value	0.9513	
	RR[3] (95% CI), P-value	1.048 (0.237, 4.622), 1.0000	
	ARR[3] (95% CI), P-value	1.056 (0.188, 5.926), 0.9510	
	ARD[4]		
	Difference (95% C.I.)	0.006 (-0.201, 0.214)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.13
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Opioid Pain Medication use at BL

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Yes	N	17	13
	Responder - n(%)	3 (17.65%)	2 (15.38%)
	Difference in responder (KRN23 vs Placebo) - %	2.3%	
	Logistic Regression[1]		
	Responder - %	17.6%	15.4%
	95% C.I.	5.5%, 44.1%	3.6%, 46.8%
	Odds ratio (KRN23 vs Placebo)	1.179	
	95% C.I. of odds ratio	0.153, 9.100	
	P-value	0.8704	
	RR[3] (95% CI), P-value	1.147 (0.223, 5.896), 1.0000	
	ARR[3] (95% CI), P-value	1.179 (0.167, 8.331), 0.8692	
	ARD[4]		
	Difference (95% C.I.)	0.023 (-0.244, 0.290)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.13
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Opioid Pain Medication use at BL

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
No	N	51	53
	Responder - n(%)	11 (21.57%)	9 (16.98%)
	Difference in responder (KRN23 vs Placebo) - %	4.6%	
	Logistic Regression[1]		
	Responder - %	21.6%	17.0%
	95% C.I.	12.3%, 35.1%	9.0%, 29.7%
	Odds ratio (KRN23 vs Placebo)	1.344	
	95% C.I. of odds ratio	0.499, 3.623	
	P-value	0.5550	
	RR[3] (95% CI), P-value	1.270 (0.575, 2.806), 0.6234	
	ARR[3] (95% CI), P-value	1.344 (0.505, 3.580), 0.5537	
	ARD[4]		
	Difference (95% C.I.)	0.046 (-0.106, 0.197)	
	P-value	0.6234	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.14
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Active fractures and pseudofractures at BL

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Yes	N	32	38
	Responder - n(%)	9 (28.13%)	8 (21.05%)
	Difference in responder (KRN23 vs Placebo) - %	7.1%	
	Logistic Regression[1]		
	Responder - %	28.1%	21.1%
	95% C.I.	15.2%, 46.2%	10.8%, 37.1%
	Odds ratio (KRN23 vs Placebo)	1.467	
	95% C.I. of odds ratio	0.481, 4.481	
	P-value	0.4953	
	RR[3] (95% CI), P-value	1.336 (0.584, 3.058), 0.5804	
	ARR[3] (95% CI), P-value	1.467 (0.490, 4.392), 0.4930	
	ARD[4]		
	Difference (95% C.I.)	0.071 (-0.132, 0.273)	
	P-value	0.5804	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.14
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
Active fractures and pseudofractures at BL

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
No	N	36	28
	Responder - n(%)	5 (13.89%)	3 (10.71%)
	Difference in responder (KRN23 vs Placebo) - %	3.2%	
	Logistic Regression[1]		
	Responder - %	13.9%	10.7%
	95% C.I.	5.8%, 29.7%	3.4%, 28.9%
	Odds ratio (KRN23 vs Placebo)	1.344	
	95% C.I. of odds ratio	0.284, 6.368	
	P-value	0.7052	
	RR[3] (95% CI), P-value	1.296 (0.338, 4.968), 1.0000	
	ARR[3] (95% CI), P-value	1.344 (0.292, 6.177), 0.7040	
	ARD[4]		
	Difference (95% C.I.)	0.032 (-0.129, 0.193)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.10.999.2.24.2
Subgroup Analysis: WOMAC Physical Functioning responder analyses(15.0 nu)
Primary Analysis Set (Week 24)
BPI Average Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
> 6.0	N	20	17
	Responder - n(%)	6 (30.00%)	5 (29.41%)
	Difference in responder (KRN23 vs Placebo) - %	0.6%	
	Logistic Regression[1]		
	Responder - %	30.0%	29.4%
	95% C.I.	13.7%, 53.6%	12.4%, 55.1%
	Odds ratio (KRN23 vs Placebo)	1.029	
	95% C.I. of odds ratio	0.237, 4.455	
	P-value	0.9691	
	RR[3] (95% CI), P-value	1.020 (0.377, 2.759), 1.0000	
	ARR[3] (95% CI), P-value	1.029 (0.250, 4.235), 0.9689	
	ARD[4]		
	Difference (95% C.I.)	0.006 (-0.289, 0.301)	
	P-value	1.0000	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Paindiary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: t-logistic-womac_15percent.sas

Table 2.1.2.4.9.24
Summary of Interaction Test: Change from baseline to post-baseline visits in the Pain score of WOMAC
GEE Model

Subgroup Variables	Week 24
BPI Average Pain at BL	0.3476
BPI Worst Pain at BL	0.5240
Region	0.0123
Sex	0.6269
Race Group	0.1163
Age Category	0.7974
WOMAC Stiffness at BL cat	0.5753
WOMAC Physical Function at BL cat	0.7405
WOMAC Pain at BL cat	0.9514
WOMAC Total Score at BL	0.8847
Pain Medication Use at BL cat	0.9733
Opioid Pain Medication Use at BL	0.9867
Active fractures and pseudo-fractures at BL	0.3923
6MWT score at BL cat	0.7756

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
P value of Interaction is from the GEE model which includes the change from baseline for Pain Score of WOMAC as the dependent variable, region, visit, treatment, actual randomization stratification, visit by treatment, subgroup and subgroup by treatment as fixed factors, and baseline for Pain Score of WOMAC as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: Interaction_womac.sas

Table 2.2.2.4.24.1
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6		N_1	27	17	44
	Baseline	n	27	16	43
		Mean	41.48	33.75	38.60
		SD, SE	13.855, 2.666	14.888, 3.722	14.570, 2.222
		Median	45.00	35.00	40.00
		Q1, Q3	35.00, 50.00	25.00, 40.00	30.00, 45.00
		Min, Max	10.0, 70.0	10.0, 70.0	10.0, 70.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.1
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Baseline			
		n	27	16	43
		Mean	41.48	33.75	38.60
		SD, SE	13.855, 2.666	14.888, 3.722	14.570, 2.222
		Median	45.00	35.00	40.00
		Q1, Q3	35.00, 50.00	25.00, 40.00	30.00, 45.00
		Min, Max	10.0, 70.0	10.0, 70.0	10.0, 70.0
		Observed			
		n	27	17	44
		Mean	34.07	28.24	31.82
		SD, SE	15.753, 3.032	10.146, 2.461	14.022, 2.114
		Median	35.00	30.00	30.00
		Q1, Q3	20.00, 45.00	20.00, 35.00	20.00, 40.00
		Min, Max	5.0, 70.0	10.0, 45.0	5.0, 70.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.1
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Change from Baseline			
		n	27	16	43
		Mean	-7.41	-6.25	-6.98
		SD, SE	16.015, 3.082	12.845, 3.211	14.766, 2.252
		Median	-10.00	-5.00	-5.00
		Q1, Q3	-20.00, 5.00	-15.00, 2.50	-15.00, 5.00
		Min, Max	-35.0, 20.0	-40.0, 10.0	-40.0, 20.0
		GEE Estimates			
		LS Mean (SE)	-7.00 (4.234)	-11.12 (4.071)	
		95% CI	(-15.30, 1.30)	(-19.10, -3.14)	
		LS Mean Difference (SE)		-4.13 (3.206)	
		95% CI		(-10.41, 2.16)	
		p-value		0.1982	
		HedgesG (95% CI)		0.074 (-0.544, 0.693)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.1
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Baseline			
		n	27	16	43
		Mean	41.48	33.75	38.60
		SD, SE	13.855, 2.666	14.888, 3.722	14.570, 2.222
		Median	45.00	35.00	40.00
		Q1, Q3	35.00, 50.00	25.00, 40.00	30.00, 45.00
		Min, Max	10.0, 70.0	10.0, 70.0	10.0, 70.0
		Observed			
		n	27	17	44
		Mean	37.78	33.24	36.02
		SD, SE	14.500, 2.791	14.246, 3.455	14.410, 2.172
		Median	40.00	35.00	40.00
		Q1, Q3	30.00, 50.00	15.00, 40.00	25.00, 45.00
		Min, Max	10.0, 65.0	15.0, 55.0	10.0, 65.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.1
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Change from Baseline			
		n	27	16	43
		Mean	-3.70	-0.94	-2.67
		SD, SE	16.326, 3.142	15.299, 3.825	15.825, 2.413
		Median	0.00	0.00	0.00
		Q1, Q3	-15.00, 5.00	-5.00, 10.00	-15.00, 5.00
		Min, Max	-30.0, 35.0	-35.0, 20.0	-35.0, 35.0
		GEE Estimates			
		LS Mean (SE)	-3.29 (4.216)	-5.81 (5.689)	
		95% CI	(-11.56, 4.97)	(-16.96, 5.34)	
		LS Mean Difference (SE)		-2.52 (4.150)	
		95% CI		(-10.65, 5.62)	
		p-value		0.5443	
		HedgesG (95% CI)		0.166 (-0.453, 0.786)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.1
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6		N_1	39	51	90
	Baseline	n	39	51	90
		Mean	52.44	55.98	54.44
		SD, SE	15.212, 2.436	15.525, 2.174	15.405, 1.624
		Median	50.00	55.00	55.00
		Q1, Q3	40.00, 60.00	50.00, 65.00	45.00, 65.00
		Min, Max	25.0, 90.0	10.0, 100.0	10.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.1
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Baseline			
		n	39	51	90
		Mean	52.44	55.98	54.44
		SD, SE	15.212, 2.436	15.525, 2.174	15.405, 1.624
		Median	50.00	55.00	55.00
		Q1, Q3	40.00, 60.00	50.00, 65.00	45.00, 65.00
		Min, Max	25.0, 90.0	10.0, 100.0	10.0, 100.0
		Observed			
		n	39	51	90
		Mean	50.77	48.63	49.56
		SD, SE	15.667, 2.509	18.030, 2.525	16.987, 1.791
		Median	50.00	50.00	50.00
		Q1, Q3	40.00, 60.00	35.00, 60.00	35.00, 60.00
		Min, Max	25.0, 90.0	5.0, 90.0	5.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.1
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Change from Baseline			
		n	39	51	90
		Mean	-1.67	-7.35	-4.89
		SD, SE	13.196, 2.113	14.434, 2.021	14.122, 1.489
		Median	0.00	-5.00	-5.00
		Q1, Q3	-10.00, 10.00	-15.00, 5.00	-10.00, 5.00
		Min, Max	-35.0, 30.0	-50.0, 20.0	-50.0, 30.0
		GEE Estimates			
		LS Mean (SE)	2.44 (2.657)	-2.41 (2.170)	
		95% CI	(-2.76, 7.65)	(-6.66, 1.84)	
		LS Mean Difference (SE)		-4.85 (2.838)	
		95% CI		(-10.42, 0.71)	
		p-value		0.0873	
		HedgesG (95% CI)		-0.401 (-0.822, 0.020)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.1
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Baseline			
		n	38	50	88
		Mean	51.97	55.30	53.86
		SD, SE	15.136, 2.455	14.895, 2.106	15.004, 1.599
		Median	50.00	55.00	55.00
		Q1, Q3	40.00, 60.00	50.00, 65.00	45.00, 62.50
		Min, Max	25.0, 90.0	10.0, 100.0	10.0, 100.0
		Observed			
		n	38	50	88
		Mean	50.53	46.80	48.41
		SD, SE	19.165, 3.109	16.744, 2.368	17.820, 1.900
		Median	50.00	45.00	45.00
		Q1, Q3	35.00, 65.00	35.00, 60.00	35.00, 60.00
		Min, Max	20.0, 100.0	5.0, 85.0	5.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.1
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Change from Baseline			
		n	38	50	88
		Mean	-1.45	-8.50	-5.45
		SD, SE	15.063, 2.444	18.049, 2.553	17.097, 1.823
		Median	0.00	-5.00	-5.00
		Q1, Q3	-15.00, 15.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-35.0, 30.0	-50.0, 50.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	2.38 (2.893)	-3.81 (2.478)	
		95% CI	(-3.29, 8.05)	(-8.67, 1.05)	
		LS Mean Difference (SE)		-6.19 (3.226)	
		95% CI		(-12.52, 0.13)	
		p-value		0.0548	
		HedgesG (95% CI)		-0.411 (-0.837, 0.016)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.2
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6		N_1	49	48	97
	Baseline	n	49	47	96
		Mean	43.57	44.89	44.22
		SD, SE	13.346, 1.907	16.302, 2.378	14.803, 1.511
		Median	45.00	45.00	45.00
		Q1, Q3	35.00, 55.00	35.00, 55.00	35.00, 55.00
		Min, Max	10.0, 70.0	10.0, 75.0	10.0, 75.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.2
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Baseline			
		n	49	47	96
		Mean	43.57	44.89	44.22
		SD, SE	13.346, 1.907	16.302, 2.378	14.803, 1.511
		Median	45.00	45.00	45.00
		Q1, Q3	35.00, 55.00	35.00, 55.00	35.00, 55.00
		Min, Max	10.0, 70.0	10.0, 75.0	10.0, 75.0
		Observed			
		n	49	48	97
		Mean	40.20	40.21	40.21
		SD, SE	16.201, 2.314	16.372, 2.363	16.201, 1.645
		Median	40.00	40.00	40.00
		Q1, Q3	30.00, 50.00	27.50, 55.00	30.00, 50.00
		Min, Max	5.0, 80.0	10.0, 70.0	5.0, 80.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.2
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Change from Baseline			
		n	49	47	96
		Mean	-3.37	-4.68	-4.01
		SD, SE	15.322, 2.189	13.039, 1.902	14.191, 1.448
		Median	-5.00	-5.00	-5.00
		Q1, Q3	-10.00, 10.00	-10.00, 5.00	-10.00, 5.00
		Min, Max	-35.0, 30.0	-40.0, 20.0	-40.0, 30.0
		GEE Estimates			
		LS Mean (SE)	-3.79 (3.031)	-4.47 (2.649)	
		95% CI	(-9.73, 2.15)	(-9.67, 0.72)	
		LS Mean Difference (SE)		-0.69 (2.698)	
		95% CI		(-5.97, 4.60)	
		p-value		0.7995	
		HedgesG (95% CI)		-0.090 (-0.491, 0.310)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.2
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Baseline			
		n	49	47	96
		Mean	43.57	44.89	44.22
		SD, SE	13.346, 1.907	16.302, 2.378	14.803, 1.511
		Median	45.00	45.00	45.00
		Q1, Q3	35.00, 55.00	35.00, 55.00	35.00, 55.00
		Min, Max	10.0, 70.0	10.0, 75.0	10.0, 75.0
		Observed			
		n	49	48	97
		Mean	41.73	40.31	41.03
		SD, SE	15.895, 2.271	15.724, 2.270	15.744, 1.599
		Median	40.00	40.00	40.00
		Q1, Q3	30.00, 50.00	30.00, 50.00	30.00, 50.00
		Min, Max	10.0, 80.0	5.0, 75.0	5.0, 80.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.2
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Change from Baseline			
		n	49	47	96
		Mean	-1.84	-4.57	-3.18
		SD, SE	15.569, 2.224	17.062, 2.489	16.289, 1.662
		Median	0.00	-5.00	0.00
		Q1, Q3	-15.00, 5.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-30.0, 35.0	-50.0, 50.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	-2.26 (3.104)	-4.37 (2.816)	
		95% CI	(-8.34, 3.83)	(-9.89, 1.15)	
		LS Mean Difference (SE)		-2.11 (2.811)	
		95% CI		(-7.62, 3.40)	
		p-value		0.4530	
		HedgesG (95% CI)		-0.165 (-0.566, 0.236)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.2
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6		N_1	17	20	37
	Baseline	n	17	20	37
		Mean	60.59	64.25	62.57
		SD, SE	14.778, 3.584	14.352, 3.209	14.464, 2.378
		Median	60.00	62.50	60.00
		Q1, Q3	50.00, 70.00	57.50, 70.00	50.00, 70.00
		Min, Max	40.0, 90.0	35.0, 100.0	35.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.2
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Baseline			
		n	17	20	37
		Mean	60.59	64.25	62.57
		SD, SE	14.778, 3.584	14.352, 3.209	14.464, 2.378
		Median	60.00	62.50	60.00
		Q1, Q3	50.00, 70.00	57.50, 70.00	50.00, 70.00
		Min, Max	40.0, 90.0	35.0, 100.0	35.0, 100.0
		Observed			
		n	17	20	37
		Mean	54.71	51.50	52.97
		SD, SE	17.631, 4.276	21.527, 4.814	19.631, 3.227
		Median	50.00	52.50	50.00
		Q1, Q3	45.00, 60.00	35.00, 67.50	45.00, 65.00
		Min, Max	25.0, 90.0	5.0, 90.0	5.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.2
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Change from Baseline			
		n	17	20	37
		Mean	-5.88	-12.75	-9.59
		SD, SE	12.404, 3.008	14.821, 3.314	14.013, 2.304
		Median	-5.00	-12.50	-10.00
		Q1, Q3	-15.00, 5.00	-22.50, 0.00	-15.00, 0.00
		Min, Max	-35.0, 10.0	-50.0, 10.0	-50.0, 10.0
		GEE Estimates			
		LS Mean (SE)	0.42 (3.698)	-6.81 (1.864)	
		95% CI	(-6.83, 7.66)	(-10.47, -3.16)	
		LS Mean Difference (SE)		-7.23 (4.683)	
		95% CI		(-16.41, 1.95)	
		p-value		0.1227	
		HedgesG (95% CI)		-0.475 (-1.130, 0.181)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.2
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Baseline			
		n	16	19	35
		Mean	60.00	62.89	61.57
		SD, SE	15.055, 3.764	13.366, 3.066	14.026, 2.371
		Median	60.00	60.00	60.00
		Q1, Q3	50.00, 67.50	55.00, 70.00	50.00, 70.00
		Min, Max	40.0, 90.0	35.0, 100.0	35.0, 100.0
		Observed			
		n	16	19	35
		Mean	55.94	51.05	53.29
		SD, SE	21.696, 5.424	18.453, 4.233	19.850, 3.355
		Median	55.00	50.00	50.00
		Q1, Q3	42.50, 67.50	35.00, 65.00	40.00, 65.00
		Min, Max	20.0, 100.0	20.0, 85.0	20.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.2
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Change from Baseline			
		n	16	19	35
		Mean	-4.06	-11.84	-8.29
		SD, SE	15.729, 3.932	18.349, 4.210	17.403, 2.942
		Median	-7.50	-5.00	-5.00
		Q1, Q3	-15.00, 10.00	-30.00, 0.00	-20.00, 5.00
		Min, Max	-35.0, 20.0	-50.0, 10.0	-50.0, 20.0
		GEE Estimates			
		LS Mean (SE)	1.84 (4.471)	-6.25 (1.975)	
		95% CI	(-6.92, 10.60)	(-10.12, -2.38)	
		LS Mean Difference (SE)		-8.09 (5.553)	
		95% CI		(-18.97, 2.79)	
		p-value		0.1452	
		HedgesG (95% CI)		-0.429 (-1.102, 0.244)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.3
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU		N_1	58	58	116
	Baseline	n	58	57	115
		Mean	48.97	52.63	50.78
		SD, SE	15.297, 2.009	16.478, 2.183	15.930, 1.485
		Median	47.50	55.00	50.00
		Q1, Q3	40.00, 60.00	40.00, 65.00	40.00, 60.00
		Min, Max	15.0, 90.0	15.0, 100.0	15.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.3
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Baseline			
		n	58	57	115
		Mean	48.97	52.63	50.78
		SD, SE	15.297, 2.009	16.478, 2.183	15.930, 1.485
		Median	47.50	55.00	50.00
		Q1, Q3	40.00, 60.00	40.00, 65.00	40.00, 60.00
		Min, Max	15.0, 90.0	15.0, 100.0	15.0, 100.0
		Observed			
		n	58	58	116
		Mean	45.78	44.14	44.96
		SD, SE	16.853, 2.213	17.799, 2.337	17.276, 1.604
		Median	45.00	40.00	45.00
		Q1, Q3	35.00, 60.00	35.00, 60.00	35.00, 60.00
		Min, Max	20.0, 90.0	5.0, 90.0	5.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.3
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Change from Baseline			
		n	58	57	115
		Mean	-3.19	-8.42	-5.78
		SD, SE	14.947, 1.963	14.084, 1.865	14.699, 1.371
		Median	-2.50	-5.00	-5.00
		Q1, Q3	-15.00, 10.00	-15.00, 0.00	-15.00, 5.00
		Min, Max	-35.0, 30.0	-50.0, 20.0	-50.0, 30.0
		GEE Estimates			
		LS Mean (SE)	-3.55 (1.818)	-7.37 (1.927)	
		95% CI	(-7.11, 0.01)	(-11.14, -3.59)	
		LS Mean Difference (SE)		-3.81 (2.568)	
		95% CI		(-8.85, 1.22)	
		p-value		0.1376	
		HedgesG (95% CI)		-0.355 (-0.723, 0.014)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.3
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Baseline			
		n	57	56	113
		Mean	48.60	51.96	50.27
		SD, SE	15.170, 2.009	15.831, 2.115	15.524, 1.460
		Median	45.00	55.00	50.00
		Q1, Q3	40.00, 60.00	40.00, 62.50	40.00, 60.00
		Min, Max	15.0, 90.0	15.0, 100.0	15.0, 100.0
		Observed			
		n	57	57	114
		Mean	46.84	42.98	44.91
		SD, SE	16.999, 2.252	16.579, 2.196	16.828, 1.576
		Median	45.00	40.00	45.00
		Q1, Q3	35.00, 55.00	35.00, 55.00	35.00, 55.00
		Min, Max	15.0, 100.0	5.0, 75.0	5.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.3
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Change from Baseline			
		n	57	56	113
		Mean	-1.75	-8.93	-5.31
		SD, SE	15.512, 2.055	16.479, 2.202	16.329, 1.536
		Median	0.00	-5.00	-5.00
		Q1, Q3	-15.00, 5.00	-15.00, 2.50	-15.00, 5.00
		Min, Max	-35.0, 35.0	-50.0, 20.0	-50.0, 35.0
		GEE Estimates			
		LS Mean (SE)	-2.29 (1.971)	-8.10 (2.020)	
		95% CI	(-6.15, 1.57)	(-12.06, -4.14)	
		LS Mean Difference (SE)		-5.81 (2.684)	
		95% CI		(-11.07, -0.55)	
		p-value		0.0304	
		HedgesG (95% CI)		-0.441 (-0.815, -0.068)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.3
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia		N_1	8	10	18
	Baseline	n	8	10	18
		Mean	40.63	39.50	40.00
		SD, SE	16.353, 5.782	22.907, 7.244	19.704, 4.644
		Median	40.00	42.50	40.00
		Q1, Q3	35.00, 50.00	15.00, 55.00	30.00, 55.00
		Min, Max	10.0, 65.0	10.0, 75.0	10.0, 75.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.3
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Baseline			
		n	8	10	18
		Mean	40.63	39.50	40.00
		SD, SE	16.353, 5.782	22.907, 7.244	19.704, 4.644
		Median	40.00	42.50	40.00
		Q1, Q3	35.00, 50.00	15.00, 55.00	30.00, 55.00
		Min, Max	10.0, 65.0	10.0, 75.0	10.0, 75.0
		Observed			
		n	8	10	18
		Mean	30.63	40.00	35.83
		SD, SE	18.601, 6.576	23.570, 7.454	21.437, 5.053
		Median	30.00	40.00	35.00
		Q1, Q3	17.50, 42.50	20.00, 60.00	20.00, 55.00
		Min, Max	5.0, 60.0	10.0, 80.0	5.0, 80.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.3
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Change from Baseline			
		n	8	10	18
		Mean	-10.00	0.50	-4.17
		SD, SE	10.351, 3.660	11.168, 3.532	11.789, 2.779
		Median	-7.50	2.50	-2.50
		Q1, Q3	-15.00, -2.50	-5.00, 10.00	-10.00, 5.00
		Min, Max	-30.0, 0.0	-20.0, 15.0	-30.0, 15.0
		GEE Estimates			
		LS Mean (SE)	-10.09 (6.251)	0.50 (4.439)	
		95% CI	(-22.35, 2.16)	(-8.20, 9.20)	
		LS Mean Difference (SE)		10.60 (5.607)	
		95% CI		(-0.39, 21.58)	
		p-value		0.0588	
		HedgesG (95% CI)		0.872 (-0.101, 1.844)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.3
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Baseline			
		n	8	10	18
		Mean	40.63	39.50	40.00
		SD, SE	16.353, 5.782	22.907, 7.244	19.704, 4.644
		Median	40.00	42.50	40.00
		Q1, Q3	35.00, 50.00	15.00, 55.00	30.00, 55.00
		Min, Max	10.0, 65.0	10.0, 75.0	10.0, 75.0
		Observed			
		n	8	10	18
		Mean	33.75	45.50	40.28
		SD, SE	24.604, 8.699	20.743, 6.560	22.653, 5.339
		Median	27.50	45.00	42.50
		Q1, Q3	12.50, 50.00	40.00, 55.00	15.00, 55.00
		Min, Max	10.0, 80.0	15.0, 85.0	10.0, 85.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.3
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Change from Baseline			
		n	8	10	18
		Mean	-6.88	6.00	0.28
		SD, SE	15.797, 5.585	19.264, 6.092	18.509, 4.363
		Median	-10.00	5.00	0.00
		Q1, Q3	-20.00, 7.50	-10.00, 10.00	-15.00, 10.00
		Min, Max	-25.0, 15.0	-15.0, 50.0	-25.0, 50.0
		GEE Estimates			
		LS Mean (SE)	-6.97 (6.957)	6.00 (5.000)	
		95% CI	(-20.60, 6.67)	(-3.80, 15.80)	
		LS Mean Difference (SE)		12.97 (6.840)	
		95% CI		(-0.44, 26.38)	
		p-value		0.0579	
		HedgesG (95% CI)		0.648 (-0.305, 1.602)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male		N_1	23	24	47
	Baseline	n	23	23	46
		Mean	43.48	47.17	45.33
		SD, SE	14.494, 3.022	19.178, 3.999	16.912, 2.493
		Median	45.00	50.00	45.00
		Q1, Q3	35.00, 50.00	30.00, 60.00	35.00, 55.00
		Min, Max	15.0, 85.0	15.0, 90.0	15.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Baseline			
		n	23	23	46
		Mean	43.48	47.17	45.33
		SD, SE	14.494, 3.022	19.178, 3.999	16.912, 2.493
		Median	45.00	50.00	45.00
		Q1, Q3	35.00, 50.00	30.00, 60.00	35.00, 55.00
		Min, Max	15.0, 85.0	15.0, 90.0	15.0, 90.0
		Observed			
		n	23	24	47
		Mean	40.00	40.63	40.32
		SD, SE	19.424, 4.050	16.037, 3.274	17.582, 2.565
		Median	35.00	40.00	35.00
		Q1, Q3	30.00, 50.00	30.00, 52.50	30.00, 50.00
		Min, Max	5.0, 90.0	15.0, 70.0	5.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Change from Baseline			
		n	23	23	46
		Mean	-3.48	-6.52	-5.00
		SD, SE	15.258, 3.182	15.406, 3.212	15.239, 2.247
		Median	-5.00	-5.00	-5.00
		Q1, Q3	-15.00, 10.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-30.0, 30.0	-40.0, 15.0	-40.0, 30.0
		GEE Estimates			
		LS Mean (SE)	0.53 (5.476)	-1.89 (4.506)	
		95% CI	(-10.21, 11.26)	(-10.72, 6.94)	
		LS Mean Difference (SE)		-2.42 (4.207)	
		95% CI		(-10.67, 5.82)	
		p-value		0.5651	
		HedgesG (95% CI)		-0.191 (-0.770, 0.388)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Baseline			
		n	23	22	45
		Mean	43.48	45.23	44.33
		SD, SE	14.494, 3.022	17.146, 3.656	15.689, 2.339
		Median	45.00	47.50	45.00
		Q1, Q3	35.00, 50.00	30.00, 55.00	35.00, 55.00
		Min, Max	15.0, 85.0	15.0, 75.0	15.0, 85.0
		Observed			
		n	23	23	46
		Mean	43.91	38.04	40.98
		SD, SE	20.723, 4.321	13.292, 2.772	17.468, 2.576
		Median	40.00	40.00	40.00
		Q1, Q3	30.00, 50.00	30.00, 45.00	30.00, 50.00
		Min, Max	10.0, 100.0	15.0, 70.0	10.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Change from Baseline			
		n	23	22	45
		Mean	0.43	-7.27	-3.33
		SD, SE	17.511, 3.651	15.866, 3.383	16.989, 2.533
		Median	0.00	-5.00	-5.00
		Q1, Q3	-15.00, 15.00	-15.00, 5.00	-15.00, 10.00
		Min, Max	-30.0, 30.0	-35.0, 20.0	-35.0, 30.0
		GEE Estimates			
		LS Mean (SE)	4.44 (5.891)	-3.27 (4.448)	
		95% CI	(-7.11, 15.99)	(-11.99, 5.45)	
		LS Mean Difference (SE)		-7.71 (4.296)	
		95% CI		(-16.13, 0.71)	
		p-value		0.0727	
		HedgesG (95% CI)		-0.443 (-1.034, 0.149)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female		N_1	43	44	87
	Baseline	n	43	44	87
		Mean	50.35	52.50	51.44
		SD, SE	15.713, 2.396	17.304, 2.609	16.476, 1.766
		Median	50.00	55.00	55.00
		Q1, Q3	40.00, 60.00	40.00, 62.50	40.00, 60.00
		Min, Max	10.0, 90.0	10.0, 100.0	10.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Baseline			
		n	43	44	87
		Mean	50.35	52.50	51.44
		SD, SE	15.713, 2.396	17.304, 2.609	16.476, 1.766
		Median	50.00	55.00	55.00
		Q1, Q3	40.00, 60.00	40.00, 62.50	40.00, 60.00
		Min, Max	10.0, 90.0	10.0, 100.0	10.0, 100.0
		Observed			
		n	43	44	87
		Mean	46.05	45.11	45.57
		SD, SE	16.459, 2.510	19.868, 2.995	18.163, 1.947
		Median	45.00	45.00	45.00
		Q1, Q3	35.00, 60.00	32.50, 60.00	35.00, 60.00
		Min, Max	10.0, 90.0	5.0, 90.0	5.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Change from Baseline			
		n	43	44	87
		Mean	-4.30	-7.39	-5.86
		SD, SE	14.375, 2.192	13.359, 2.014	13.877, 1.488
		Median	-5.00	-5.00	-5.00
		Q1, Q3	-10.00, 5.00	-15.00, 0.00	-15.00, 5.00
		Min, Max	-35.0, 20.0	-50.0, 20.0	-50.0, 20.0
		GEE Estimates			
		LS Mean (SE)	-2.80 (3.084)	-5.45 (2.794)	
		95% CI	(-8.85, 3.24)	(-10.92, 0.03)	
		LS Mean Difference (SE)		-2.64 (2.887)	
		95% CI		(-8.30, 3.02)	
		p-value		0.3604	
		HedgesG (95% CI)		-0.218 (-0.639, 0.204)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Baseline			
		n	42	44	86
		Mean	49.88	52.50	51.22
		SD, SE	15.597, 2.407	17.304, 2.609	16.448, 1.774
		Median	50.00	55.00	55.00
		Q1, Q3	40.00, 60.00	40.00, 62.50	40.00, 60.00
		Min, Max	10.0, 90.0	10.0, 100.0	10.0, 100.0
		Observed			
		n	42	44	86
		Mean	45.95	46.14	46.05
		SD, SE	17.188, 2.652	18.327, 2.763	17.675, 1.906
		Median	45.00	45.00	45.00
		Q1, Q3	35.00, 55.00	35.00, 60.00	35.00, 60.00
		Min, Max	10.0, 95.0	5.0, 85.0	5.0, 95.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Change from Baseline			
		n	42	44	86
		Mean	-3.93	-6.36	-5.17
		SD, SE	14.294, 2.206	18.595, 2.803	16.582, 1.788
		Median	-2.50	0.00	0.00
		Q1, Q3	-15.00, 5.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-35.0, 35.0	-50.0, 50.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	-2.64 (3.153)	-4.42 (3.032)	
		95% CI	(-8.82, 3.54)	(-10.37, 1.52)	
		LS Mean Difference (SE)		-1.78 (3.036)	
		95% CI		(-7.73, 4.17)	
		p-value		0.5578	
		HedgesG (95% CI)		-0.143 (-0.567, 0.280)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White		N_1	53	55	108
	Baseline	n	53	54	107
		Mean	47.92	52.87	50.42
		SD, SE	14.821, 2.036	15.314, 2.084	15.205, 1.470
		Median	45.00	55.00	50.00
		Q1, Q3	40.00, 60.00	40.00, 65.00	40.00, 60.00
		Min, Max	15.0, 90.0	15.0, 100.0	15.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Baseline			
		n	53	54	107
		Mean	47.92	52.87	50.42
		SD, SE	14.821, 2.036	15.314, 2.084	15.205, 1.470
		Median	45.00	55.00	50.00
		Q1, Q3	40.00, 60.00	40.00, 65.00	40.00, 60.00
		Min, Max	15.0, 90.0	15.0, 100.0	15.0, 100.0
		Observed			
		n	53	55	108
		Mean	44.34	44.45	44.40
		SD, SE	16.292, 2.238	17.445, 2.352	16.810, 1.618
		Median	45.00	40.00	45.00
		Q1, Q3	30.00, 50.00	35.00, 60.00	35.00, 60.00
		Min, Max	20.0, 90.0	5.0, 90.0	5.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Change from Baseline			
		n	53	54	107
		Mean	-3.58	-8.33	-5.98
		SD, SE	15.360, 2.110	14.341, 1.952	14.975, 1.448
		Median	-5.00	-5.00	-5.00
		Q1, Q3	-15.00, 10.00	-15.00, 0.00	-15.00, 5.00
		Min, Max	-35.0, 30.0	-50.0, 20.0	-50.0, 30.0
		GEE Estimates			
		LS Mean (SE)	-4.46 (1.946)	-7.10 (2.042)	
		95% CI	(-8.28, -0.65)	(-11.10, -3.10)	
		LS Mean Difference (SE)		-2.63 (2.707)	
		95% CI		(-7.94, 2.67)	
		p-value		0.3307	
		HedgesG (95% CI)		-0.314 (-0.696, 0.067)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Baseline			
		n	53	54	107
		Mean	47.92	52.87	50.42
		SD, SE	14.821, 2.036	15.314, 2.084	15.205, 1.470
		Median	45.00	55.00	50.00
		Q1, Q3	40.00, 60.00	40.00, 65.00	40.00, 60.00
		Min, Max	15.0, 90.0	15.0, 100.0	15.0, 100.0
		Observed			
		n	53	55	108
		Mean	46.13	43.55	44.81
		SD, SE	15.892, 2.183	16.434, 2.216	16.147, 1.554
		Median	45.00	40.00	45.00
		Q1, Q3	35.00, 55.00	35.00, 55.00	35.00, 55.00
		Min, Max	15.0, 95.0	5.0, 75.0	5.0, 95.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Change from Baseline			
		n	53	54	107
		Mean	-1.79	-9.26	-5.56
		SD, SE	15.723, 2.160	16.666, 2.268	16.559, 1.601
		Median	0.00	-5.00	-5.00
		Q1, Q3	-15.00, 5.00	-15.00, 0.00	-15.00, 5.00
		Min, Max	-35.0, 35.0	-50.0, 20.0	-50.0, 35.0
		GEE Estimates			
		LS Mean (SE)	-2.67 (2.024)	-8.02 (2.084)	
		95% CI	(-6.64, 1.29)	(-12.11, -3.94)	
		LS Mean Difference (SE)		-5.35 (2.734)	
		95% CI		(-10.71, 0.01)	
		p-value		0.0503	
		HedgesG (95% CI)		-0.453 (-0.837, -0.069)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White		N_1	13	13	26
	Baseline	n	13	13	26
		Mean	48.08	41.54	44.81
		SD, SE	18.879, 5.236	25.198, 6.989	22.067, 4.328
		Median	45.00	35.00	45.00
		Q1, Q3	35.00, 55.00	20.00, 55.00	35.00, 55.00
		Min, Max	10.0, 85.0	10.0, 90.0	10.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Baseline			
		n	13	13	26
		Mean	48.08	41.54	44.81
		SD, SE	18.879, 5.236	25.198, 6.989	22.067, 4.328
		Median	45.00	35.00	45.00
		Q1, Q3	35.00, 55.00	20.00, 55.00	35.00, 55.00
		Min, Max	10.0, 85.0	10.0, 90.0	10.0, 90.0
		Observed			
		n	13	13	26
		Mean	42.31	39.62	40.96
		SD, SE	23.059, 6.395	23.315, 6.466	22.760, 4.464
		Median	50.00	35.00	40.00
		Q1, Q3	25.00, 55.00	20.00, 60.00	20.00, 60.00
		Min, Max	5.0, 90.0	10.0, 80.0	5.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Change from Baseline			
		n	13	13	26
		Mean	-5.77	-1.92	-3.85
		SD, SE	11.152, 3.093	11.463, 3.179	11.252, 2.207
		Median	-5.00	0.00	0.00
		Q1, Q3	-10.00, 0.00	-10.00, 5.00	-10.00, 5.00
		Min, Max	-30.0, 10.0	-20.0, 15.0	-30.0, 15.0
		GEE Estimates			
		LS Mean (SE)	-3.20 (4.344)	-0.57 (3.434)	
		95% CI	(-11.71, 5.31)	(-7.30, 6.16)	
		LS Mean Difference (SE)		2.63 (4.803)	
		95% CI		(-6.78, 12.04)	
		p-value		0.5841	
		HedgesG (95% CI)		0.316 (-0.457, 1.090)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Baseline			
		n	12	12	24
		Mean	46.25	37.50	41.88
		SD, SE	18.479, 5.334	21.479, 6.201	20.098, 4.103
		Median	45.00	35.00	42.50
		Q1, Q3	35.00, 55.00	17.50, 55.00	32.50, 55.00
		Min, Max	10.0, 85.0	10.0, 75.0	10.0, 85.0
		Observed			
		n	12	12	24
		Mean	41.25	42.50	41.88
		SD, SE	27.396, 7.909	20.725, 5.983	23.766, 4.851
		Median	37.50	42.50	40.00
		Q1, Q3	20.00, 50.00	27.50, 55.00	20.00, 52.50
		Min, Max	10.0, 100.0	15.0, 85.0	10.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.4
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Change from Baseline			
		n	12	12	24
		Mean	-5.00	5.00	0.00
		SD, SE	14.924, 4.308	17.710, 5.112	16.811, 3.432
		Median	-2.50	5.00	0.00
		Q1, Q3	-20.00, 7.50	-7.50, 10.00	-15.00, 10.00
		Min, Max	-25.0, 15.0	-15.0, 50.0	-25.0, 50.0
		GEE Estimates			
		LS Mean (SE)	-2.81 (5.028)	5.39 (4.420)	
		95% CI	(-12.67, 7.04)	(-3.27, 14.06)	
		LS Mean Difference (SE)		8.21 (5.604)	
		95% CI		(-2.78, 19.19)	
		p-value		0.1431	
		HedgesG (95% CI)		0.564 (-0.251, 1.380)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.6
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years		N_1	36	31	67
	Baseline	n	36	30	66
		Mean	47.08	49.33	48.11
		SD, SE	14.754, 2.459	15.185, 2.772	14.878, 1.831
		Median	45.00	55.00	50.00
		Q1, Q3	40.00, 55.00	35.00, 60.00	35.00, 60.00
		Min, Max	10.0, 85.0	15.0, 75.0	10.0, 85.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.6
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Baseline			
		n	36	30	66
		Mean	47.08	49.33	48.11
		SD, SE	14.754, 2.459	15.185, 2.772	14.878, 1.831
		Median	45.00	55.00	50.00
		Q1, Q3	40.00, 55.00	35.00, 60.00	35.00, 60.00
		Min, Max	10.0, 85.0	15.0, 75.0	10.0, 85.0
		Observed			
		n	36	31	67
		Mean	43.47	42.42	42.99
		SD, SE	18.471, 3.078	17.314, 3.110	17.818, 2.177
		Median	42.50	45.00	45.00
		Q1, Q3	30.00, 55.00	30.00, 60.00	30.00, 60.00
		Min, Max	5.0, 90.0	5.0, 75.0	5.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.6
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Change from Baseline			
		n	36	30	66
		Mean	-3.61	-6.83	-5.08
		SD, SE	14.571, 2.428	15.227, 2.780	14.845, 1.827
		Median	-2.50	-5.00	-5.00
		Q1, Q3	-10.00, 7.50	-15.00, 5.00	-15.00, 5.00
		Min, Max	-35.0, 30.0	-40.0, 20.0	-40.0, 30.0
		GEE Estimates			
		LS Mean (SE)	-3.81 (3.968)	-6.53 (3.735)	
		95% CI	(-11.59, 3.96)	(-13.85, 0.79)	
		LS Mean Difference (SE)		-2.72 (3.563)	
		95% CI		(-9.70, 4.27)	
		p-value		0.4460	
		HedgesG (95% CI)		-0.211 (-0.697, 0.275)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.6
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Baseline			
		n	36	30	66
		Mean	47.08	49.33	48.11
		SD, SE	14.754, 2.459	15.185, 2.772	14.878, 1.831
		Median	45.00	55.00	50.00
		Q1, Q3	40.00, 55.00	35.00, 60.00	35.00, 60.00
		Min, Max	10.0, 85.0	15.0, 75.0	10.0, 85.0
		Observed			
		n	36	31	67
		Mean	42.22	41.94	42.09
		SD, SE	19.400, 3.233	17.305, 3.108	18.323, 2.238
		Median	40.00	40.00	40.00
		Q1, Q3	30.00, 50.00	35.00, 55.00	30.00, 50.00
		Min, Max	10.0, 100.0	5.0, 75.0	5.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.6
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Change from Baseline			
		n	36	30	66
		Mean	-4.86	-7.33	-5.98
		SD, SE	15.743, 2.624	17.207, 3.142	16.343, 2.012
		Median	-2.50	-2.50	-2.50
		Q1, Q3	-20.00, 5.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-35.0, 35.0	-50.0, 20.0	-50.0, 35.0
		GEE Estimates			
		LS Mean (SE)	-5.06 (4.239)	-7.03 (3.803)	
		95% CI	(-13.37, 3.25)	(-14.48, 0.43)	
		LS Mean Difference (SE)		-1.97 (3.850)	
		95% CI		(-9.51, 5.58)	
		p-value		0.6097	
		HedgesG (95% CI)		-0.146 (-0.632, 0.339)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.6
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years		N_1	30	37	67
	Baseline	n	30	37	67
		Mean	49.00	51.76	50.52
		SD, SE	16.630, 3.036	20.146, 3.312	18.569, 2.269
		Median	45.00	55.00	50.00
		Q1, Q3	40.00, 60.00	40.00, 65.00	40.00, 65.00
		Min, Max	15.0, 90.0	10.0, 100.0	10.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.6
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Baseline			
		n	30	37	67
		Mean	49.00	51.76	50.52
		SD, SE	16.630, 3.036	20.146, 3.312	18.569, 2.269
		Median	45.00	55.00	50.00
		Q1, Q3	40.00, 60.00	40.00, 65.00	40.00, 65.00
		Min, Max	15.0, 90.0	10.0, 100.0	10.0, 100.0
		Observed			
		n	30	37	67
		Mean	44.50	44.46	44.48
		SD, SE	16.884, 3.083	19.818, 3.258	18.425, 2.251
		Median	45.00	40.00	45.00
		Q1, Q3	30.00, 55.00	35.00, 60.00	35.00, 60.00
		Min, Max	20.0, 90.0	10.0, 90.0	10.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.6
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Change from Baseline			
		n	30	37	67
		Mean	-4.50	-7.30	-6.04
		SD, SE	14.818, 2.705	13.102, 2.154	13.859, 1.693
		Median	-5.00	-5.00	-5.00
		Q1, Q3	-15.00, 5.00	-15.00, 0.00	-15.00, 5.00
		Min, Max	-35.0, 20.0	-50.0, 15.0	-50.0, 20.0
		GEE Estimates			
		LS Mean (SE)	-1.73 (3.384)	-3.25 (2.934)	
		95% CI	(-8.36, 4.90)	(-9.00, 2.50)	
		LS Mean Difference (SE)		-1.52 (3.262)	
		95% CI		(-7.91, 4.87)	
		p-value		0.6410	
		HedgesG (95% CI)		-0.196 (-0.679, 0.287)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.6
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Baseline			
		n	29	36	65
		Mean	48.28	50.69	49.62
		SD, SE	16.436, 3.052	19.352, 3.225	18.013, 2.234
		Median	45.00	52.50	50.00
		Q1, Q3	40.00, 60.00	40.00, 65.00	40.00, 60.00
		Min, Max	15.0, 90.0	10.0, 100.0	10.0, 100.0
		Observed			
		n	29	36	65
		Mean	48.97	44.58	46.54
		SD, SE	16.604, 3.083	17.087, 2.848	16.885, 2.094
		Median	50.00	42.50	45.00
		Q1, Q3	40.00, 60.00	32.50, 57.50	35.00, 60.00
		Min, Max	25.0, 95.0	15.0, 85.0	15.0, 95.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.6
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Change from Baseline			
		n	29	36	65
		Mean	0.69	-6.11	-3.08
		SD, SE	14.924, 2.771	18.170, 3.028	17.018, 2.111
		Median	0.00	-5.00	0.00
		Q1, Q3	-10.00, 5.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-25.0, 30.0	-50.0, 50.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	3.15 (3.583)	-2.44 (3.096)	
		95% CI	(-3.88, 10.17)	(-8.51, 3.62)	
		LS Mean Difference (SE)		-5.59 (3.352)	
		95% CI		(-12.16, 0.98)	
		p-value		0.0953	
		HedgesG (95% CI)		-0.394 (-0.887, 0.100)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.7
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5		N_1	41	39	80
	Baseline	n	41	38	79
		Mean	44.76	43.42	44.11
		SD, SE	15.287, 2.387	16.320, 2.648	15.705, 1.767
		Median	40.00	45.00	45.00
		Q1, Q3	35.00, 55.00	35.00, 55.00	35.00, 55.00
		Min, Max	10.0, 90.0	10.0, 70.0	10.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.7
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline			
		n	41	38	79
		Mean	44.76	43.42	44.11
		SD, SE	15.287, 2.387	16.320, 2.648	15.705, 1.767
		Median	40.00	45.00	45.00
		Q1, Q3	35.00, 55.00	35.00, 55.00	35.00, 55.00
		Min, Max	10.0, 90.0	10.0, 70.0	10.0, 90.0
		Observed			
		n	41	39	80
		Mean	41.34	38.46	39.94
		SD, SE	17.924, 2.799	17.326, 2.774	17.583, 1.966
		Median	40.00	35.00	40.00
		Q1, Q3	30.00, 50.00	25.00, 55.00	27.50, 50.00
		Min, Max	5.0, 90.0	5.0, 70.0	5.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.7
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline			
		n	41	38	79
		Mean	-3.41	-5.00	-4.18
		SD, SE	15.550, 2.428	13.203, 2.142	14.399, 1.620
		Median	0.00	-5.00	-5.00
		Q1, Q3	-10.00, 5.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-35.0, 30.0	-40.0, 20.0	-40.0, 30.0
		GEE Estimates			
		LS Mean (SE)	-4.23 (3.730)	-6.54 (3.383)	
		95% CI	(-11.54, 3.08)	(-13.17, 0.09)	
		LS Mean Difference (SE)		-2.31 (3.133)	
		95% CI		(-8.46, 3.83)	
		p-value		0.4600	
		HedgesG (95% CI)		-0.107 (-0.549, 0.335)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.7
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline			
		n	41	38	79
		Mean	44.76	43.42	44.11
		SD, SE	15.287, 2.387	16.320, 2.648	15.705, 1.767
		Median	40.00	45.00	45.00
		Q1, Q3	35.00, 55.00	35.00, 55.00	35.00, 55.00
		Min, Max	10.0, 90.0	10.0, 70.0	10.0, 90.0
		Observed			
		n	41	39	80
		Mean	42.20	40.38	41.31
		SD, SE	18.168, 2.837	15.576, 2.494	16.872, 1.886
		Median	40.00	40.00	40.00
		Q1, Q3	30.00, 50.00	35.00, 50.00	30.00, 50.00
		Min, Max	10.0, 95.0	15.0, 75.0	10.0, 95.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.7
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline			
		n	41	38	79
		Mean	-2.56	-3.03	-2.78
		SD, SE	16.997, 2.655	16.338, 2.650	16.578, 1.865
		Median	-5.00	0.00	0.00
		Q1, Q3	-15.00, 10.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-35.0, 35.0	-40.0, 50.0	-40.0, 50.0
		GEE Estimates			
		LS Mean (SE)	-3.38 (3.961)	-4.57 (3.656)	
		95% CI	(-11.14, 4.39)	(-11.74, 2.59)	
		LS Mean Difference (SE)		-1.19 (3.287)	
		95% CI		(-7.64, 5.25)	
		p-value		0.7162	
		HedgesG (95% CI)		-0.027 (-0.469, 0.414)	

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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.7
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5		N_1	25	29	54
	Baseline	n	25	29	54
		Mean	53.20	60.17	56.94
		SD, SE	14.782, 2.956	15.725, 2.920	15.553, 2.117
		Median	50.00	60.00	60.00
		Q1, Q3	45.00, 65.00	55.00, 70.00	45.00, 65.00
		Min, Max	20.0, 85.0	25.0, 100.0	20.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.7
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline			
		n	25	29	54
		Mean	53.20	60.17	56.94
		SD, SE	14.782, 2.956	15.725, 2.920	15.553, 2.117
		Median	50.00	60.00	60.00
		Q1, Q3	45.00, 65.00	55.00, 70.00	45.00, 65.00
		Min, Max	20.0, 85.0	25.0, 100.0	20.0, 100.0
		Observed			
		n	25	29	54
		Mean	48.20	50.34	49.35
		SD, SE	16.638, 3.328	18.368, 3.411	17.457, 2.376
		Median	50.00	50.00	50.00
		Q1, Q3	35.00, 60.00	35.00, 65.00	35.00, 60.00
		Min, Max	25.0, 90.0	15.0, 90.0	15.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.7
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline			
		n	25	29	54
		Mean	-5.00	-9.83	-7.59
		SD, SE	13.070, 2.614	14.729, 2.735	14.067, 1.914
		Median	-5.00	-10.00	-5.00
		Q1, Q3	-15.00, 5.00	-20.00, 0.00	-20.00, 5.00
		Min, Max	-35.0, 15.0	-50.0, 15.0	-50.0, 15.0
		GEE Estimates			
		LS Mean (SE)	-1.31 (2.908)	-3.36 (2.914)	
		95% CI	(-7.01, 4.39)	(-9.07, 2.35)	
		LS Mean Difference (SE)		-2.05 (3.726)	
		95% CI		(-9.35, 5.25)	
		p-value		0.5823	
		HedgesG (95% CI)		-0.334 (-0.872, 0.205)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.7
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline			
		n	24	28	52
		Mean	52.50	59.11	56.06
		SD, SE	14.670, 2.995	14.910, 2.818	15.027, 2.084
		Median	50.00	60.00	57.50
		Q1, Q3	45.00, 62.50	55.00, 67.50	45.00, 65.00
		Min, Max	20.0, 85.0	25.0, 100.0	20.0, 100.0
		Observed			
		n	24	28	52
		Mean	50.42	47.50	48.85
		SD, SE	17.932, 3.660	18.534, 3.503	18.139, 2.515
		Median	50.00	45.00	50.00
		Q1, Q3	37.50, 60.00	32.50, 65.00	35.00, 62.50
		Min, Max	25.0, 100.0	5.0, 85.0	5.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.7
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline			
		n	24	28	52
		Mean	-2.08	-11.61	-7.21
		SD, SE	12.931, 2.640	18.361, 3.470	16.640, 2.307
		Median	0.00	-10.00	-5.00
		Q1, Q3	-12.50, 5.00	-25.00, 0.00	-15.00, 5.00
		Min, Max	-20.0, 25.0	-50.0, 15.0	-50.0, 25.0
		GEE Estimates			
		LS Mean (SE)	1.28 (2.909)	-5.50 (2.833)	
		95% CI	(-4.43, 6.98)	(-11.06, 0.05)	
		LS Mean Difference (SE)		-6.78 (4.022)	
		95% CI		(-14.66, 1.10)	
		p-value		0.0919	
		HedgesG (95% CI)		-0.572 (-1.128, -0.015)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.8
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	38.78	38.17	38.51
		SD, SE	10.891, 1.791	15.508, 2.831	13.056, 1.595
		Median	40.00	35.00	40.00
		Q1, Q3	35.00, 45.00	30.00, 50.00	30.00, 45.00
		Min, Max	10.0, 55.0	10.0, 70.0	10.0, 70.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.8
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline			
		n	37	30	67
		Mean	38.78	38.17	38.51
		SD, SE	10.891, 1.791	15.508, 2.831	13.056, 1.595
		Median	40.00	35.00	40.00
		Q1, Q3	35.00, 45.00	30.00, 50.00	30.00, 45.00
		Min, Max	10.0, 55.0	10.0, 70.0	10.0, 70.0
		Observed			
		n	37	30	67
		Mean	37.84	31.67	35.07
		SD, SE	14.603, 2.401	13.087, 2.389	14.182, 1.733
		Median	35.00	35.00	35.00
		Q1, Q3	30.00, 50.00	20.00, 40.00	25.00, 45.00
		Min, Max	5.0, 65.0	5.0, 65.0	5.0, 65.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.8
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-0.95	-6.50	-3.43
		SD, SE	13.634, 2.241	12.328, 2.251	13.263, 1.620
		Median	0.00	-5.00	-5.00
		Q1, Q3	-10.00, 10.00	-15.00, 0.00	-15.00, 10.00
		Min, Max	-30.0, 20.0	-30.0, 15.0	-30.0, 20.0
		GEE Estimates			
		LS Mean (SE)	-5.44 (3.986)	-11.54 (3.533)	
		95% CI	(-13.25, 2.37)	(-18.46, -4.61)	
		LS Mean Difference (SE)		-6.10 (2.817)	
		95% CI		(-11.62, -0.57)	
		p-value		0.0305	
		HedgesG (95% CI)		-0.414 (-0.900, 0.073)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.8
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline			
		n	37	30	67
		Mean	38.78	38.17	38.51
		SD, SE	10.891, 1.791	15.508, 2.831	13.056, 1.595
		Median	40.00	35.00	40.00
		Q1, Q3	35.00, 45.00	30.00, 50.00	30.00, 45.00
		Min, Max	10.0, 55.0	10.0, 70.0	10.0, 70.0
		Observed			
		n	37	30	67
		Mean	36.49	34.83	35.75
		SD, SE	14.666, 2.411	14.884, 2.717	14.675, 1.793
		Median	35.00	35.00	35.00
		Q1, Q3	25.00, 45.00	25.00, 40.00	25.00, 45.00
		Min, Max	10.0, 75.0	5.0, 75.0	5.0, 75.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.8
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-2.30	-3.33	-2.76
		SD, SE	16.898, 2.778	17.682, 3.228	17.129, 2.093
		Median	0.00	-2.50	0.00
		Q1, Q3	-15.00, 5.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-30.0, 35.0	-50.0, 50.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	-6.79 (3.873)	-8.37 (4.094)	
		95% CI	(-14.38, 0.80)	(-16.39, -0.35)	
		LS Mean Difference (SE)		-1.58 (3.448)	
		95% CI		(-8.34, 5.18)	
		p-value		0.6472	
		HedgesG (95% CI)		-0.058 (-0.540, 0.423)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.8
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8		N_1	29	38	67
	Baseline	n	29	37	66
		Mean	59.66	60.81	60.30
		SD, SE	12.459, 2.314	12.830, 2.109	12.584, 1.549
		Median	60.00	60.00	60.00
		Q1, Q3	50.00, 65.00	55.00, 65.00	50.00, 65.00
		Min, Max	40.0, 90.0	35.0, 100.0	35.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.8
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline			
		n	29	37	66
		Mean	59.66	60.81	60.30
		SD, SE	12.459, 2.314	12.830, 2.109	12.584, 1.549
		Median	60.00	60.00	60.00
		Q1, Q3	50.00, 65.00	55.00, 65.00	50.00, 65.00
		Min, Max	40.0, 90.0	35.0, 100.0	35.0, 100.0
		Observed			
		n	29	38	67
		Mean	51.72	52.89	52.39
		SD, SE	18.336, 3.405	16.991, 2.756	17.459, 2.133
		Median	50.00	55.00	55.00
		Q1, Q3	40.00, 65.00	40.00, 65.00	40.00, 65.00
		Min, Max	20.0, 90.0	15.0, 90.0	15.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.8
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline			
		n	29	37	66
		Mean	-7.93	-7.57	-7.73
		SD, SE	15.031, 2.791	15.349, 2.523	15.094, 1.858
		Median	-5.00	-5.00	-5.00
		Q1, Q3	-15.00, 0.00	-15.00, 5.00	-15.00, 0.00
		Min, Max	-35.0, 30.0	-50.0, 20.0	-50.0, 30.0
		GEE Estimates			
		LS Mean (SE)	-3.82 (3.064)	-3.09 (2.094)	
		95% CI	(-9.83, 2.18)	(-7.19, 1.02)	
		LS Mean Difference (SE)		0.73 (3.782)	
		95% CI		(-6.68, 8.15)	
		p-value		0.8461	
		HedgesG (95% CI)		0.023 (-0.463, 0.509)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.8
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline			
		n	28	36	64
		Mean	59.29	60.00	59.69
		SD, SE	12.525, 2.367	12.012, 2.002	12.146, 1.518
		Median	60.00	60.00	60.00
		Q1, Q3	50.00, 65.00	52.50, 65.00	50.00, 65.00
		Min, Max	40.0, 90.0	35.0, 100.0	35.0, 100.0
		Observed			
		n	28	37	65
		Mean	56.79	50.27	53.08
		SD, SE	16.455, 3.110	15.765, 2.592	16.267, 2.018
		Median	52.50	50.00	50.00
		Q1, Q3	45.00, 65.00	40.00, 60.00	45.00, 65.00
		Min, Max	30.0, 100.0	20.0, 85.0	20.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.8
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-2.50	-9.44	-6.41
		SD, SE	13.777, 2.604	17.311, 2.885	16.121, 2.015
		Median	0.00	-5.00	-2.50
		Q1, Q3	-10.00, 5.00	-20.00, 2.50	-15.00, 5.00
		Min, Max	-35.0, 20.0	-50.0, 20.0	-50.0, 20.0
		GEE Estimates			
		LS Mean (SE)	1.40 (2.773)	-5.30 (2.014)	
		95% CI	(-4.03, 6.83)	(-9.25, -1.35)	
		LS Mean Difference (SE)		-6.70 (3.597)	
		95% CI		(-13.75, 0.35)	
		p-value		0.0625	
		HedgesG (95% CI)		-0.425 (-0.925, 0.074)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.9
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50		N_1	42	32	74
	Baseline	n	42	32	74
		Mean	38.81	35.78	37.50
		SD, SE	9.678, 1.493	11.921, 2.107	10.735, 1.248
		Median	40.00	35.00	40.00
		Q1, Q3	35.00, 45.00	30.00, 45.00	35.00, 45.00
		Min, Max	10.0, 50.0	10.0, 50.0	10.0, 50.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.9
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Baseline			
		n	42	32	74
		Mean	38.81	35.78	37.50
		SD, SE	9.678, 1.493	11.921, 2.107	10.735, 1.248
		Median	40.00	35.00	40.00
		Q1, Q3	35.00, 45.00	30.00, 45.00	35.00, 45.00
		Min, Max	10.0, 50.0	10.0, 50.0	10.0, 50.0
		Observed			
		n	42	32	74
		Mean	38.33	32.66	35.88
		SD, SE	15.209, 2.347	14.311, 2.530	14.997, 1.743
		Median	35.00	35.00	35.00
		Q1, Q3	30.00, 50.00	20.00, 40.00	25.00, 45.00
		Min, Max	5.0, 80.0	5.0, 65.0	5.0, 80.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.9
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Change from Baseline			
		n	42	32	74
		Mean	-0.48	-3.13	-1.62
		SD, SE	13.651, 2.106	12.748, 2.253	13.244, 1.540
		Median	0.00	-2.50	0.00
		Q1, Q3	-10.00, 10.00	-10.00, 7.50	-10.00, 10.00
		Min, Max	-30.0, 30.0	-35.0, 20.0	-35.0, 30.0
		GEE Estimates			
		LS Mean (SE)	-1.92 (4.385)	-6.41 (3.780)	
		95% CI	(-10.51, 6.68)	(-13.82, 0.99)	
		LS Mean Difference (SE)		-4.49 (3.211)	
		95% CI		(-10.79, 1.80)	
		p-value		0.1617	
		HedgesG (95% CI)		-0.195 (-0.656, 0.266)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.9
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Baseline			
		n	42	32	74
		Mean	38.81	35.78	37.50
		SD, SE	9.678, 1.493	11.921, 2.107	10.735, 1.248
		Median	40.00	35.00	40.00
		Q1, Q3	35.00, 45.00	30.00, 45.00	35.00, 45.00
		Min, Max	10.0, 50.0	10.0, 50.0	10.0, 50.0
		Observed			
		n	42	32	74
		Mean	39.17	36.56	38.04
		SD, SE	15.923, 2.457	12.791, 2.261	14.614, 1.699
		Median	40.00	37.50	40.00
		Q1, Q3	30.00, 50.00	30.00, 45.00	30.00, 50.00
		Min, Max	10.0, 75.0	15.0, 60.0	10.0, 75.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.9
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Change from Baseline			
		n	42	32	74
		Mean	0.36	0.78	0.54
		SD, SE	16.056, 2.477	14.148, 2.501	15.161, 1.762
		Median	0.00	0.00	0.00
		Q1, Q3	-15.00, 15.00	-5.00, 5.00	-10.00, 10.00
		Min, Max	-30.0, 35.0	-30.0, 50.0	-30.0, 50.0
		GEE Estimates			
		LS Mean (SE)	-1.09 (4.583)	-2.51 (3.810)	
		95% CI	(-10.07, 7.90)	(-9.97, 4.96)	
		LS Mean Difference (SE)		-1.42 (3.147)	
		95% CI		(-7.59, 4.75)	
		p-value		0.6516	
		HedgesG (95% CI)		0.027 (-0.433, 0.487)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.9
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50		N_1	24	35	59
	Baseline	n	24	35	59
		Mean	63.96	64.29	64.15
		SD, SE	9.778, 1.996	10.010, 1.692	9.833, 1.280
		Median	60.00	60.00	60.00
		Q1, Q3	55.00, 70.00	55.00, 70.00	55.00, 70.00
		Min, Max	55.0, 90.0	55.0, 100.0	55.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.9
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Baseline			
		n	24	35	59
		Mean	63.96	64.29	64.15
		SD, SE	9.778, 1.996	10.010, 1.692	9.833, 1.280
		Median	60.00	60.00	60.00
		Q1, Q3	55.00, 70.00	55.00, 70.00	55.00, 70.00
		Min, Max	55.0, 90.0	55.0, 100.0	55.0, 100.0
		Observed			
		n	24	35	59
		Mean	53.75	53.57	53.64
		SD, SE	17.585, 3.590	16.741, 2.830	16.939, 2.205
		Median	52.50	55.00	55.00
		Q1, Q3	45.00, 65.00	40.00, 65.00	45.00, 65.00
		Min, Max	20.0, 90.0	15.0, 90.0	15.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.9
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Change from Baseline			
		n	24	35	59
		Mean	-10.21	-10.71	-10.51
		SD, SE	14.331, 2.925	14.253, 2.409	14.163, 1.844
		Median	-5.00	-10.00	-5.00
		Q1, Q3	-25.00, 0.00	-20.00, 0.00	-25.00, 0.00
		Min, Max	-35.0, 10.0	-50.0, 10.0	-50.0, 10.0
		GEE Estimates			
		LS Mean (SE)	-5.95 (3.211)	-5.82 (2.398)	
		95% CI	(-12.24, 0.34)	(-10.52, -1.12)	
		LS Mean Difference (SE)		0.13 (3.894)	
		95% CI		(-7.50, 7.76)	
		p-value		0.9738	
		HedgesG (95% CI)		-0.034 (-0.554, 0.485)	

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The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.9
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Baseline			
		n	23	34	57
		Mean	63.70	63.53	63.60
		SD, SE	9.911, 2.067	9.090, 1.559	9.342, 1.237
		Median	60.00	60.00	60.00
		Q1, Q3	55.00, 70.00	55.00, 70.00	55.00, 70.00
		Min, Max	55.0, 90.0	55.0, 100.0	55.0, 100.0
		Observed			
		n	23	34	57
		Mean	56.30	49.85	52.46
		SD, SE	17.659, 3.682	18.525, 3.177	18.301, 2.424
		Median	50.00	47.50	50.00
		Q1, Q3	45.00, 65.00	40.00, 65.00	40.00, 65.00
		Min, Max	35.0, 100.0	5.0, 85.0	5.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.9
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Change from Baseline			
		n	23	34	57
		Mean	-7.39	-13.68	-11.14
		SD, SE	13.388, 2.792	17.851, 3.061	16.367, 2.168
		Median	-10.00	-15.00	-10.00
		Q1, Q3	-20.00, 5.00	-30.00, 0.00	-20.00, 0.00
		Min, Max	-35.0, 15.0	-50.0, 20.0	-50.0, 20.0
		GEE Estimates			
		LS Mean (SE)	-3.28 (3.191)	-8.99 (2.647)	
		95% CI	(-9.53, 2.98)	(-14.18, -3.80)	
		LS Mean Difference (SE)		-5.71 (4.105)	
		95% CI		(-13.76, 2.33)	
		p-value		0.1641	
		HedgesG (95% CI)		-0.376 (-0.909, 0.158)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.10
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5		N_1	37	30	67
	Baseline	n	37	29	66
		Mean	38.78	36.21	37.65
		SD, SE	10.891, 1.791	13.605, 2.526	12.128, 1.493
		Median	40.00	35.00	40.00
		Q1, Q3	35.00, 45.00	30.00, 45.00	30.00, 45.00
		Min, Max	10.0, 55.0	10.0, 60.0	10.0, 60.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.10
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Baseline			
		n	37	29	66
		Mean	38.78	36.21	37.65
		SD, SE	10.891, 1.791	13.605, 2.526	12.128, 1.493
		Median	40.00	35.00	40.00
		Q1, Q3	35.00, 45.00	30.00, 45.00	30.00, 45.00
		Min, Max	10.0, 55.0	10.0, 60.0	10.0, 60.0
		Observed			
		n	37	30	67
		Mean	37.84	32.50	35.45
		SD, SE	14.603, 2.401	13.756, 2.511	14.374, 1.756
		Median	35.00	35.00	35.00
		Q1, Q3	30.00, 50.00	20.00, 40.00	25.00, 45.00
		Min, Max	5.0, 65.0	5.0, 65.0	5.0, 65.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.10
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Change from Baseline			
		n	37	29	66
		Mean	-0.95	-3.97	-2.27
		SD, SE	13.634, 2.241	12.913, 2.398	13.306, 1.638
		Median	0.00	-5.00	-2.50
		Q1, Q3	-10.00, 10.00	-15.00, 5.00	-10.00, 10.00
		Min, Max	-30.0, 20.0	-30.0, 20.0	-30.0, 20.0
		GEE Estimates			
		LS Mean (SE)	-5.36 (3.993)	-10.16 (3.571)	
		95% CI	(-13.18, 2.47)	(-17.16, -3.16)	
		LS Mean Difference (SE)		-4.81 (3.014)	
		95% CI		(-10.71, 1.10)	
		p-value		0.1108	
		HedgesG (95% CI)		-0.221 (-0.708, 0.267)	

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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.10
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Baseline			
		n	37	29	66
		Mean	38.78	36.21	37.65
		SD, SE	10.891, 1.791	13.605, 2.526	12.128, 1.493
		Median	40.00	35.00	40.00
		Q1, Q3	35.00, 45.00	30.00, 45.00	30.00, 45.00
		Min, Max	10.0, 55.0	10.0, 60.0	10.0, 60.0
		Observed			
		n	37	30	67
		Mean	36.49	34.50	35.60
		SD, SE	14.666, 2.411	13.088, 2.390	13.913, 1.700
		Median	35.00	37.50	35.00
		Q1, Q3	25.00, 45.00	30.00, 40.00	25.00, 45.00
		Min, Max	10.0, 75.0	5.0, 60.0	5.0, 75.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.10
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Change from Baseline			
		n	37	29	66
		Mean	-2.30	-1.90	-2.12
		SD, SE	16.898, 2.778	17.082, 3.172	16.849, 2.074
		Median	0.00	0.00	0.00
		Q1, Q3	-15.00, 5.00	-10.00, 5.00	-15.00, 5.00
		Min, Max	-30.0, 35.0	-50.0, 50.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	-6.71 (3.879)	-8.09 (4.014)	
		95% CI	(-14.31, 0.90)	(-15.96, -0.23)	
		LS Mean Difference (SE)		-1.38 (3.353)	
		95% CI		(-7.96, 5.19)	
		p-value		0.6796	
		HedgesG (95% CI)		0.023 (-0.463, 0.509)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.10
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	59.66	61.71	60.82
		SD, SE	12.459, 2.314	12.207, 1.980	12.266, 1.499
		Median	60.00	60.00	60.00
		Q1, Q3	50.00, 65.00	55.00, 70.00	55.00, 70.00
		Min, Max	40.0, 90.0	35.0, 100.0	35.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.10
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Baseline			
		n	29	38	67
		Mean	59.66	61.71	60.82
		SD, SE	12.459, 2.314	12.207, 1.980	12.266, 1.499
		Median	60.00	60.00	60.00
		Q1, Q3	50.00, 65.00	55.00, 70.00	55.00, 70.00
		Min, Max	40.0, 90.0	35.0, 100.0	35.0, 100.0
		Observed			
		n	29	38	67
		Mean	51.72	52.24	52.01
		SD, SE	18.336, 3.405	17.387, 2.820	17.668, 2.159
		Median	50.00	55.00	55.00
		Q1, Q3	40.00, 65.00	35.00, 65.00	35.00, 65.00
		Min, Max	20.0, 90.0	15.0, 90.0	15.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.10
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-7.93	-9.47	-8.81
		SD, SE	15.031, 2.791	14.463, 2.346	14.619, 1.786
		Median	-5.00	-5.00	-5.00
		Q1, Q3	-15.00, 0.00	-20.00, 0.00	-20.00, 0.00
		Min, Max	-35.0, 30.0	-50.0, 10.0	-50.0, 30.0
		GEE Estimates			
		LS Mean (SE)	-3.26 (3.100)	-4.27 (2.008)	
		95% CI	(-9.34, 2.81)	(-8.21, -0.33)	
		LS Mean Difference (SE)		-1.01 (3.728)	
		95% CI		(-8.31, 6.30)	
		p-value		0.7870	
		HedgesG (95% CI)		-0.102 (-0.586, 0.381)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.10
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Baseline			
		n	28	37	65
		Mean	59.29	60.95	60.23
		SD, SE	12.525, 2.367	11.416, 1.877	11.840, 1.469
		Median	60.00	60.00	60.00
		Q1, Q3	50.00, 65.00	55.00, 65.00	55.00, 65.00
		Min, Max	40.0, 90.0	35.0, 100.0	35.0, 100.0
		Observed			
		n	28	37	65
		Mean	56.79	50.54	53.23
		SD, SE	16.455, 3.110	16.741, 2.752	16.781, 2.081
		Median	52.50	50.00	50.00
		Q1, Q3	45.00, 65.00	40.00, 65.00	45.00, 65.00
		Min, Max	30.0, 100.0	20.0, 85.0	20.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.10
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Change from Baseline			
		n	28	37	65
		Mean	-2.50	-10.41	-7.00
		SD, SE	13.777, 2.604	17.336, 2.850	16.269, 2.018
		Median	0.00	-10.00	-5.00
		Q1, Q3	-10.00, 5.00	-25.00, 0.00	-15.00, 5.00
		Min, Max	-35.0, 20.0	-50.0, 20.0	-50.0, 20.0
		GEE Estimates			
		LS Mean (SE)	1.97 (2.803)	-5.47 (2.003)	
		95% CI	(-3.53, 7.46)	(-9.40, -1.55)	
		LS Mean Difference (SE)		-7.44 (3.677)	
		95% CI		(-14.65, -0.24)	
		p-value		0.0430	
		HedgesG (95% CI)		-0.483 (-0.981, 0.015)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.11
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes		N_1	44	47	91
	Baseline	n	44	46	90
		Mean	49.32	55.00	52.22
		SD, SE	14.887, 2.244	15.670, 2.310	15.472, 1.631
		Median	45.00	55.00	55.00
		Q1, Q3	40.00, 60.00	45.00, 65.00	40.00, 60.00
		Min, Max	20.0, 85.0	15.0, 100.0	15.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.11
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	44	46	90
		Mean	49.32	55.00	52.22
		SD, SE	14.887, 2.244	15.670, 2.310	15.472, 1.631
		Median	45.00	55.00	55.00
		Q1, Q3	40.00, 60.00	45.00, 65.00	40.00, 60.00
		Min, Max	20.0, 85.0	15.0, 100.0	15.0, 100.0
		Observed			
		n	44	47	91
		Mean	44.77	47.34	46.10
		SD, SE	16.029, 2.416	17.750, 2.589	16.895, 1.771
		Median	45.00	45.00	45.00
		Q1, Q3	30.00, 57.50	35.00, 60.00	35.00, 60.00
		Min, Max	20.0, 90.0	15.0, 90.0	15.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.11
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	44	46	90
		Mean	-4.55	-7.50	-6.06
		SD, SE	15.470, 2.332	13.693, 2.019	14.582, 1.537
		Median	-5.00	-5.00	-5.00
		Q1, Q3	-15.00, 10.00	-15.00, 0.00	-15.00, 5.00
		Min, Max	-35.0, 20.0	-50.0, 20.0	-50.0, 20.0
		GEE Estimates			
		LS Mean (SE)	-6.24 (3.093)	-6.70 (2.753)	
		95% CI	(-12.30, -0.18)	(-12.09, -1.30)	
		LS Mean Difference (SE)		-0.46 (3.010)	
		95% CI		(-6.36, 5.44)	
		p-value		0.8792	
		HedgesG (95% CI)		-0.199 (-0.613, 0.216)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.11
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	43	45	88
		Mean	48.84	54.22	51.59
		SD, SE	14.713, 2.244	14.922, 2.224	14.982, 1.597
		Median	45.00	55.00	52.50
		Q1, Q3	40.00, 60.00	45.00, 65.00	40.00, 60.00
		Min, Max	20.0, 85.0	15.0, 100.0	15.0, 100.0
		Observed			
		n	43	46	89
		Mean	46.74	44.67	45.67
		SD, SE	16.105, 2.456	16.846, 2.484	16.432, 1.742
		Median	45.00	42.50	45.00
		Q1, Q3	35.00, 60.00	35.00, 55.00	35.00, 55.00
		Min, Max	20.0, 100.0	5.0, 75.0	5.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.11
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	43	45	88
		Mean	-2.09	-9.44	-5.85
		SD, SE	15.362, 2.343	15.927, 2.374	15.996, 1.705
		Median	0.00	-5.00	-5.00
		Q1, Q3	-15.00, 5.00	-15.00, 0.00	-15.00, 5.00
		Min, Max	-35.0, 35.0	-50.0, 20.0	-50.0, 35.0
		GEE Estimates			
		LS Mean (SE)	-3.99 (3.142)	-8.92 (2.453)	
		95% CI	(-10.15, 2.17)	(-13.73, -4.11)	
		LS Mean Difference (SE)		-4.93 (3.063)	
		95% CI		(-10.94, 1.07)	
		p-value		0.1075	
		HedgesG (95% CI)		-0.460 (-0.884, -0.037)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.11
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No		N_1	22	21	43
	Baseline	n	22	21	43
		Mean	45.23	41.19	43.26
		SD, SE	16.795, 3.581	19.487, 4.253	18.057, 2.754
		Median	45.00	35.00	45.00
		Q1, Q3	35.00, 55.00	30.00, 60.00	35.00, 55.00
		Min, Max	10.0, 90.0	10.0, 75.0	10.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.11
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Baseline			
		n	22	21	43
		Mean	45.23	41.19	43.26
		SD, SE	16.795, 3.581	19.487, 4.253	18.057, 2.754
		Median	45.00	35.00	45.00
		Q1, Q3	35.00, 55.00	30.00, 60.00	35.00, 55.00
		Min, Max	10.0, 90.0	10.0, 75.0	10.0, 90.0
		Observed			
		n	22	21	43
		Mean	42.27	35.00	38.72
		SD, SE	20.801, 4.435	18.028, 3.934	19.612, 2.991
		Median	42.50	35.00	35.00
		Q1, Q3	25.00, 50.00	20.00, 45.00	25.00, 50.00
		Min, Max	5.0, 90.0	5.0, 80.0	5.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.11
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Change from Baseline			
		n	22	21	43
		Mean	-2.95	-6.19	-4.53
		SD, SE	12.878, 2.746	14.908, 3.253	13.836, 2.110
		Median	-2.50	0.00	0.00
		Q1, Q3	-10.00, 5.00	-15.00, 5.00	-10.00, 5.00
		Min, Max	-30.0, 30.0	-40.0, 15.0	-40.0, 30.0
		GEE Estimates			
		LS Mean (SE)	-1.45 (4.388)	-6.55 (3.312)	
		95% CI	(-10.05, 7.16)	(-13.04, -0.05)	
		LS Mean Difference (SE)		-5.10 (4.576)	
		95% CI		(-14.07, 3.87)	
		p-value		0.2651	
		HedgesG (95% CI)		-0.223 (-0.823, 0.377)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.11
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Baseline			
		n	22	21	43
		Mean	45.23	41.19	43.26
		SD, SE	16.795, 3.581	19.487, 4.253	18.057, 2.754
		Median	45.00	35.00	45.00
		Q1, Q3	35.00, 55.00	30.00, 60.00	35.00, 55.00
		Min, Max	10.0, 90.0	10.0, 75.0	10.0, 90.0
		Observed			
		n	22	21	43
		Mean	42.27	40.48	41.40
		SD, SE	22.293, 4.753	17.742, 3.872	19.980, 3.047
		Median	45.00	40.00	40.00
		Q1, Q3	25.00, 50.00	30.00, 50.00	25.00, 50.00
		Min, Max	10.0, 95.0	15.0, 85.0	10.0, 95.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.11
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Change from Baseline			
		n	22	21	43
		Mean	-2.95	-0.71	-1.86
		SD, SE	16.158, 3.445	19.893, 4.341	17.896, 2.729
		Median	0.00	0.00	0.00
		Q1, Q3	-20.00, 15.00	-10.00, 10.00	-15.00, 10.00
		Min, Max	-30.0, 25.0	-40.0, 50.0	-40.0, 50.0
		GEE Estimates			
		LS Mean (SE)	-1.45 (4.896)	-1.07 (3.696)	
		95% CI	(-11.04, 8.15)	(-8.31, 6.17)	
		LS Mean Difference (SE)		0.38 (5.050)	
		95% CI		(-9.52, 10.27)	
		p-value		0.9405	
		HedgesG (95% CI)		0.119 (-0.480, 0.717)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.12
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes		N_1	13	17	30
	Baseline	n	13	17	30
		Mean	46.54	57.65	52.83
		SD, SE	14.051, 3.897	19.852, 4.815	18.179, 3.319
		Median	45.00	55.00	52.50
		Q1, Q3	40.00, 60.00	45.00, 65.00	40.00, 65.00
		Min, Max	25.0, 70.0	15.0, 100.0	15.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.12
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	13	17	30
		Mean	46.54	57.65	52.83
		SD, SE	14.051, 3.897	19.852, 4.815	18.179, 3.319
		Median	45.00	55.00	52.50
		Q1, Q3	40.00, 60.00	45.00, 65.00	40.00, 65.00
		Min, Max	25.0, 70.0	15.0, 100.0	15.0, 100.0
		Observed			
		n	13	17	30
		Mean	44.23	49.71	47.33
		SD, SE	15.117, 4.193	22.463, 5.448	19.508, 3.562
		Median	45.00	50.00	50.00
		Q1, Q3	35.00, 60.00	30.00, 70.00	30.00, 60.00
		Min, Max	20.0, 65.0	15.0, 90.0	15.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.12
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	13	17	30
		Mean	-2.31	-7.94	-5.50
		SD, SE	18.553, 5.146	15.315, 3.715	16.731, 3.055
		Median	5.00	-5.00	-5.00
		Q1, Q3	-20.00, 10.00	-10.00, 0.00	-20.00, 5.00
		Min, Max	-35.0, 20.0	-50.0, 10.0	-50.0, 20.0
		GEE Estimates			
		LS Mean (SE)	-4.27 (3.990)	-4.82 (4.146)	
		95% CI	(-12.09, 3.55)	(-12.95, 3.31)	
		LS Mean Difference (SE)		-0.55 (5.806)	
		95% CI		(-11.92, 10.83)	
		p-value		0.9251	
		HedgesG (95% CI)		-0.316 (-1.042, 0.411)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.12
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	13	16	29
		Mean	46.54	55.63	51.55
		SD, SE	14.051, 3.897	18.608, 4.652	17.066, 3.169
		Median	45.00	55.00	50.00
		Q1, Q3	40.00, 60.00	42.50, 65.00	40.00, 65.00
		Min, Max	25.0, 70.0	15.0, 100.0	15.0, 100.0
		Observed			
		n	13	16	29
		Mean	46.54	48.13	47.41
		SD, SE	15.328, 4.251	18.154, 4.539	16.670, 3.096
		Median	50.00	50.00	50.00
		Q1, Q3	30.00, 60.00	35.00, 60.00	35.00, 60.00
		Min, Max	25.0, 75.0	15.0, 75.0	15.0, 75.0

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The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.12
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	13	16	29
		Mean	0.00	-7.50	-4.14
		SD, SE	17.795, 4.935	17.512, 4.378	17.732, 3.293
		Median	-5.00	-2.50	-5.00
		Q1, Q3	-10.00, 10.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-20.0, 35.0	-50.0, 15.0	-50.0, 35.0
		GEE Estimates			
		LS Mean (SE)	-1.97 (4.006)	-5.18 (3.949)	
		95% CI	(-9.82, 5.89)	(-12.92, 2.56)	
		LS Mean Difference (SE)		-3.21 (5.400)	
		95% CI		(-13.80, 7.37)	
		p-value		0.5516	
		HedgesG (95% CI)		-0.399 (-1.138, 0.340)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.12
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No		N_1	53	51	104
	Baseline	n	53	50	103
		Mean	48.30	48.30	48.30
		SD, SE	15.991, 2.197	16.891, 2.389	16.353, 1.611
		Median	45.00	50.00	50.00
		Q1, Q3	40.00, 55.00	35.00, 60.00	35.00, 60.00
		Min, Max	10.0, 90.0	10.0, 75.0	10.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.12
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Baseline			
		n	53	50	103
		Mean	48.30	48.30	48.30
		SD, SE	15.991, 2.197	16.891, 2.389	16.353, 1.611
		Median	45.00	50.00	50.00
		Q1, Q3	40.00, 55.00	35.00, 60.00	35.00, 60.00
		Min, Max	10.0, 90.0	10.0, 75.0	10.0, 90.0
		Observed			
		n	53	51	104
		Mean	43.87	41.47	42.69
		SD, SE	18.336, 2.519	16.891, 2.365	17.597, 1.726
		Median	45.00	40.00	40.00
		Q1, Q3	30.00, 50.00	30.00, 55.00	30.00, 55.00
		Min, Max	5.0, 90.0	5.0, 80.0	5.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.12
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Change from Baseline			
		n	53	50	103
		Mean	-4.43	-6.80	-5.58
		SD, SE	13.611, 1.870	13.656, 1.931	13.618, 1.342
		Median	-5.00	-5.00	-5.00
		Q1, Q3	-10.00, 5.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-35.0, 30.0	-40.0, 20.0	-40.0, 30.0
		GEE Estimates			
		LS Mean (SE)	-3.00 (3.059)	-5.46 (2.579)	
		95% CI	(-9.00, 3.00)	(-10.51, -0.41)	
		LS Mean Difference (SE)		-2.46 (2.590)	
		95% CI		(-7.54, 2.62)	
		p-value		0.3422	
		HedgesG (95% CI)		-0.171 (-0.558, 0.217)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.12
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Baseline			
		n	52	50	102
		Mean	47.88	48.30	48.09
		SD, SE	15.853, 2.198	16.891, 2.389	16.290, 1.613
		Median	45.00	50.00	50.00
		Q1, Q3	40.00, 55.00	35.00, 60.00	35.00, 60.00
		Min, Max	10.0, 90.0	10.0, 75.0	10.0, 90.0
		Observed			
		n	52	51	103
		Mean	44.90	41.86	43.40
		SD, SE	19.187, 2.661	16.672, 2.335	17.963, 1.770
		Median	45.00	40.00	40.00
		Q1, Q3	32.50, 50.00	30.00, 55.00	30.00, 50.00
		Min, Max	10.0, 100.0	5.0, 85.0	5.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.12
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Change from Baseline			
		n	52	50	102
		Mean	-2.98	-6.40	-4.66
		SD, SE	15.025, 2.084	17.815, 2.519	16.460, 1.630
		Median	0.00	-5.00	0.00
		Q1, Q3	-15.00, 5.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-35.0, 30.0	-50.0, 50.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	-1.72 (3.270)	-5.06 (2.818)	
		95% CI	(-8.13, 4.69)	(-10.58, 0.46)	
		LS Mean Difference (SE)		-3.34 (2.902)	
		95% CI		(-9.03, 2.35)	
		p-value		0.2502	
		HedgesG (95% CI)		-0.204 (-0.593, 0.185)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.14
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes		N_1	38	32	70
	Baseline	n	38	32	70
		Mean	49.08	51.88	50.36
		SD, SE	12.458, 2.021	21.355, 3.775	17.032, 2.036
		Median	47.50	55.00	50.00
		Q1, Q3	40.00, 60.00	37.50, 65.00	40.00, 60.00
		Min, Max	25.0, 80.0	10.0, 100.0	10.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.14
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Baseline			
		n	38	32	70
		Mean	49.08	51.88	50.36
		SD, SE	12.458, 2.021	21.355, 3.775	17.032, 2.036
		Median	47.50	55.00	50.00
		Q1, Q3	40.00, 60.00	37.50, 65.00	40.00, 60.00
		Min, Max	25.0, 80.0	10.0, 100.0	10.0, 100.0
		Observed			
		n	38	32	70
		Mean	45.53	42.19	44.00
		SD, SE	15.457, 2.507	19.631, 3.470	17.437, 2.084
		Median	50.00	35.00	42.50
		Q1, Q3	30.00, 60.00	30.00, 60.00	30.00, 60.00
		Min, Max	20.0, 80.0	10.0, 90.0	10.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.14
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Change from Baseline			
		n	38	32	70
		Mean	-3.55	-9.69	-6.36
		SD, SE	14.515, 2.355	13.497, 2.386	14.293, 1.708
		Median	-5.00	-10.00	-5.00
		Q1, Q3	-15.00, 10.00	-20.00, 0.00	-15.00, 5.00
		Min, Max	-35.0, 30.0	-40.0, 10.0	-40.0, 30.0
		GEE Estimates			
		LS Mean (SE)	-0.25 (2.898)	-5.05 (2.556)	
		95% CI	(-5.93, 5.43)	(-10.06, -0.04)	
		LS Mean Difference (SE)		-4.80 (3.117)	
		95% CI		(-10.91, 1.31)	
		p-value		0.1237	
		HedgesG (95% CI)		-0.425 (-0.901, 0.050)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.14
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Baseline			
		n	37	31	68
		Mean	48.51	50.65	49.49
		SD, SE	12.126, 1.993	20.524, 3.686	16.394, 1.988
		Median	45.00	55.00	50.00
		Q1, Q3	40.00, 60.00	35.00, 60.00	40.00, 60.00
		Min, Max	25.0, 80.0	10.0, 100.0	10.0, 100.0
		Observed			
		n	37	31	68
		Mean	46.49	42.90	44.85
		SD, SE	14.086, 2.316	18.293, 3.285	16.115, 1.954
		Median	45.00	40.00	45.00
		Q1, Q3	35.00, 55.00	30.00, 55.00	35.00, 55.00
		Min, Max	20.0, 80.0	15.0, 85.0	15.0, 85.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.14
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Change from Baseline			
		n	37	31	68
		Mean	-2.03	-7.74	-4.63
		SD, SE	15.919, 2.617	20.201, 3.628	18.086, 2.193
		Median	0.00	-5.00	-5.00
		Q1, Q3	-15.00, 5.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-35.0, 35.0	-50.0, 50.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	0.98 (3.038)	-3.57 (2.909)	
		95% CI	(-4.98, 6.93)	(-9.28, 2.13)	
		LS Mean Difference (SE)		-4.55 (3.412)	
		95% CI		(-11.24, 2.14)	
		p-value		0.1824	
		HedgesG (95% CI)		-0.309 (-0.789, 0.171)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.14
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No		N_1	28	36	64
	Baseline	n	28	35	63
		Mean	46.43	49.57	48.17
		SD, SE	19.093, 3.608	14.520, 2.454	16.639, 2.096
		Median	45.00	50.00	50.00
		Q1, Q3	35.00, 55.00	35.00, 60.00	35.00, 60.00
		Min, Max	10.0, 90.0	10.0, 70.0	10.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.14
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Baseline			
		n	28	35	63
		Mean	46.43	49.57	48.17
		SD, SE	19.093, 3.608	14.520, 2.454	16.639, 2.096
		Median	45.00	50.00	50.00
		Q1, Q3	35.00, 55.00	35.00, 60.00	35.00, 60.00
		Min, Max	10.0, 90.0	10.0, 70.0	10.0, 90.0
		Observed			
		n	28	36	64
		Mean	41.79	44.72	43.44
		SD, SE	20.331, 3.842	17.846, 2.974	18.875, 2.359
		Median	40.00	45.00	45.00
		Q1, Q3	30.00, 50.00	35.00, 60.00	35.00, 57.50
		Min, Max	5.0, 90.0	5.0, 75.0	5.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.14
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Change from Baseline			
		n	28	35	63
		Mean	-4.64	-4.71	-4.68
		SD, SE	14.903, 2.816	14.191, 2.399	14.393, 1.813
		Median	0.00	-5.00	0.00
		Q1, Q3	-12.50, 5.00	-10.00, 5.00	-10.00, 5.00
		Min, Max	-35.0, 20.0	-50.0, 20.0	-50.0, 20.0
		GEE Estimates			
		LS Mean (SE)	-6.18 (4.753)	-5.86 (4.332)	
		95% CI	(-15.50, 3.13)	(-14.35, 2.62)	
		LS Mean Difference (SE)		0.32 (3.485)	
		95% CI		(-6.51, 7.15)	
		p-value		0.9271	
		HedgesG (95% CI)		-0.005 (-0.502, 0.492)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.14
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Baseline			
		n	28	35	63
		Mean	46.43	49.57	48.17
		SD, SE	19.093, 3.608	14.520, 2.454	16.639, 2.096
		Median	45.00	50.00	50.00
		Q1, Q3	35.00, 55.00	35.00, 60.00	35.00, 60.00
		Min, Max	10.0, 90.0	10.0, 70.0	10.0, 90.0
		Observed			
		n	28	36	64
		Mean	43.57	43.75	43.67
		SD, SE	23.048, 4.356	16.273, 2.712	19.360, 2.420
		Median	42.50	40.00	40.00
		Q1, Q3	27.50, 50.00	35.00, 55.00	30.00, 55.00
		Min, Max	10.0, 100.0	5.0, 75.0	5.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.14
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Change from Baseline			
		n	28	35	63
		Mean	-2.86	-5.71	-4.44
		SD, SE	15.241, 2.880	15.202, 2.570	15.163, 1.910
		Median	0.00	0.00	0.00
		Q1, Q3	-15.00, 5.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-30.0, 30.0	-50.0, 20.0	-50.0, 30.0
		GEE Estimates			
		LS Mean (SE)	-4.40 (4.915)	-6.86 (4.343)	
		95% CI	(-14.03, 5.24)	(-15.38, 1.65)	
		LS Mean Difference (SE)		-2.47 (3.715)	
		95% CI		(-9.75, 4.81)	
		p-value		0.5067	
		HedgesG (95% CI)		-0.182 (-0.680, 0.316)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.15
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High		N_1	29	37	66
	Baseline	n	29	37	66
		Mean	53.79	54.46	54.17
		SD, SE	13.205, 2.452	18.589, 3.056	16.328, 2.010
		Median	55.00	55.00	55.00
		Q1, Q3	40.00, 60.00	45.00, 65.00	45.00, 65.00
		Min, Max	35.0, 85.0	10.0, 100.0	10.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.15
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Baseline			
		n	29	37	66
		Mean	53.79	54.46	54.17
		SD, SE	13.205, 2.452	18.589, 3.056	16.328, 2.010
		Median	55.00	55.00	55.00
		Q1, Q3	40.00, 60.00	45.00, 65.00	45.00, 65.00
		Min, Max	35.0, 85.0	10.0, 100.0	10.0, 100.0
		Observed			
		n	29	37	66
		Mean	52.24	48.78	50.30
		SD, SE	15.844, 2.942	19.840, 3.262	18.142, 2.233
		Median	50.00	55.00	50.00
		Q1, Q3	45.00, 60.00	35.00, 65.00	35.00, 65.00
		Min, Max	25.0, 90.0	15.0, 90.0	15.0, 90.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.15
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Change from Baseline			
		n	29	37	66
		Mean	-1.55	-5.68	-3.86
		SD, SE	15.125, 2.809	14.961, 2.460	15.059, 1.854
		Median	0.00	-5.00	0.00
		Q1, Q3	-15.00, 10.00	-10.00, 5.00	-15.00, 5.00
		Min, Max	-35.0, 30.0	-50.0, 20.0	-50.0, 30.0
		GEE Estimates			
		LS Mean (SE)	1.68 (2.737)	-2.75 (2.537)	
		95% CI	(-3.68, 7.05)	(-7.72, 2.23)	
		LS Mean Difference (SE)		-4.43 (3.600)	
		95% CI		(-11.48, 2.63)	
		p-value		0.2188	
		HedgesG (95% CI)		-0.267 (-0.755, 0.221)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.15
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Baseline			
		n	28	36	64
		Mean	53.21	53.47	53.36
		SD, SE	13.068, 2.470	17.841, 2.974	15.813, 1.977
		Median	52.50	55.00	55.00
		Q1, Q3	40.00, 60.00	45.00, 65.00	42.50, 65.00
		Min, Max	35.0, 85.0	10.0, 100.0	10.0, 100.0
		Observed			
		n	28	36	64
		Mean	51.25	48.33	49.61
		SD, SE	17.031, 3.219	17.071, 2.845	16.980, 2.123
		Median	50.00	47.50	50.00
		Q1, Q3	40.00, 62.50	37.50, 60.00	40.00, 60.00
		Min, Max	20.0, 100.0	15.0, 85.0	15.0, 100.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.15
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-1.96	-5.14	-3.75
		SD, SE	14.359, 2.714	18.535, 3.089	16.785, 2.098
		Median	0.00	0.00	0.00
		Q1, Q3	-12.50, 7.50	-15.00, 5.00	-15.00, 5.00
		Min, Max	-35.0, 30.0	-50.0, 50.0	-50.0, 50.0
		GEE Estimates			
		LS Mean (SE)	0.90 (2.854)	-2.61 (2.740)	
		95% CI	(-4.69, 6.49)	(-7.98, 2.76)	
		LS Mean Difference (SE)		-3.51 (3.517)	
		95% CI		(-10.40, 3.38)	
		p-value		0.3184	
		HedgesG (95% CI)		-0.183 (-0.678, 0.312)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.15
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low		N_1	36	30	66
	Baseline	n	36	30	66
		Mean	42.08	46.00	43.86
		SD, SE	13.958, 2.326	16.369, 2.988	15.110, 1.860
		Median	45.00	47.50	45.00
		Q1, Q3	35.00, 50.00	35.00, 60.00	35.00, 55.00
		Min, Max	10.0, 70.0	10.0, 75.0	10.0, 75.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.15
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Baseline			
		n	36	30	66
		Mean	42.08	46.00	43.86
		SD, SE	13.958, 2.326	16.369, 2.988	15.110, 1.860
		Median	45.00	47.50	45.00
		Q1, Q3	35.00, 50.00	35.00, 60.00	35.00, 55.00
		Min, Max	10.0, 70.0	10.0, 75.0	10.0, 75.0
		Observed			
		n	36	30	66
		Mean	35.97	37.17	36.52
		SD, SE	13.929, 2.322	15.295, 2.792	14.464, 1.780
		Median	35.00	40.00	35.00
		Q1, Q3	25.00, 45.00	25.00, 45.00	25.00, 45.00
		Min, Max	5.0, 65.0	5.0, 65.0	5.0, 65.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.15
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Change from Baseline			
		n	36	30	66
		Mean	-6.11	-8.83	-7.35
		SD, SE	14.198, 2.366	12.709, 2.320	13.508, 1.663
		Median	-5.00	-10.00	-5.00
		Q1, Q3	-12.50, 5.00	-20.00, 0.00	-15.00, 0.00
		Min, Max	-35.0, 15.0	-30.0, 15.0	-35.0, 15.0
		GEE Estimates			
		LS Mean (SE)	-17.08 (2.035)	-18.41 (2.608)	
		95% CI	(-21.06, -13.09)	(-23.52, -13.29)	
		LS Mean Difference (SE)		-1.33 (2.830)	
		95% CI		(-6.88, 4.22)	
		p-value		0.6386	
		HedgesG (95% CI)		-0.196 (-0.681, 0.290)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.15
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Baseline			
		n	36	30	66
		Mean	42.08	46.00	43.86
		SD, SE	13.958, 2.326	16.369, 2.988	15.110, 1.860
		Median	45.00	47.50	45.00
		Q1, Q3	35.00, 50.00	35.00, 60.00	35.00, 55.00
		Min, Max	10.0, 70.0	10.0, 75.0	10.0, 75.0
		Observed			
		n	36	30	66
		Mean	39.17	37.50	38.41
		SD, SE	16.013, 2.669	15.743, 2.874	15.791, 1.944
		Median	40.00	37.50	40.00
		Q1, Q3	27.50, 50.00	30.00, 45.00	30.00, 50.00
		Min, Max	10.0, 70.0	5.0, 75.0	5.0, 75.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.2.2.4.24.15
Subgroup Analysis: Change from baseline to week 24 in the Pain score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Change from Baseline			
		n	36	30	66
		Mean	-2.92	-8.50	-5.45
		SD, SE	16.707, 2.784	16.565, 3.024	16.750, 2.062
		Median	-2.50	-5.00	-5.00
		Q1, Q3	-17.50, 5.00	-15.00, 5.00	-15.00, 5.00
		Min, Max	-30.0, 35.0	-50.0, 20.0	-50.0, 35.0
		GEE Estimates			
		LS Mean (SE)	-13.88 (2.388)	-18.07 (2.812)	
		95% CI	(-18.56, -9.20)	(-23.58, -12.56)	
		LS Mean Difference (SE)		-4.19 (3.374)	
		95% CI		(-10.80, 2.42)	
		p-value		0.2142	
		HedgesG (95% CI)		-0.326 (-0.814, 0.161)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Pain Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Pain Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t_womac_pain_SUB.sas

Table 2.1.2.5.9.24
Summary of Interaction Test: Change from baseline to post-baseline visits in the Total score of WOMAC
GEE Model

Subgroup Variables	Week 24
BPI Average Pain at BL	0.1606
BPI Worst Pain at BL	0.3452
Region	0.1739
Sex	0.2921
Race Group	0.6187
Age Category	0.3980
WOMAC Stiffness at BL cat	0.1435
WOMAC Physical Function at BL cat	0.6348
WOMAC Pain at BL cat	0.5623
WOMAC Total Score at BL	0.3469
Pain Medication Use at BL cat	0.9204
Opioid Pain Medication Use at BL	0.8575
Active fractures and pseudo-fractures at BL	0.2490
6MWT score at BL cat	0.6750

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
P value of Interaction is from the GEE model which includes the change from baseline for Total Score of WOMAC as the dependent variable, region, treatment, actual randomization stratification, visit by treatment, subgroup and subgroup by treatment as fixed factors, and baseline for Total Score of WOMAC as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWOMAC.sas7bdat, ADSL.sas7bdat Program source: Interaction_womac.sas

Table 2.2.2.5.24.1
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6		N_1	27	17	44
	Baseline	n	27	16	43
		Mean	39.39	34.96	37.74
		SD, SE	17.245, 3.319	14.343, 3.586	16.195, 2.470
		Median	41.67	35.94	39.58
		Q1, Q3	28.13, 53.13	24.48, 44.27	28.13, 52.08
		Min, Max	7.3, 66.7	12.5, 58.3	7.3, 66.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.1
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Baseline			
		n	27	16	43
		Mean	39.39	34.96	37.74
		SD, SE	17.245, 3.319	14.343, 3.586	16.195, 2.470
		Median	41.67	35.94	39.58
		Q1, Q3	28.13, 53.13	24.48, 44.27	28.13, 52.08
		Min, Max	7.3, 66.7	12.5, 58.3	7.3, 66.7
		Observed			
		n	27	17	44
		Mean	34.03	30.15	32.53
		SD, SE	15.596, 3.001	12.377, 3.002	14.413, 2.173
		Median	33.33	31.25	31.77
		Q1, Q3	19.79, 47.92	22.92, 36.46	19.79, 45.83
		Min, Max	8.3, 58.3	9.4, 52.1	8.3, 58.3

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.1
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Change from Baseline			
		n	27	16	43
		Mean	-5.36	-6.18	-5.67
		SD, SE	11.061, 2.129	9.842, 2.460	10.511, 1.603
		Median	-4.17	-3.13	-3.13
		Q1, Q3	-9.38, 1.04	-14.58, 0.00	-9.38, 0.00
		Min, Max	-39.6, 12.5	-24.0, 11.5	-39.6, 12.5
		GEE Estimates			
		LS Mean (SE)	-4.97 (2.909)	-7.47 (2.973)	
		95% CI	(-10.67, 0.74)	(-13.30, -1.65)	
		LS Mean Difference (SE)		-2.51 (2.551)	
		95% CI		(-7.51, 2.49)	
		p-value		0.3257	
		HedgesG (95% CI)		-0.074 (-0.693, 0.544)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.1
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Baseline			
		n	27	16	43
		Mean	39.39	34.96	37.74
		SD, SE	17.245, 3.319	14.343, 3.586	16.195, 2.470
		Median	41.67	35.94	39.58
		Q1, Q3	28.13, 53.13	24.48, 44.27	28.13, 52.08
		Min, Max	7.3, 66.7	12.5, 58.3	7.3, 66.7
		Observed			
		n	27	17	44
		Mean	37.00	33.27	35.56
		SD, SE	16.400, 3.156	14.935, 3.622	15.779, 2.379
		Median	40.63	32.29	34.90
		Q1, Q3	25.00, 47.92	25.00, 41.67	25.00, 46.88
		Min, Max	5.2, 70.8	8.3, 57.3	5.2, 70.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.1
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Change from Baseline			
		n	27	16	43
		Mean	-2.39	-3.19	-2.69
		SD, SE	12.297, 2.367	10.694, 2.674	11.602, 1.769
		Median	-1.04	-4.17	-4.17
		Q1, Q3	-12.50, 1.04	-7.81, 2.60	-10.42, 2.08
		Min, Max	-26.0, 29.2	-25.0, 17.7	-26.0, 29.2
		GEE Estimates			
		LS Mean (SE)	-1.99 (3.048)	-4.48 (4.328)	
		95% CI	(-7.97, 3.98)	(-12.96, 4.00)	
		LS Mean Difference (SE)		-2.48 (3.193)	
		95% CI		(-8.74, 3.77)	
		p-value		0.4367	
		HedgesG (95% CI)		-0.065 (-0.684, 0.553)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.1
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6		N_1	39	51	90
	Baseline	n	39	51	90
		Mean	50.91	57.19	54.47
		SD, SE	16.694, 2.673	16.277, 2.279	16.662, 1.756
		Median	51.04	59.38	56.25
		Q1, Q3	38.54, 64.58	47.92, 68.75	43.75, 66.67
		Min, Max	6.3, 92.7	11.5, 93.8	6.3, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.1
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Baseline			
		n	39	51	90
		Mean	50.91	57.19	54.47
		SD, SE	16.694, 2.673	16.277, 2.279	16.662, 1.756
		Median	51.04	59.38	56.25
		Q1, Q3	38.54, 64.58	47.92, 68.75	43.75, 66.67
		Min, Max	6.3, 92.7	11.5, 93.8	6.3, 93.8
		Observed			
		n	39	51	90
		Mean	48.82	48.90	48.87
		SD, SE	18.931, 3.031	19.200, 2.689	18.977, 2.000
		Median	45.83	50.00	46.35
		Q1, Q3	35.42, 60.42	35.42, 62.50	35.42, 60.42
		Min, Max	17.7, 95.8	5.2, 84.4	5.2, 95.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.1
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Change from Baseline			
		n	39	51	90
		Mean	-2.08	-8.29	-5.60
		SD, SE	13.321, 2.133	12.103, 1.695	12.947, 1.365
		Median	-2.08	-8.33	-5.21
		Q1, Q3	-11.46, 7.29	-13.54, 2.08	-12.50, 4.17
		Min, Max	-28.1, 21.9	-43.8, 10.4	-43.8, 21.9
		GEE Estimates			
		LS Mean (SE)	3.15 (2.780)	-2.54 (2.139)	
		95% CI	(-2.30, 8.59)	(-6.74, 1.65)	
		LS Mean Difference (SE)		-5.69 (2.682)	
		95% CI		(-10.95, -0.43)	
		p-value		0.0339	
		HedgesG (95% CI)		-0.481 (-0.904, -0.059)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.1
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Baseline			
		n	38	50	88
		Mean	50.55	56.54	53.95
		SD, SE	16.764, 2.720	15.764, 2.229	16.383, 1.746
		Median	50.00	58.33	55.73
		Q1, Q3	38.54, 63.54	47.92, 66.67	43.23, 66.15
		Min, Max	6.3, 92.7	11.5, 93.8	6.3, 93.8
		Observed			
		n	38	50	88
		Mean	50.11	47.54	48.65
		SD, SE	21.994, 3.568	17.332, 2.451	19.405, 2.069
		Median	45.83	47.92	47.40
		Q1, Q3	35.42, 65.63	32.29, 62.50	32.29, 62.50
		Min, Max	10.4, 97.9	11.5, 84.4	10.4, 97.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.1
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Change from Baseline			
		n	38	50	88
		Mean	-0.44	-9.00	-5.30
		SD, SE	14.657, 2.378	16.061, 2.271	15.964, 1.702
		Median	1.56	-7.81	-6.25
		Q1, Q3	-10.42, 7.29	-15.63, -1.04	-13.54, 4.17
		Min, Max	-28.1, 34.4	-42.7, 54.2	-42.7, 54.2
		GEE Estimates			
		LS Mean (SE)	4.75 (2.926)	-3.37 (2.768)	
		95% CI	(-0.98, 10.48)	(-8.80, 2.05)	
		LS Mean Difference (SE)		-8.12 (3.056)	
		95% CI		(-14.11, -2.13)	
		p-value		0.0079	
		HedgesG (95% CI)		-0.542 (-0.972, -0.113)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.2
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6		N_1	49	48	97
	Baseline	n	49	47	96
		Mean	41.86	45.83	43.80
		SD, SE	16.355, 2.336	15.690, 2.289	16.073, 1.640
		Median	42.71	47.92	44.27
		Q1, Q3	30.21, 53.13	34.38, 57.29	34.38, 56.77
		Min, Max	6.3, 69.8	11.5, 75.0	6.3, 75.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.2
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Baseline			
		n	49	47	96
		Mean	41.86	45.83	43.80
		SD, SE	16.355, 2.336	15.690, 2.289	16.073, 1.640
		Median	42.71	47.92	44.27
		Q1, Q3	30.21, 53.13	34.38, 57.29	34.38, 56.77
		Min, Max	6.3, 69.8	11.5, 75.0	6.3, 75.0
		Observed			
		n	49	48	97
		Mean	38.69	40.10	39.39
		SD, SE	17.253, 2.465	17.409, 2.513	17.255, 1.752
		Median	37.50	38.02	37.50
		Q1, Q3	27.08, 46.88	28.65, 54.69	28.13, 50.00
		Min, Max	8.3, 83.3	9.4, 76.0	8.3, 83.3

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.2
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Change from Baseline			
		n	49	47	96
		Mean	-3.17	-5.98	-4.55
		SD, SE	11.756, 1.679	11.063, 1.614	11.450, 1.169
		Median	-4.17	-3.13	-3.13
		Q1, Q3	-9.38, 5.21	-13.54, 3.13	-10.42, 3.65
		Min, Max	-39.6, 20.8	-38.5, 11.5	-39.6, 20.8
		GEE Estimates			
		LS Mean (SE)	-0.89 (2.528)	-2.85 (2.199)	
		95% CI	(-5.85, 4.06)	(-7.17, 1.46)	
		LS Mean Difference (SE)		-1.96 (2.301)	
		95% CI		(-6.47, 2.55)	
		p-value		0.3936	
		HedgesG (95% CI)		-0.242 (-0.644, 0.160)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.2
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Baseline			
		n	49	47	96
		Mean	41.86	45.83	43.80
		SD, SE	16.355, 2.336	15.690, 2.289	16.073, 1.640
		Median	42.71	47.92	44.27
		Q1, Q3	30.21, 53.13	34.38, 57.29	34.38, 56.77
		Min, Max	6.3, 69.8	11.5, 75.0	6.3, 75.0
		Observed			
		n	49	48	97
		Mean	40.71	40.86	40.79
		SD, SE	18.281, 2.612	16.173, 2.334	17.180, 1.744
		Median	40.63	38.54	39.58
		Q1, Q3	29.17, 48.96	29.69, 54.17	29.17, 51.04
		Min, Max	5.2, 92.7	8.3, 72.9	5.2, 92.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.2
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Change from Baseline			
		n	49	47	96
		Mean	-1.15	-5.32	-3.19
		SD, SE	12.634, 1.805	14.626, 2.133	13.734, 1.402
		Median	0.00	-5.21	-3.65
		Q1, Q3	-8.33, 4.17	-13.54, 2.08	-11.46, 3.13
		Min, Max	-28.1, 29.2	-35.4, 54.2	-35.4, 54.2
		GEE Estimates			
		LS Mean (SE)	1.13 (2.640)	-2.19 (2.577)	
		95% CI	(-4.05, 6.30)	(-7.24, 2.86)	
		LS Mean Difference (SE)		-3.32 (2.518)	
		95% CI		(-8.25, 1.62)	
		p-value		0.1877	
		HedgesG (95% CI)		-0.300 (-0.702, 0.102)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.2
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6		N_1	17	20	37
	Baseline	n	17	20	37
		Mean	58.70	66.09	62.70
		SD, SE	15.849, 3.844	16.651, 3.723	16.490, 2.711
		Median	62.50	68.75	63.54
		Q1, Q3	51.04, 66.67	59.38, 76.04	56.25, 70.83
		Min, Max	22.9, 92.7	28.1, 93.8	22.9, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.2
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Baseline			
		n	17	20	37
		Mean	58.70	66.09	62.70
		SD, SE	15.849, 3.844	16.651, 3.723	16.490, 2.711
		Median	62.50	68.75	63.54
		Q1, Q3	51.04, 66.67	59.38, 76.04	56.25, 70.83
		Min, Max	22.9, 92.7	28.1, 93.8	22.9, 93.8
		Observed			
		n	17	20	37
		Mean	54.53	54.06	54.28
		SD, SE	19.330, 4.688	20.989, 4.693	19.966, 3.282
		Median	51.04	55.73	53.13
		Q1, Q3	38.54, 62.50	41.15, 72.40	38.54, 70.83
		Min, Max	28.1, 95.8	5.2, 84.4	5.2, 95.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.2
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Change from Baseline			
		n	17	20	37
		Mean	-4.17	-12.03	-8.42
		SD, SE	14.681, 3.561	11.894, 2.659	13.647, 2.244
		Median	-2.08	-9.38	-7.29
		Q1, Q3	-16.67, 4.17	-19.79, -4.17	-16.67, 2.08
		Min, Max	-28.1, 21.9	-43.8, 4.2	-43.8, 21.9
		GEE Estimates			
		LS Mean (SE)	-1.81 (3.907)	-9.34 (1.646)	
		95% CI	(-9.47, 5.85)	(-12.57, -6.11)	
		LS Mean Difference (SE)		-7.53 (4.523)	
		95% CI		(-16.40, 1.33)	
		p-value		0.0959	
		HedgesG (95% CI)		-0.565 (-1.225, 0.094)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.2
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Baseline			
		n	16	19	35
		Mean	58.33	64.86	61.88
		SD, SE	16.294, 4.073	16.137, 3.702	16.305, 2.756
		Median	60.42	68.75	62.50
		Q1, Q3	50.52, 67.71	59.38, 75.00	55.21, 70.83
		Min, Max	22.9, 92.7	28.1, 93.8	22.9, 93.8
		Observed			
		n	16	19	35
		Mean	56.77	51.64	53.99
		SD, SE	23.738, 5.935	19.713, 4.523	21.472, 3.629
		Median	56.77	53.13	54.17
		Q1, Q3	38.54, 73.44	32.29, 67.71	35.42, 70.83
		Min, Max	16.7, 97.9	13.5, 84.4	13.5, 97.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.2
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Change from Baseline			
		n	16	19	35
		Mean	-1.56	-13.21	-7.89
		SD, SE	16.887, 4.222	15.059, 3.455	16.749, 2.831
		Median	1.04	-11.46	-8.33
		Q1, Q3	-15.10, 7.29	-20.83, -2.08	-17.71, 4.17
		Min, Max	-28.1, 34.4	-42.7, 4.2	-42.7, 34.4
		GEE Estimates			
		LS Mean (SE)	0.87 (4.523)	-10.62 (1.714)	
		95% CI	(-7.99, 9.74)	(-13.98, -7.26)	
		LS Mean Difference (SE)		-11.49 (5.249)	
		95% CI		(-21.78, -1.21)	
		p-value		0.0285	
		HedgesG (95% CI)		-0.694 (-1.379, -0.010)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.3
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU		N_1	58	58	116
	Baseline	n	58	57	115
		Mean	48.19	53.18	50.66
		SD, SE	16.495, 2.166	16.734, 2.217	16.730, 1.560
		Median	47.92	53.13	51.04
		Q1, Q3	38.54, 62.50	40.63, 64.58	38.54, 62.50
		Min, Max	6.3, 92.7	14.6, 93.8	6.3, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.3
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Baseline			
		n	58	57	115
		Mean	48.19	53.18	50.66
		SD, SE	16.495, 2.166	16.734, 2.217	16.730, 1.560
		Median	47.92	53.13	51.04
		Q1, Q3	38.54, 62.50	40.63, 64.58	38.54, 62.50
		Min, Max	6.3, 92.7	14.6, 93.8	6.3, 93.8
		Observed			
		n	58	58	116
		Mean	44.38	44.77	44.58
		SD, SE	17.744, 2.330	18.620, 2.445	18.109, 1.681
		Median	45.31	41.67	43.23
		Q1, Q3	33.33, 54.17	31.25, 59.38	31.77, 57.81
		Min, Max	12.5, 95.8	5.2, 84.4	5.2, 95.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.3
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Change from Baseline			
		n	58	57	115
		Mean	-3.81	-8.53	-6.15
		SD, SE	12.870, 1.690	11.930, 1.580	12.584, 1.173
		Median	-3.65	-8.33	-5.21
		Q1, Q3	-10.42, 4.17	-13.54, 1.04	-13.54, 3.13
		Min, Max	-39.6, 21.9	-43.8, 11.5	-43.8, 21.9
		GEE Estimates			
		LS Mean (SE)	-4.20 (1.719)	-7.89 (1.659)	
		95% CI	(-7.57, -0.83)	(-11.14, -4.64)	
		LS Mean Difference (SE)		-3.69 (2.290)	
		95% CI		(-8.17, 0.80)	
		p-value		0.1075	
		HedgesG (95% CI)		-0.375 (-0.744, -0.006)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.3
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Baseline			
		n	57	56	113
		Mean	47.90	52.53	50.19
		SD, SE	16.494, 2.185	16.143, 2.157	16.414, 1.544
		Median	47.92	52.60	51.04
		Q1, Q3	38.54, 59.38	40.10, 64.06	38.54, 62.50
		Min, Max	6.3, 92.7	14.6, 93.8	6.3, 93.8
		Observed			
		n	57	57	114
		Mean	46.42	43.20	44.81
		SD, SE	18.912, 2.505	16.830, 2.229	17.895, 1.676
		Median	42.71	40.63	41.67
		Q1, Q3	31.25, 59.38	30.21, 57.29	31.25, 58.33
		Min, Max	10.4, 97.9	11.5, 75.0	10.4, 97.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.3
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Change from Baseline			
		n	57	56	113
		Mean	-1.48	-9.58	-5.49
		SD, SE	13.938, 1.846	13.141, 1.756	14.088, 1.325
		Median	0.00	-7.29	-5.21
		Q1, Q3	-12.50, 5.21	-16.15, -0.52	-13.54, 3.13
		Min, Max	-28.1, 34.4	-42.7, 14.6	-42.7, 34.4
		GEE Estimates			
		LS Mean (SE)	-1.87 (1.922)	-9.04 (1.742)	
		95% CI	(-5.64, 1.89)	(-12.45, -5.62)	
		LS Mean Difference (SE)		-7.16 (2.402)	
		95% CI		(-11.87, -2.45)	
		p-value		0.0029	
		HedgesG (95% CI)		-0.588 (-0.965, -0.212)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.3
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia		N_1	8	10	18
	Baseline	n	8	10	18
		Mean	31.77	44.48	38.83
		SD, SE	20.826, 7.363	25.872, 8.182	23.983, 5.653
		Median	27.08	48.44	36.98
		Q1, Q3	15.63, 45.83	15.63, 62.50	15.63, 61.46
		Min, Max	7.3, 69.8	11.5, 87.5	7.3, 87.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.3
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Baseline			
		n	8	10	18
		Mean	31.77	44.48	38.83
		SD, SE	20.826, 7.363	25.872, 8.182	23.983, 5.653
		Median	27.08	48.44	36.98
		Q1, Q3	15.63, 45.83	15.63, 62.50	15.63, 61.46
		Min, Max	7.3, 69.8	11.5, 87.5	7.3, 87.5
		Observed			
		n	8	10	18
		Mean	31.12	40.94	36.57
		SD, SE	24.647, 8.714	24.670, 7.801	24.445, 5.762
		Median	26.56	44.79	34.38
		Q1, Q3	12.50, 39.58	16.67, 60.42	13.54, 48.96
		Min, Max	8.3, 83.3	9.4, 82.3	8.3, 83.3

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.3
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Change from Baseline			
		n	8	10	18
		Mean	-0.65	-3.54	-2.26
		SD, SE	9.131, 3.228	8.494, 2.686	8.644, 2.037
		Median	-3.65	-3.13	-3.13
		Q1, Q3	-8.85, 7.81	-8.33, 4.17	-8.33, 5.21
		Min, Max	-9.4, 13.5	-16.7, 9.4	-16.7, 13.5
		GEE Estimates			
		LS Mean (SE)	-4.99 (4.232)	-4.89 (3.401)	
		95% CI	(-13.28, 3.31)	(-11.56, 1.78)	
		LS Mean Difference (SE)		0.10 (4.590)	
		95% CI		(-8.90, 9.09)	
		p-value		0.9830	
		HedgesG (95% CI)		-0.296 (-1.230, 0.639)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.3
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Baseline			
		n	8	10	18
		Mean	31.77	44.48	38.83
		SD, SE	20.826, 7.363	25.872, 8.182	23.983, 5.653
		Median	27.08	48.44	36.98
		Q1, Q3	15.63, 45.83	15.63, 62.50	15.63, 61.46
		Min, Max	7.3, 69.8	11.5, 87.5	7.3, 87.5
		Observed			
		n	8	10	18
		Mean	32.16	48.02	40.97
		SD, SE	29.643, 10.481	23.123, 7.312	26.658, 6.283
		Median	28.13	48.44	47.40
		Q1, Q3	6.77, 44.79	46.88, 61.46	11.46, 57.29
		Min, Max	5.2, 92.7	8.3, 84.4	5.2, 92.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.3
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Change from Baseline			
		n	8	10	18
		Mean	0.39	3.54	2.14
		SD, SE	12.173, 4.304	20.567, 6.504	16.957, 3.997
		Median	-1.56	-3.65	-3.65
		Q1, Q3	-9.37, 7.29	-9.37, 12.50	-9.37, 12.50
		Min, Max	-12.5, 22.9	-14.6, 54.2	-14.6, 54.2
		GEE Estimates			
		LS Mean (SE)	-3.95 (4.807)	2.19 (5.942)	
		95% CI	(-13.37, 5.48)	(-9.45, 13.84)	
		LS Mean Difference (SE)		6.14 (7.107)	
		95% CI		(-7.79, 20.07)	
		p-value		0.3877	
		HedgesG (95% CI)		0.163 (-0.769, 1.094)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.4
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male		N_1	23	24	47
	Baseline	n	23	23	46
		Mean	43.03	47.74	45.38
		SD, SE	15.601, 3.253	18.749, 3.909	17.220, 2.539
		Median	42.71	42.71	42.71
		Q1, Q3	30.21, 55.21	33.33, 61.46	33.33, 58.33
		Min, Max	9.4, 69.8	14.6, 89.6	9.4, 89.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.4
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Baseline			
		n	23	23	46
		Mean	43.03	47.74	45.38
		SD, SE	15.601, 3.253	18.749, 3.909	17.220, 2.539
		Median	42.71	42.71	42.71
		Q1, Q3	30.21, 55.21	33.33, 61.46	33.33, 58.33
		Min, Max	9.4, 69.8	14.6, 89.6	9.4, 89.6
		Observed			
		n	23	24	47
		Mean	42.84	41.06	41.93
		SD, SE	22.546, 4.701	16.903, 3.450	19.667, 2.869
		Median	37.50	36.46	37.50
		Q1, Q3	22.92, 54.17	30.21, 52.60	29.17, 53.13
		Min, Max	8.3, 88.5	14.6, 76.0	8.3, 88.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.4
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Change from Baseline			
		n	23	23	46
		Mean	-0.18	-7.16	-3.67
		SD, SE	13.137, 2.739	11.660, 2.431	12.778, 1.884
		Median	-3.13	-8.33	-4.69
		Q1, Q3	-10.42, 12.50	-13.54, 1.04	-10.42, 4.17
		Min, Max	-25.0, 21.9	-38.5, 11.5	-38.5, 21.9
		GEE Estimates			
		LS Mean (SE)	3.68 (4.870)	-3.19 (3.741)	
		95% CI	(-5.87, 13.23)	(-10.52, 4.14)	
		LS Mean Difference (SE)		-6.87 (3.717)	
		95% CI		(-14.16, 0.41)	
		p-value		0.0645	
		HedgesG (95% CI)		-0.540 (-1.128, 0.049)	

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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.4
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Baseline			
		n	23	22	45
		Mean	43.03	45.83	44.40
		SD, SE	15.601, 3.253	16.766, 3.574	16.058, 2.394
		Median	42.71	41.67	42.71
		Q1, Q3	30.21, 55.21	33.33, 59.38	33.33, 57.29
		Min, Max	9.4, 69.8	14.6, 77.1	9.4, 77.1
		Observed			
		n	23	23	46
		Mean	45.43	39.95	42.69
		SD, SE	23.391, 4.877	14.422, 3.007	19.413, 2.862
		Median	41.67	38.54	39.58
		Q1, Q3	31.25, 60.42	28.13, 56.25	29.17, 57.29
		Min, Max	5.2, 92.7	13.5, 64.6	5.2, 92.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.4
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Change from Baseline			
		n	23	22	45
		Mean	2.40	-6.68	-2.04
		SD, SE	15.490, 3.230	12.134, 2.587	14.536, 2.167
		Median	1.04	-7.81	-6.25
		Q1, Q3	-10.42, 16.67	-14.58, 2.08	-12.50, 7.29
		Min, Max	-28.1, 29.2	-26.0, 17.7	-28.1, 29.2
		GEE Estimates			
		LS Mean (SE)	6.26 (5.206)	-2.98 (3.839)	
		95% CI	(-3.94, 16.46)	(-10.51, 4.54)	
		LS Mean Difference (SE)		-9.25 (3.911)	
		95% CI		(-16.91, -1.58)	
		p-value		0.0181	
		HedgesG (95% CI)		-0.625 (-1.223, -0.026)	

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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.4
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female		N_1	43	44	87
	Baseline	n	43	44	87
		Mean	47.89	54.05	51.01
		SD, SE	18.727, 2.856	18.054, 2.722	18.543, 1.988
		Median	50.00	55.21	52.08
		Q1, Q3	36.46, 63.54	44.79, 65.63	38.54, 63.54
		Min, Max	6.3, 92.7	11.5, 93.8	6.3, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.4
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Baseline			
		n	43	44	87
		Mean	47.89	54.05	51.01
		SD, SE	18.727, 2.856	18.054, 2.722	18.543, 1.988
		Median	50.00	55.21	52.08
		Q1, Q3	36.46, 63.54	44.79, 65.63	38.54, 63.54
		Min, Max	6.3, 92.7	11.5, 93.8	6.3, 93.8
		Observed			
		n	43	44	87
		Mean	42.73	45.93	44.35
		SD, SE	17.079, 2.605	20.701, 3.121	18.955, 2.032
		Median	43.75	46.88	44.79
		Q1, Q3	32.29, 51.04	30.73, 59.90	31.25, 58.33
		Min, Max	11.5, 95.8	5.2, 84.4	5.2, 95.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.4
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Change from Baseline			
		n	43	44	87
		Mean	-5.16	-8.12	-6.66
		SD, SE	11.879, 1.812	11.640, 1.755	11.784, 1.263
		Median	-4.17	-6.77	-4.17
		Q1, Q3	-9.38, 4.17	-14.58, 1.56	-13.54, 3.13
		Min, Max	-39.6, 14.6	-43.8, 10.4	-43.8, 14.6
		GEE Estimates			
		LS Mean (SE)	-2.55 (2.726)	-4.46 (2.204)	
		95% CI	(-7.89, 2.79)	(-8.78, -0.14)	
		LS Mean Difference (SE)		-1.91 (2.587)	
		95% CI		(-6.98, 3.16)	
		p-value		0.4597	
		HedgesG (95% CI)		-0.247 (-0.669, 0.175)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.4
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Baseline			
		n	42	44	86
		Mean	47.50	54.05	50.85
		SD, SE	18.770, 2.896	18.054, 2.722	18.592, 2.005
		Median	49.48	55.21	52.08
		Q1, Q3	36.46, 62.50	44.79, 65.63	38.54, 63.54
		Min, Max	6.3, 92.7	11.5, 93.8	6.3, 93.8
		Observed			
		n	42	44	86
		Mean	44.25	46.00	45.14
		SD, SE	19.473, 3.005	19.134, 2.884	19.206, 2.071
		Median	41.67	48.44	44.27
		Q1, Q3	29.17, 54.17	32.29, 62.50	31.25, 60.42
		Min, Max	5.2, 97.9	8.3, 84.4	5.2, 97.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.4
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Change from Baseline			
		n	42	44	86
		Mean	-3.25	-8.05	-5.70
		SD, SE	12.285, 1.896	16.457, 2.481	14.684, 1.583
		Median	-0.52	-4.17	-3.13
		Q1, Q3	-12.50, 3.13	-14.58, -0.52	-13.54, 2.08
		Min, Max	-28.1, 34.4	-42.7, 54.2	-42.7, 54.2
		GEE Estimates			
		LS Mean (SE)	-0.65 (2.753)	-4.39 (2.926)	
		95% CI	(-6.05, 4.74)	(-10.13, 1.34)	
		LS Mean Difference (SE)		-3.74 (2.832)	
		95% CI		(-9.29, 1.81)	
		p-value		0.1868	
		HedgesG (95% CI)		-0.323 (-0.748, 0.103)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.5
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White		N_1	53	55	108
	Baseline	n	53	54	107
		Mean	47.86	52.97	50.44
		SD, SE	16.814, 2.310	16.271, 2.214	16.663, 1.611
		Median	47.92	53.65	51.04
		Q1, Q3	38.54, 59.38	40.63, 64.58	38.54, 62.50
		Min, Max	6.3, 92.7	14.6, 93.8	6.3, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.5
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Baseline			
		n	53	54	107
		Mean	47.86	52.97	50.44
		SD, SE	16.814, 2.310	16.271, 2.214	16.663, 1.611
		Median	47.92	53.65	51.04
		Q1, Q3	38.54, 59.38	40.63, 64.58	38.54, 62.50
		Min, Max	6.3, 92.7	14.6, 93.8	6.3, 93.8
		Observed			
		n	53	55	108
		Mean	43.04	44.72	43.89
		SD, SE	17.290, 2.375	18.441, 2.487	17.821, 1.715
		Median	40.63	42.71	41.67
		Q1, Q3	32.29, 53.13	31.25, 59.38	31.25, 56.77
		Min, Max	12.5, 95.8	5.2, 84.4	5.2, 95.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.5
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Change from Baseline			
		n	53	54	107
		Mean	-4.82	-8.39	-6.62
		SD, SE	12.742, 1.750	12.236, 1.665	12.559, 1.214
		Median	-4.17	-7.81	-5.21
		Q1, Q3	-11.46, 4.17	-15.63, 1.04	-13.54, 3.13
		Min, Max	-39.6, 20.8	-43.8, 11.5	-43.8, 20.8
		GEE Estimates			
		LS Mean (SE)	-5.55 (1.755)	-7.95 (1.734)	
		95% CI	(-8.99, -2.11)	(-11.35, -4.55)	
		LS Mean Difference (SE)		-2.40 (2.353)	
		95% CI		(-7.02, 2.21)	
		p-value		0.3072	
		HedgesG (95% CI)		-0.282 (-0.662, 0.099)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.5
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Baseline			
		n	53	54	107
		Mean	47.86	52.97	50.44
		SD, SE	16.814, 2.310	16.271, 2.214	16.663, 1.611
		Median	47.92	53.65	51.04
		Q1, Q3	38.54, 59.38	40.63, 64.58	38.54, 62.50
		Min, Max	6.3, 92.7	14.6, 93.8	6.3, 93.8
		Observed			
		n	53	55	108
		Mean	46.07	43.52	44.77
		SD, SE	18.401, 2.528	17.047, 2.299	17.687, 1.702
		Median	42.71	40.63	41.67
		Q1, Q3	31.25, 59.38	30.21, 57.29	30.73, 58.85
		Min, Max	10.4, 97.9	11.5, 75.0	10.4, 97.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.5
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Change from Baseline			
		n	53	54	107
		Mean	-1.79	-9.70	-5.78
		SD, SE	13.954, 1.917	13.370, 1.819	14.167, 1.370
		Median	0.00	-7.29	-5.21
		Q1, Q3	-12.50, 5.21	-16.67, 0.00	-13.54, 3.13
		Min, Max	-28.1, 34.4	-42.7, 14.6	-42.7, 34.4
		GEE Estimates			
		LS Mean (SE)	-2.52 (1.981)	-9.26 (1.800)	
		95% CI	(-6.41, 1.36)	(-12.79, -5.74)	
		LS Mean Difference (SE)		-6.74 (2.474)	
		95% CI		(-11.59, -1.89)	
		p-value		0.0064	
		HedgesG (95% CI)		-0.570 (-0.956, -0.183)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.5
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White		N_1	13	13	26
	Baseline	n	13	13	26
		Mean	39.42	47.36	43.39
		SD, SE	20.403, 5.659	25.803, 7.156	23.146, 4.539
		Median	39.58	42.71	41.15
		Q1, Q3	26.04, 50.00	34.38, 62.50	26.04, 62.50
		Min, Max	7.3, 69.8	11.5, 89.6	7.3, 89.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.5
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Baseline			
		n	13	13	26
		Mean	39.42	47.36	43.39
		SD, SE	20.403, 5.659	25.803, 7.156	23.146, 4.539
		Median	39.58	42.71	41.15
		Q1, Q3	26.04, 50.00	34.38, 62.50	26.04, 62.50
		Min, Max	7.3, 69.8	11.5, 89.6	7.3, 89.6
		Observed			
		n	13	13	26
		Mean	41.67	42.07	41.87
		SD, SE	25.611, 7.103	24.028, 6.664	24.331, 4.772
		Median	43.75	43.75	43.75
		Q1, Q3	19.79, 48.96	23.96, 60.42	19.79, 60.42
		Min, Max	8.3, 88.5	9.4, 82.3	8.3, 88.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.5
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Change from Baseline			
		n	13	13	26
		Mean	2.24	-5.29	-1.52
		SD, SE	9.715, 2.694	8.141, 2.258	9.584, 1.880
		Median	-1.04	-5.21	-2.60
		Q1, Q3	-5.21, 9.38	-11.46, -2.08	-8.33, 6.25
		Min, Max	-9.4, 21.9	-16.7, 9.4	-16.7, 21.9
		GEE Estimates			
		LS Mean (SE)	3.23 (3.857)	-3.53 (3.427)	
		95% CI	(-4.33, 10.79)	(-10.25, 3.19)	
		LS Mean Difference (SE)		-6.76 (3.907)	
		95% CI		(-14.42, 0.89)	
		p-value		0.0835	
		HedgesG (95% CI)		-0.782 (-1.580, 0.016)	

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The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.5
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Baseline			
		n	12	12	24
		Mean	37.33	43.84	40.58
		SD, SE	19.793, 5.714	23.467, 6.774	21.490, 4.387
		Median	38.54	41.15	39.58
		Q1, Q3	21.88, 49.48	25.00, 61.98	21.88, 59.38
		Min, Max	7.3, 69.8	11.5, 87.5	7.3, 87.5
		Observed			
		n	12	12	24
		Mean	38.45	45.75	42.10
		SD, SE	29.280, 8.452	21.598, 6.235	25.436, 5.192
		Median	35.42	47.92	43.75
		Q1, Q3	16.15, 50.52	34.38, 59.38	23.96, 54.17
		Min, Max	5.2, 92.7	8.3, 84.4	5.2, 92.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.5
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Change from Baseline			
		n	12	12	24
		Mean	1.13	1.91	1.52
		SD, SE	12.551, 3.623	18.990, 5.482	15.747, 3.214
		Median	0.52	-4.17	-3.65
		Q1, Q3	-9.37, 7.29	-7.81, 6.25	-8.85, 7.29
		Min, Max	-13.5, 22.9	-14.6, 54.2	-14.6, 54.2
		GEE Estimates			
		LS Mean (SE)	1.87 (4.419)	3.16 (6.058)	
		95% CI	(-6.79, 10.53)	(-8.72, 15.03)	
		LS Mean Difference (SE)		1.29 (6.237)	
		95% CI		(-10.93, 13.52)	
		p-value		0.8360	
		HedgesG (95% CI)		0.045 (-0.755, 0.845)	

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The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.6
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years		N_1	36	31	67
	Baseline	n	36	30	66
		Mean	42.56	49.97	45.93
		SD, SE	18.526, 3.088	14.406, 2.630	17.064, 2.100
		Median	40.63	50.00	46.35
		Q1, Q3	28.65, 60.42	39.58, 61.46	34.38, 61.46
		Min, Max	6.3, 71.9	19.8, 77.1	6.3, 77.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.6
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Baseline			
		n	36	30	66
		Mean	42.56	49.97	45.93
		SD, SE	18.526, 3.088	14.406, 2.630	17.064, 2.100
		Median	40.63	50.00	46.35
		Q1, Q3	28.65, 60.42	39.58, 61.46	34.38, 61.46
		Min, Max	6.3, 71.9	19.8, 77.1	6.3, 77.1
		Observed			
		n	36	31	67
		Mean	39.18	42.51	40.72
		SD, SE	19.369, 3.228	17.493, 3.142	18.462, 2.255
		Median	35.42	43.75	35.42
		Q1, Q3	27.60, 46.35	28.13, 57.29	28.13, 52.08
		Min, Max	8.3, 88.5	5.2, 75.0	5.2, 88.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.6
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Change from Baseline			
		n	36	30	66
		Mean	-3.39	-7.78	-5.38
		SD, SE	14.043, 2.340	11.524, 2.104	13.050, 1.606
		Median	-4.17	-8.33	-5.21
		Q1, Q3	-10.94, 6.25	-16.67, 2.08	-12.50, 4.17
		Min, Max	-39.6, 21.9	-28.1, 11.5	-39.6, 21.9
		GEE Estimates			
		LS Mean (SE)	-1.58 (3.276)	-4.84 (2.929)	
		95% CI	(-8.00, 4.84)	(-10.58, 0.90)	
		LS Mean Difference (SE)		-3.26 (3.258)	
		95% CI		(-9.64, 3.13)	
		p-value		0.3176	
		HedgesG (95% CI)		-0.330 (-0.818, 0.158)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.6
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Baseline			
		n	36	30	66
		Mean	42.56	49.97	45.93
		SD, SE	18.526, 3.088	14.406, 2.630	17.064, 2.100
		Median	40.63	50.00	46.35
		Q1, Q3	28.65, 60.42	39.58, 61.46	34.38, 61.46
		Min, Max	6.3, 71.9	19.8, 77.1	6.3, 77.1
		Observed			
		n	36	31	67
		Mean	39.58	43.31	41.31
		SD, SE	21.583, 3.597	17.838, 3.204	19.879, 2.429
		Median	38.54	43.75	38.54
		Q1, Q3	26.56, 48.44	29.17, 57.29	27.08, 56.25
		Min, Max	5.2, 92.7	11.5, 75.0	5.2, 92.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.6
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Change from Baseline			
		n	36	30	66
		Mean	-2.98	-7.12	-4.86
		SD, SE	14.436, 2.406	13.651, 2.492	14.130, 1.739
		Median	-5.21	-6.77	-6.25
		Q1, Q3	-13.02, 6.25	-14.58, 4.17	-13.54, 4.17
		Min, Max	-28.1, 22.9	-42.7, 17.7	-42.7, 22.9
		GEE Estimates			
		LS Mean (SE)	-1.18 (3.474)	-4.18 (3.049)	
		95% CI	(-7.98, 5.63)	(-10.15, 1.80)	
		LS Mean Difference (SE)		-3.00 (3.394)	
		95% CI		(-9.65, 3.65)	
		p-value		0.3765	
		HedgesG (95% CI)		-0.286 (-0.773, 0.201)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.5.24.6
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years		N_1	30	37	67
	Baseline	n	30	37	67
		Mean	50.56	53.43	52.15
		SD, SE	15.955, 2.913	21.169, 3.480	18.931, 2.313
		Median	51.56	54.17	53.13
		Q1, Q3	41.67, 59.38	39.58, 66.67	40.63, 63.54
		Min, Max	9.4, 92.7	11.5, 93.8	9.4, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.5.24.6
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Baseline			
		n	30	37	67
		Mean	50.56	53.43	52.15
		SD, SE	15.955, 2.913	21.169, 3.480	18.931, 2.313
		Median	51.56	54.17	53.13
		Q1, Q3	41.67, 59.38	39.58, 66.67	40.63, 63.54
		Min, Max	9.4, 92.7	11.5, 93.8	9.4, 93.8
		Observed			
		n	30	37	67
		Mean	47.08	45.64	46.28
		SD, SE	17.891, 3.266	21.095, 3.468	19.593, 2.394
		Median	46.88	42.71	46.88
		Q1, Q3	35.42, 58.33	31.25, 60.42	34.38, 60.42
		Min, Max	12.5, 95.8	9.4, 84.4	9.4, 95.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.6
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Change from Baseline			
		n	30	37	67
		Mean	-3.47	-7.80	-5.86
		SD, SE	10.493, 1.916	11.761, 1.934	11.337, 1.385
		Median	-2.60	-5.21	-3.13
		Q1, Q3	-9.38, 4.17	-13.54, 0.00	-12.50, 3.13
		Min, Max	-26.0, 15.6	-43.8, 10.4	-43.8, 15.6
		GEE Estimates			
		LS Mean (SE)	0.30 (3.015)	-3.25 (2.482)	
		95% CI	(-5.61, 6.21)	(-8.12, 1.61)	
		LS Mean Difference (SE)		-3.55 (2.756)	
		95% CI		(-8.95, 1.85)	
		p-value		0.1975	
		HedgesG (95% CI)		-0.376 (-0.861, 0.110)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.6
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Baseline			
		n	29	36	65
		Mean	50.07	52.43	51.38
		SD, SE	16.012, 2.973	20.556, 3.426	18.565, 2.303
		Median	51.04	54.17	52.08
		Q1, Q3	41.67, 58.33	39.06, 65.63	40.63, 62.50
		Min, Max	9.4, 92.7	11.5, 93.8	9.4, 93.8
		Observed			
		n	29	36	65
		Mean	50.97	44.44	47.36
		SD, SE	18.145, 3.369	17.972, 2.995	18.203, 2.258
		Median	47.92	44.27	46.88
		Q1, Q3	40.63, 61.46	32.29, 58.85	32.29, 61.46
		Min, Max	24.0, 97.9	8.3, 84.4	8.3, 97.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.6
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Change from Baseline			
		n	29	36	65
		Mean	0.90	-7.99	-4.02
		SD, SE	12.542, 2.329	16.344, 2.724	15.320, 1.900
		Median	1.04	-5.73	-3.13
		Q1, Q3	-6.25, 4.17	-14.58, -1.56	-12.50, 2.08
		Min, Max	-21.9, 34.4	-42.7, 54.2	-42.7, 54.2
		GEE Estimates			
		LS Mean (SE)	4.68 (3.170)	-3.62 (3.233)	
		95% CI	(-1.53, 10.89)	(-9.96, 2.71)	
		LS Mean Difference (SE)		-8.31 (3.016)	
		95% CI		(-14.22, -2.39)	
		p-value		0.0059	
		HedgesG (95% CI)		-0.585 (-1.084, -0.086)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.7
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5		N_1	41	39	80
	Baseline	n	41	38	79
		Mean	41.54	43.01	42.25
		SD, SE	18.375, 2.870	16.137, 2.618	17.240, 1.940
		Median	41.67	44.27	42.71
		Q1, Q3	29.17, 52.08	32.29, 55.21	30.21, 54.17
		Min, Max	6.3, 92.7	11.5, 72.9	6.3, 92.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.7
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline			
		n	41	38	79
		Mean	41.54	43.01	42.25
		SD, SE	18.375, 2.870	16.137, 2.618	17.240, 1.940
		Median	41.67	44.27	42.71
		Q1, Q3	29.17, 52.08	32.29, 55.21	30.21, 54.17
		Min, Max	6.3, 92.7	11.5, 72.9	6.3, 92.7
		Observed			
		n	41	39	80
		Mean	38.74	38.76	38.75
		SD, SE	18.345, 2.865	19.139, 3.065	18.617, 2.081
		Median	36.46	35.42	35.94
		Q1, Q3	28.13, 46.88	23.96, 52.08	24.48, 50.00
		Min, Max	8.3, 95.8	5.2, 76.0	5.2, 95.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.7
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline			
		n	41	38	79
		Mean	-2.79	-4.61	-3.67
		SD, SE	11.770, 1.838	11.327, 1.838	11.521, 1.296
		Median	-4.17	-2.60	-3.13
		Q1, Q3	-9.38, 4.17	-9.38, 3.13	-9.38, 4.17
		Min, Max	-28.1, 20.8	-38.5, 11.5	-38.5, 20.8
		GEE Estimates			
		LS Mean (SE)	-1.76 (2.988)	-3.57 (2.837)	
		95% CI	(-7.61, 4.10)	(-9.13, 1.99)	
		LS Mean Difference (SE)		-1.81 (2.594)	
		95% CI		(-6.89, 3.27)	
		p-value		0.4852	
		HedgesG (95% CI)		-0.153 (-0.595, 0.289)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.7
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline			
		n	41	38	79
		Mean	41.54	43.01	42.25
		SD, SE	18.375, 2.870	16.137, 2.618	17.240, 1.940
		Median	41.67	44.27	42.71
		Q1, Q3	29.17, 52.08	32.29, 55.21	30.21, 54.17
		Min, Max	6.3, 92.7	11.5, 72.9	6.3, 92.7
		Observed			
		n	41	39	80
		Mean	40.22	39.80	40.01
		SD, SE	21.056, 3.288	16.915, 2.709	19.030, 2.128
		Median	39.58	36.46	38.54
		Q1, Q3	26.04, 47.92	27.08, 57.29	27.08, 51.04
		Min, Max	5.2, 97.9	8.3, 67.7	5.2, 97.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.7
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline			
		n	41	38	79
		Mean	-1.32	-3.67	-2.45
		SD, SE	15.043, 2.349	15.161, 2.459	15.049, 1.693
		Median	-1.04	-3.13	-3.13
		Q1, Q3	-12.50, 5.21	-9.38, 2.08	-12.50, 4.17
		Min, Max	-28.1, 34.4	-42.7, 54.2	-42.7, 54.2
		GEE Estimates			
		LS Mean (SE)	-0.28 (3.411)	-2.64 (3.515)	
		95% CI	(-6.97, 6.40)	(-9.52, 4.25)	
		LS Mean Difference (SE)		-2.35 (3.109)	
		95% CI		(-8.44, 3.74)	
		p-value		0.4493	
		HedgesG (95% CI)		-0.152 (-0.594, 0.290)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.7
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5		N_1	25	29	54
	Baseline	n	25	29	54
		Mean	53.83	63.51	59.03
		SD, SE	13.825, 2.765	14.400, 2.674	14.826, 2.018
		Median	57.29	62.50	61.98
		Q1, Q3	42.71, 65.63	54.17, 71.88	46.88, 68.75
		Min, Max	22.9, 71.9	38.5, 93.8	22.9, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.7
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline			
		n	25	29	54
		Mean	53.83	63.51	59.03
		SD, SE	13.825, 2.765	14.400, 2.674	14.826, 2.018
		Median	57.29	62.50	61.98
		Q1, Q3	42.71, 65.63	54.17, 71.88	46.88, 68.75
		Min, Max	22.9, 71.9	38.5, 93.8	22.9, 93.8
		Observed			
		n	25	29	54
		Mean	49.38	51.54	50.54
		SD, SE	18.505, 3.701	17.653, 3.278	17.913, 2.438
		Median	46.88	53.13	49.48
		Q1, Q3	35.42, 60.42	37.50, 62.50	36.46, 61.46
		Min, Max	17.7, 88.5	15.6, 84.4	15.6, 88.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.7
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline			
		n	25	29	54
		Mean	-4.46	-11.96	-8.49
		SD, SE	13.709, 2.742	10.680, 1.983	12.634, 1.719
		Median	-3.13	-10.42	-8.33
		Q1, Q3	-9.38, 4.17	-18.75, -5.21	-16.67, 0.00
		Min, Max	-39.6, 21.9	-43.8, 4.2	-43.8, 21.9
		GEE Estimates			
		LS Mean (SE)	0.47 (2.874)	-5.59 (2.689)	
		95% CI	(-5.16, 6.10)	(-10.86, -0.31)	
		LS Mean Difference (SE)		-6.05 (3.631)	
		95% CI		(-13.17, 1.06)	
		p-value		0.0955	
		HedgesG (95% CI)		-0.596 (-1.143, -0.050)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.7
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline			
		n	24	28	52
		Mean	53.39	62.57	58.33
		SD, SE	13.936, 2.845	13.746, 2.598	14.457, 2.005
		Median	57.29	62.50	60.42
		Q1, Q3	42.19, 66.15	52.60, 71.35	46.35, 68.23
		Min, Max	22.9, 71.9	38.5, 93.8	22.9, 93.8
		Observed			
		n	24	28	52
		Mean	52.26	49.67	50.86
		SD, SE	18.270, 3.729	17.650, 3.336	17.809, 2.470
		Median	51.56	48.96	48.96
		Q1, Q3	39.58, 63.02	33.85, 62.50	38.02, 63.02
		Min, Max	24.0, 92.7	11.5, 84.4	11.5, 92.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.7
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline			
		n	24	28	52
		Mean	-1.13	-12.91	-7.47
		SD, SE	11.206, 2.287	13.452, 2.542	13.697, 1.899
		Median	0.52	-10.94	-6.25
		Q1, Q3	-8.33, 4.17	-20.83, -3.13	-14.06, 2.08
		Min, Max	-26.0, 22.9	-42.7, 4.2	-42.7, 22.9
		GEE Estimates			
		LS Mean (SE)	3.86 (2.601)	-6.61 (2.697)	
		95% CI	(-1.24, 8.96)	(-11.90, -1.32)	
		LS Mean Difference (SE)		-10.47 (3.410)	
		95% CI		(-17.15, -3.78)	
		p-value		0.0021	
		HedgesG (95% CI)		-0.912 (-1.485, -0.340)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.8
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	33.70	35.66	34.58
		SD, SE	12.039, 1.979	11.534, 2.106	11.767, 1.438
		Median	37.50	38.54	38.54
		Q1, Q3	28.13, 42.71	30.21, 43.75	28.13, 43.75
		Min, Max	6.3, 49.0	11.5, 51.0	6.3, 51.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.8
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline			
		n	37	30	67
		Mean	33.70	35.66	34.58
		SD, SE	12.039, 1.979	11.534, 2.106	11.767, 1.438
		Median	37.50	38.54	38.54
		Q1, Q3	28.13, 42.71	30.21, 43.75	28.13, 43.75
		Min, Max	6.3, 49.0	11.5, 51.0	6.3, 51.0
		Observed			
		n	37	30	67
		Mean	32.55	28.85	30.89
		SD, SE	12.825, 2.108	11.375, 2.077	12.247, 1.496
		Median	34.38	30.73	33.33
		Q1, Q3	20.83, 43.75	18.75, 37.50	19.79, 40.63
		Min, Max	8.3, 54.2	5.2, 49.0	5.2, 54.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.8
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-1.15	-6.81	-3.68
		SD, SE	9.419, 1.549	9.671, 1.766	9.874, 1.206
		Median	-2.08	-6.77	-3.13
		Q1, Q3	-7.29, 6.25	-13.54, -1.04	-9.38, 3.13
		Min, Max	-25.0, 20.8	-28.1, 11.5	-28.1, 20.8
		GEE Estimates			
		LS Mean (SE)	-3.00 (2.798)	-7.90 (2.787)	
		95% CI	(-8.49, 2.48)	(-13.36, -2.44)	
		LS Mean Difference (SE)		-4.90 (2.238)	
		95% CI		(-9.28, -0.51)	
		p-value		0.0287	
		HedgesG (95% CI)		-0.577 (-1.069, -0.086)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.8
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline			
		n	37	30	67
		Mean	33.70	35.66	34.58
		SD, SE	12.039, 1.979	11.534, 2.106	11.767, 1.438
		Median	37.50	38.54	38.54
		Q1, Q3	28.13, 42.71	30.21, 43.75	28.13, 43.75
		Min, Max	6.3, 49.0	11.5, 51.0	6.3, 51.0
		Observed			
		n	37	30	67
		Mean	32.57	32.43	32.51
		SD, SE	13.985, 2.299	13.167, 2.404	13.523, 1.652
		Median	31.25	31.77	31.25
		Q1, Q3	25.00, 41.67	25.00, 38.54	25.00, 40.63
		Min, Max	5.2, 70.8	8.3, 65.6	5.2, 70.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.8
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-1.13	-3.23	-2.07
		SD, SE	12.436, 2.044	15.354, 2.803	13.749, 1.680
		Median	-1.04	-5.21	-4.17
		Q1, Q3	-8.33, 4.17	-10.42, 2.08	-10.42, 3.13
		Min, Max	-28.1, 29.2	-35.4, 54.2	-35.4, 54.2
		GEE Estimates			
		LS Mean (SE)	-2.98 (2.966)	-4.32 (3.545)	
		95% CI	(-8.79, 2.84)	(-11.27, 2.62)	
		LS Mean Difference (SE)		-1.35 (2.899)	
		95% CI		(-7.03, 4.33)	
		p-value		0.6421	
		HedgesG (95% CI)		-0.148 (-0.630, 0.334)	

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The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.8
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8		N_1	29	38	67
	Baseline	n	29	37	66
		Mean	62.14	65.03	63.76
		SD, SE	8.600, 1.597	10.799, 1.775	9.927, 1.222
		Median	62.50	62.50	62.50
		Q1, Q3	57.29, 66.67	57.29, 70.83	57.29, 68.75
		Min, Max	50.0, 92.7	49.0, 93.8	49.0, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.8
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline			
		n	29	37	66
		Mean	62.14	65.03	63.76
		SD, SE	8.600, 1.597	10.799, 1.775	9.927, 1.222
		Median	62.50	62.50	62.50
		Q1, Q3	57.29, 66.67	57.29, 70.83	57.29, 68.75
		Min, Max	50.0, 92.7	49.0, 93.8	49.0, 93.8
		Observed			
		n	29	38	67
		Mean	55.82	56.33	56.11
		SD, SE	17.635, 3.275	15.557, 2.524	16.361, 1.999
		Median	54.17	58.85	57.29
		Q1, Q3	44.79, 62.50	48.96, 66.67	45.83, 66.67
		Min, Max	27.1, 95.8	15.6, 84.4	15.6, 95.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.8
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline			
		n	29	37	66
		Mean	-6.32	-8.59	-7.59
		SD, SE	15.197, 2.822	12.981, 2.134	13.932, 1.715
		Median	-4.17	-7.29	-6.77
		Q1, Q3	-17.71, 4.17	-13.54, 2.08	-16.67, 3.13
		Min, Max	-39.6, 21.9	-43.8, 10.4	-43.8, 21.9
		GEE Estimates			
		LS Mean (SE)	-2.15 (3.060)	-4.02 (2.082)	
		95% CI	(-8.15, 3.84)	(-8.10, 0.06)	
		LS Mean Difference (SE)		-1.87 (3.682)	
		95% CI		(-9.08, 5.35)	
		p-value		0.6123	
		HedgesG (95% CI)		-0.157 (-0.644, 0.329)	

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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.8
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline			
		n	28	36	64
		Mean	62.05	64.35	63.35
		SD, SE	8.745, 1.653	10.112, 1.685	9.534, 1.192
		Median	62.50	62.50	62.50
		Q1, Q3	56.77, 66.67	56.77, 70.83	56.77, 68.75
		Min, Max	50.0, 92.7	49.0, 93.8	49.0, 93.8
		Observed			
		n	28	37	65
		Mean	60.64	53.24	56.43
		SD, SE	17.222, 3.255	15.520, 2.551	16.561, 2.054
		Median	59.90	53.13	57.29
		Q1, Q3	45.83, 69.27	47.92, 62.50	46.88, 65.63
		Min, Max	35.4, 97.9	13.5, 84.4	13.5, 97.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.8
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-1.41	-11.23	-6.93
		SD, SE	15.362, 2.903	14.022, 2.337	15.312, 1.914
		Median	0.52	-7.29	-4.17
		Q1, Q3	-13.02, 6.25	-20.83, -1.04	-15.63, 2.60
		Min, Max	-28.1, 34.4	-42.7, 9.4	-42.7, 34.4
		GEE Estimates			
		LS Mean (SE)	2.86 (3.139)	-6.81 (2.051)	
		95% CI	(-3.29, 9.01)	(-10.83, -2.78)	
		LS Mean Difference (SE)		-9.66 (3.663)	
		95% CI		(-16.84, -2.48)	
		p-value		0.0083	
		HedgesG (95% CI)		-0.653 (-1.159, -0.146)	

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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.9
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50		N_1	42	32	74
	Baseline	n	42	32	74
		Mean	37.18	38.70	37.84
		SD, SE	14.295, 2.206	14.241, 2.518	14.194, 1.650
		Median	39.06	39.06	39.06
		Q1, Q3	28.13, 46.88	31.25, 48.96	29.17, 47.92
		Min, Max	6.3, 62.5	11.5, 62.5	6.3, 62.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.9
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Baseline			
		n	42	32	74
		Mean	37.18	38.70	37.84
		SD, SE	14.295, 2.206	14.241, 2.518	14.194, 1.650
		Median	39.06	39.06	39.06
		Q1, Q3	28.13, 46.88	31.25, 48.96	29.17, 47.92
		Min, Max	6.3, 62.5	11.5, 62.5	6.3, 62.5
		Observed			
		n	42	32	74
		Mean	36.93	32.98	35.22
		SD, SE	16.575, 2.558	15.495, 2.739	16.129, 1.875
		Median	35.94	33.33	34.90
		Q1, Q3	21.88, 47.92	20.83, 41.67	21.88, 46.88
		Min, Max	8.3, 81.3	5.2, 65.6	5.2, 81.3

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.5.24.9
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Change from Baseline			
		n	42	32	74
		Mean	-0.25	-5.73	-2.62
		SD, SE	9.491, 1.464	11.232, 1.985	10.566, 1.228
		Median	-0.52	-5.21	-3.13
		Q1, Q3	-7.29, 6.25	-12.50, 3.65	-9.38, 4.17
		Min, Max	-25.0, 20.8	-38.5, 11.5	-38.5, 20.8
		GEE Estimates			
		LS Mean (SE)	1.81 (3.528)	-3.97 (3.044)	
		95% CI	(-5.11, 8.72)	(-9.94, 2.00)	
		LS Mean Difference (SE)		-5.78 (2.589)	
		95% CI		(-10.85, -0.70)	
		p-value		0.0257	
		HedgesG (95% CI)		-0.521 (-0.988, -0.053)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.9
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Baseline			
		n	42	32	74
		Mean	37.18	38.70	37.84
		SD, SE	14.295, 2.206	14.241, 2.518	14.194, 1.650
		Median	39.06	39.06	39.06
		Q1, Q3	28.13, 46.88	31.25, 48.96	29.17, 47.92
		Min, Max	6.3, 62.5	11.5, 62.5	6.3, 62.5
		Observed			
		n	42	32	74
		Mean	38.37	36.10	37.39
		SD, SE	18.782, 2.898	14.074, 2.488	16.838, 1.957
		Median	38.54	33.33	34.90
		Q1, Q3	26.04, 48.96	26.04, 47.40	26.04, 47.92
		Min, Max	5.2, 85.4	8.3, 65.6	5.2, 85.4

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Table 2.2.2.5.24.9
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Change from Baseline			
		n	42	32	74
		Mean	1.19	-2.60	-0.45
		SD, SE	12.975, 2.002	14.426, 2.550	13.657, 1.588
		Median	1.04	-4.17	-1.04
		Q1, Q3	-6.25, 5.21	-9.38, 2.08	-8.33, 4.17
		Min, Max	-28.1, 34.4	-29.2, 54.2	-29.2, 54.2
		GEE Estimates			
		LS Mean (SE)	3.24 (3.949)	-0.85 (3.629)	
		95% CI	(-4.50, 10.98)	(-7.96, 6.27)	
		LS Mean Difference (SE)		-4.09 (2.897)	
		95% CI		(-9.77, 1.59)	
		p-value		0.1580	
		HedgesG (95% CI)		-0.272 (-0.734, 0.190)	

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Table 2.2.2.5.24.9
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50		N_1	24	35	59
	Baseline	n	24	35	59
		Mean	61.98	63.93	63.14
		SD, SE	10.769, 2.198	12.635, 2.136	11.853, 1.543
		Median	63.54	62.50	63.54
		Q1, Q3	56.77, 67.19	55.21, 71.88	56.25, 69.79
		Min, Max	37.5, 92.7	40.6, 93.8	37.5, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.5.24.9
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Baseline			
		n	24	35	59
		Mean	61.98	63.93	63.14
		SD, SE	10.769, 2.198	12.635, 2.136	11.853, 1.543
		Median	63.54	62.50	63.54
		Q1, Q3	56.77, 67.19	55.21, 71.88	56.25, 69.79
		Min, Max	37.5, 92.7	40.6, 93.8	37.5, 93.8
		Observed			
		n	24	35	59
		Mean	52.99	54.26	53.74
		SD, SE	18.916, 3.861	17.396, 2.941	17.880, 2.328
		Median	46.35	58.33	53.13
		Q1, Q3	36.98, 61.46	40.63, 66.67	38.54, 66.67
		Min, Max	27.1, 95.8	15.6, 84.4	15.6, 95.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.5.24.9
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Change from Baseline			
		n	24	35	59
		Mean	-8.98	-9.67	-9.39
		SD, SE	15.088, 3.080	11.708, 1.979	13.067, 1.701
		Median	-9.38	-8.33	-8.33
		Q1, Q3	-19.27, 3.65	-18.75, 1.04	-18.75, 1.04
		Min, Max	-39.6, 21.9	-43.8, 4.2	-43.8, 21.9
		GEE Estimates			
		LS Mean (SE)	-5.54 (3.246)	-5.66 (2.351)	
		95% CI	(-11.90, 0.82)	(-10.27, -1.05)	
		LS Mean Difference (SE)		-0.12 (3.693)	
		95% CI		(-7.36, 7.12)	
		p-value		0.9739	
		HedgesG (95% CI)		-0.051 (-0.570, 0.469)	

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Table 2.2.2.5.24.9
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Baseline			
		n	23	34	57
		Mean	61.87	63.17	62.65
		SD, SE	10.996, 2.293	11.998, 2.058	11.521, 1.526
		Median	63.54	62.50	62.50
		Q1, Q3	56.25, 67.71	55.21, 70.83	56.25, 68.75
		Min, Max	37.5, 92.7	40.6, 93.8	37.5, 93.8
		Observed			
		n	23	34	57
		Mean	56.16	50.89	53.02
		SD, SE	19.584, 4.083	18.211, 3.123	18.786, 2.488
		Median	51.04	54.17	53.13
		Q1, Q3	40.63, 67.71	34.38, 64.58	39.58, 65.63
		Min, Max	24.0, 97.9	11.5, 84.4	11.5, 97.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.9
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Change from Baseline			
		n	23	34	57
		Mean	-5.71	-12.29	-9.63
		SD, SE	14.031, 2.926	14.321, 2.456	14.450, 1.914
		Median	-8.33	-10.42	-8.33
		Q1, Q3	-15.62, 3.13	-20.83, -2.08	-17.71, 2.08
		Min, Max	-28.1, 22.9	-42.7, 9.4	-42.7, 22.9
		GEE Estimates			
		LS Mean (SE)	-2.09 (3.109)	-8.35 (2.493)	
		95% CI	(-8.18, 4.01)	(-13.24, -3.47)	
		LS Mean Difference (SE)		-6.27 (3.706)	
		95% CI		(-13.53, 1.00)	
		p-value		0.0908	
		HedgesG (95% CI)		-0.449 (-0.984, 0.087)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.10
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5		N_1	37	30	67
	Baseline	n	37	29	66
		Mean	33.70	35.02	34.28
		SD, SE	12.039, 1.979	11.214, 2.082	11.613, 1.430
		Median	37.50	38.54	38.02
		Q1, Q3	28.13, 42.71	30.21, 43.75	28.13, 42.71
		Min, Max	6.3, 49.0	11.5, 49.0	6.3, 49.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.10
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Baseline			
		n	37	29	66
		Mean	33.70	35.02	34.28
		SD, SE	12.039, 1.979	11.214, 2.082	11.613, 1.430
		Median	37.50	38.54	38.02
		Q1, Q3	28.13, 42.71	30.21, 43.75	28.13, 42.71
		Min, Max	6.3, 49.0	11.5, 49.0	6.3, 49.0
		Observed			
		n	37	30	67
		Mean	32.55	30.52	31.64
		SD, SE	12.825, 2.108	13.801, 2.520	13.207, 1.614
		Median	34.38	30.73	33.33
		Q1, Q3	20.83, 43.75	18.75, 38.54	19.79, 40.63
		Min, Max	8.3, 54.2	5.2, 59.4	5.2, 59.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.10
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Change from Baseline			
		n	37	29	66
		Mean	-1.15	-5.24	-2.95
		SD, SE	9.419, 1.549	10.415, 1.934	10.002, 1.231
		Median	-2.08	-3.13	-3.13
		Q1, Q3	-7.29, 6.25	-11.46, 3.13	-9.38, 5.21
		Min, Max	-25.0, 20.8	-28.1, 11.5	-28.1, 20.8
		GEE Estimates			
		LS Mean (SE)	-3.14 (2.775)	-6.76 (2.829)	
		95% CI	(-8.58, 2.30)	(-12.31, -1.22)	
		LS Mean Difference (SE)		-3.62 (2.447)	
		95% CI		(-8.42, 1.17)	
		p-value		0.1386	
		HedgesG (95% CI)		-0.403 (-0.894, 0.088)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.10
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Baseline			
		n	37	29	66
		Mean	33.70	35.02	34.28
		SD, SE	12.039, 1.979	11.214, 2.082	11.613, 1.430
		Median	37.50	38.54	38.02
		Q1, Q3	28.13, 42.71	30.21, 43.75	28.13, 42.71
		Min, Max	6.3, 49.0	11.5, 49.0	6.3, 49.0
		Observed			
		n	37	30	67
		Mean	32.57	33.33	32.91
		SD, SE	13.985, 2.299	13.836, 2.526	13.818, 1.688
		Median	31.25	32.29	32.29
		Q1, Q3	25.00, 41.67	25.00, 40.63	25.00, 41.67
		Min, Max	5.2, 70.8	8.3, 65.6	5.2, 70.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.10
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Change from Baseline			
		n	37	29	66
		Mean	-1.13	-2.51	-1.74
		SD, SE	12.436, 2.044	15.212, 2.825	13.631, 1.678
		Median	-1.04	-4.17	-4.17
		Q1, Q3	-8.33, 4.17	-9.38, 2.08	-9.38, 3.13
		Min, Max	-28.1, 29.2	-35.4, 54.2	-35.4, 54.2
		GEE Estimates			
		LS Mean (SE)	-3.11 (2.925)	-4.03 (3.533)	
		95% CI	(-8.84, 2.62)	(-10.96, 2.89)	
		LS Mean Difference (SE)		-0.92 (2.937)	
		95% CI		(-6.68, 4.83)	
		p-value		0.7532	
		HedgesG (95% CI)		-0.098 (-0.585, 0.388)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.10
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	62.14	64.75	63.62
		SD, SE	8.600, 1.597	10.775, 1.748	9.908, 1.210
		Median	62.50	62.50	62.50
		Q1, Q3	57.29, 66.67	56.25, 70.83	56.25, 68.75
		Min, Max	50.0, 92.7	50.0, 93.8	50.0, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.10
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Baseline			
		n	29	38	67
		Mean	62.14	64.75	63.62
		SD, SE	8.600, 1.597	10.775, 1.748	9.908, 1.210
		Median	62.50	62.50	62.50
		Q1, Q3	57.29, 66.67	56.25, 70.83	56.25, 68.75
		Min, Max	50.0, 92.7	50.0, 93.8	50.0, 93.8
		Observed			
		n	29	38	67
		Mean	55.82	55.02	55.36
		SD, SE	17.635, 3.275	16.260, 2.638	16.743, 2.045
		Median	54.17	57.81	55.21
		Q1, Q3	44.79, 62.50	43.75, 66.67	43.75, 66.67
		Min, Max	27.1, 95.8	15.6, 84.4	15.6, 95.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.10
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-6.32	-9.73	-8.26
		SD, SE	15.197, 2.822	12.151, 1.971	13.552, 1.656
		Median	-4.17	-8.85	-7.29
		Q1, Q3	-17.71, 4.17	-16.67, 1.04	-17.71, 3.12
		Min, Max	-39.6, 21.9	-43.8, 4.2	-43.8, 21.9
		GEE Estimates			
		LS Mean (SE)	-1.65 (3.021)	-4.97 (1.993)	
		95% CI	(-7.57, 4.27)	(-8.88, -1.07)	
		LS Mean Difference (SE)		-3.32 (3.524)	
		95% CI		(-10.23, 3.59)	
		p-value		0.3464	
		HedgesG (95% CI)		-0.245 (-0.730, 0.240)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.10
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Baseline			
		n	28	37	65
		Mean	62.05	64.08	63.21
		SD, SE	8.745, 1.653	10.086, 1.658	9.513, 1.180
		Median	62.50	62.50	62.50
		Q1, Q3	56.77, 66.67	56.25, 70.83	56.25, 68.75
		Min, Max	50.0, 92.7	50.0, 93.8	50.0, 93.8
		Observed			
		n	28	37	65
		Mean	60.64	52.51	56.01
		SD, SE	17.222, 3.255	16.013, 2.632	16.907, 2.097
		Median	59.90	53.13	56.25
		Q1, Q3	45.83, 69.27	43.75, 62.50	44.79, 65.63
		Min, Max	35.4, 97.9	13.5, 84.4	13.5, 97.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.10
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Change from Baseline			
		n	28	37	65
		Mean	-1.41	-11.57	-7.20
		SD, SE	15.362, 2.903	13.897, 2.285	15.293, 1.897
		Median	0.52	-7.29	-5.21
		Q1, Q3	-13.02, 6.25	-20.83, -2.08	-15.63, 2.08
		Min, Max	-28.1, 34.4	-42.7, 9.4	-42.7, 34.4
		GEE Estimates			
		LS Mean (SE)	3.36 (3.110)	-6.92 (2.039)	
		95% CI	(-2.74, 9.45)	(-10.91, -2.92)	
		LS Mean Difference (SE)		-10.28 (3.596)	
		95% CI		(-17.33, -3.23)	
		p-value		0.0043	
		HedgesG (95% CI)		-0.679 (-1.184, -0.175)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.11
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes		N_1	44	47	91
	Baseline	n	44	46	90
		Mean	49.01	55.89	52.52
		SD, SE	15.597, 2.351	16.748, 2.469	16.472, 1.736
		Median	51.56	57.29	54.17
		Q1, Q3	39.06, 62.50	45.83, 66.67	41.67, 64.58
		Min, Max	6.3, 71.9	14.6, 93.8	6.3, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.11
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	44	46	90
		Mean	49.01	55.89	52.52
		SD, SE	15.597, 2.351	16.748, 2.469	16.472, 1.736
		Median	51.56	57.29	54.17
		Q1, Q3	39.06, 62.50	45.83, 66.67	41.67, 64.58
		Min, Max	6.3, 71.9	14.6, 93.8	6.3, 93.8
		Observed			
		n	44	47	91
		Mean	45.22	48.18	46.75
		SD, SE	15.387, 2.320	18.441, 2.690	17.005, 1.783
		Median	45.83	50.00	45.83
		Q1, Q3	33.85, 54.17	33.33, 60.42	33.33, 59.38
		Min, Max	17.7, 88.5	14.6, 84.4	14.6, 88.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.11
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	44	46	90
		Mean	-3.79	-7.79	-5.83
		SD, SE	12.913, 1.947	12.175, 1.795	12.632, 1.332
		Median	-4.17	-6.77	-4.17
		Q1, Q3	-9.90, 4.17	-13.54, 2.08	-13.54, 3.13
		Min, Max	-39.6, 21.9	-43.8, 11.5	-43.8, 21.9
		GEE Estimates			
		LS Mean (SE)	-5.14 (2.583)	-7.04 (2.198)	
		95% CI	(-10.20, -0.08)	(-11.35, -2.73)	
		LS Mean Difference (SE)		-1.90 (2.584)	
		95% CI		(-6.97, 3.16)	
		p-value		0.4618	
		HedgesG (95% CI)		-0.313 (-0.729, 0.103)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.11
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	43	45	88
		Mean	48.64	55.14	51.96
		SD, SE	15.593, 2.378	16.140, 2.406	16.118, 1.718
		Median	51.04	56.25	53.65
		Q1, Q3	38.54, 62.50	45.83, 66.67	41.15, 63.54
		Min, Max	6.3, 71.9	14.6, 93.8	6.3, 93.8
		Observed			
		n	43	46	89
		Mean	47.07	45.92	46.48
		SD, SE	16.243, 2.477	16.404, 2.419	16.244, 1.722
		Median	44.79	47.92	45.83
		Q1, Q3	37.50, 60.42	32.29, 59.38	33.33, 59.38
		Min, Max	16.7, 89.6	11.5, 75.0	11.5, 89.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.11
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	43	45	88
		Mean	-1.57	-9.47	-5.61
		SD, SE	13.027, 1.987	13.044, 1.945	13.554, 1.445
		Median	0.00	-7.29	-3.65
		Q1, Q3	-10.42, 4.17	-15.63, 0.00	-13.54, 3.13
		Min, Max	-28.1, 29.2	-42.7, 14.6	-42.7, 29.2
		GEE Estimates			
		LS Mean (SE)	-2.93 (2.670)	-8.87 (2.024)	
		95% CI	(-8.16, 2.31)	(-12.83, -4.90)	
		LS Mean Difference (SE)		-5.94 (2.573)	
		95% CI		(-10.98, -0.90)	
		p-value		0.0210	
		HedgesG (95% CI)		-0.593 (-1.020, -0.166)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.11
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No		N_1	22	21	43
	Baseline	n	22	21	43
		Mean	40.58	43.11	41.81
		SD, SE	20.630, 4.398	19.200, 4.190	19.748, 3.012
		Median	40.63	39.58	39.58
		Q1, Q3	28.13, 50.00	32.29, 56.25	28.13, 55.21
		Min, Max	7.3, 92.7	11.5, 87.5	7.3, 92.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.11
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Baseline			
		n	22	21	43
		Mean	40.58	43.11	41.81
		SD, SE	20.630, 4.398	19.200, 4.190	19.748, 3.012
		Median	40.63	39.58	39.58
		Q1, Q3	28.13, 50.00	32.29, 56.25	28.13, 55.21
		Min, Max	7.3, 92.7	11.5, 87.5	7.3, 92.7
		Observed			
		n	22	21	43
		Mean	37.88	35.32	36.63
		SD, SE	24.363, 5.194	19.131, 4.175	21.742, 3.316
		Median	35.42	33.33	34.38
		Q1, Q3	19.79, 48.96	23.96, 44.79	19.79, 48.96
		Min, Max	8.3, 95.8	5.2, 82.3	5.2, 95.8

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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.11
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Change from Baseline			
		n	22	21	43
		Mean	-2.70	-7.79	-5.18
		SD, SE	11.766, 2.509	10.394, 2.268	11.282, 1.721
		Median	-1.56	-8.33	-5.21
		Q1, Q3	-9.38, 6.25	-11.46, -2.08	-10.42, 4.17
		Min, Max	-28.1, 18.8	-28.1, 9.4	-28.1, 18.8
		GEE Estimates			
		LS Mean (SE)	-1.05 (3.394)	-6.09 (2.425)	
		95% CI	(-7.70, 5.61)	(-10.84, -1.34)	
		LS Mean Difference (SE)		-5.04 (3.369)	
		95% CI		(-11.65, 1.56)	
		p-value		0.1343	
		HedgesG (95% CI)		-0.439 (-1.044, 0.166)	

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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.11
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Baseline			
		n	22	21	43
		Mean	40.58	43.11	41.81
		SD, SE	20.630, 4.398	19.200, 4.190	19.748, 3.012
		Median	40.63	39.58	39.58
		Q1, Q3	28.13, 50.00	32.29, 56.25	28.13, 55.21
		Min, Max	7.3, 92.7	11.5, 87.5	7.3, 92.7
		Observed			
		n	22	21	43
		Mean	39.96	39.53	39.75
		SD, SE	27.420, 5.846	20.216, 4.412	23.887, 3.643
		Median	35.42	33.33	33.33
		Q1, Q3	23.96, 50.00	27.08, 48.96	25.00, 50.00
		Min, Max	5.2, 97.9	8.3, 84.4	5.2, 97.9

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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.11
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Change from Baseline			
		n	22	21	43
		Mean	-0.62	-3.57	-2.06
		SD, SE	15.118, 3.223	18.413, 4.018	16.672, 2.542
		Median	-2.08	-4.17	-4.17
		Q1, Q3	-12.50, 5.21	-8.33, 0.00	-10.42, 4.17
		Min, Max	-28.1, 34.4	-42.7, 54.2	-42.7, 54.2
		GEE Estimates			
		LS Mean (SE)	1.04 (4.247)	-1.87 (3.922)	
		95% CI	(-7.29, 9.36)	(-9.56, 5.81)	
		LS Mean Difference (SE)		-2.91 (4.699)	
		95% CI		(-12.12, 6.30)	
		p-value		0.5356	
		HedgesG (95% CI)		-0.169 (-0.768, 0.430)	

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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.12
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes		N_1	13	17	30
	Baseline	n	13	17	30
		Mean	44.15	58.58	52.33
		SD, SE	16.751, 4.646	20.328, 4.930	19.924, 3.638
		Median	43.75	62.50	54.17
		Q1, Q3	29.17, 56.25	43.75, 70.83	34.38, 68.75
		Min, Max	20.8, 68.8	19.8, 93.8	19.8, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.5.24.12
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	13	17	30
		Mean	44.15	58.58	52.33
		SD, SE	16.751, 4.646	20.328, 4.930	19.924, 3.638
		Median	43.75	62.50	54.17
		Q1, Q3	29.17, 56.25	43.75, 70.83	34.38, 68.75
		Min, Max	20.8, 68.8	19.8, 93.8	19.8, 93.8
		Observed			
		n	13	17	30
		Mean	42.79	51.29	47.60
		SD, SE	15.199, 4.216	22.261, 5.399	19.681, 3.593
		Median	46.88	48.96	46.88
		Q1, Q3	33.33, 51.04	35.42, 73.96	33.33, 66.67
		Min, Max	17.7, 70.8	15.6, 84.4	15.6, 84.4

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Table 2.2.2.5.24.12
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	13	17	30
		Mean	-1.36	-7.29	-4.72
		SD, SE	16.229, 4.501	14.034, 3.404	15.052, 2.748
		Median	3.13	-5.21	-1.04
		Q1, Q3	-3.13, 8.33	-13.54, 3.13	-13.54, 4.17
		Min, Max	-39.6, 20.8	-43.8, 11.5	-43.8, 20.8
		GEE Estimates			
		LS Mean (SE)	-3.16 (3.555)	-3.80 (3.496)	
		95% CI	(-10.13, 3.81)	(-10.65, 3.06)	
		LS Mean Difference (SE)		-0.64 (5.170)	
		95% CI		(-10.77, 9.50)	
		p-value		0.9018	
		HedgesG (95% CI)		-0.371 (-1.099, 0.357)	

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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.12
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	13	16	29
		Mean	44.15	56.64	51.04
		SD, SE	16.751, 4.646	19.305, 4.826	18.970, 3.523
		Median	43.75	60.42	53.13
		Q1, Q3	29.17, 56.25	42.19, 70.83	34.38, 66.67
		Min, Max	20.8, 68.8	19.8, 93.8	19.8, 93.8
		Observed			
		n	13	16	29
		Mean	45.75	48.37	47.20
		SD, SE	15.587, 4.323	17.492, 4.373	16.426, 3.050
		Median	43.75	52.08	46.88
		Q1, Q3	38.54, 59.38	32.29, 64.58	32.29, 60.42
		Min, Max	24.0, 70.8	22.9, 75.0	22.9, 75.0

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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.12
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	13	16	29
		Mean	1.60	-8.27	-3.84
		SD, SE	12.591, 3.492	14.401, 3.600	14.283, 2.652
		Median	3.13	-4.17	-1.04
		Q1, Q3	-4.17, 5.21	-12.50, 2.08	-9.38, 4.17
		Min, Max	-26.0, 21.9	-42.7, 4.2	-42.7, 21.9
		GEE Estimates			
		LS Mean (SE)	-0.19 (2.858)	-5.21 (3.174)	
		95% CI	(-5.80, 5.41)	(-11.43, 1.02)	
		LS Mean Difference (SE)		-5.01 (4.076)	
		95% CI		(-13.00, 2.98)	
		p-value		0.2190	
		HedgesG (95% CI)		-0.679 (-1.432, 0.073)	

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Table 2.2.2.5.24.12
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No		N_1	53	51	104
	Baseline	n	53	50	103
		Mean	46.70	49.60	48.11
		SD, SE	18.083, 2.484	17.331, 2.451	17.696, 1.744
		Median	46.88	51.56	48.96
		Q1, Q3	37.50, 62.50	38.54, 61.46	38.54, 62.50
		Min, Max	6.3, 92.7	11.5, 87.5	6.3, 92.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Table 2.2.2.5.24.12
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Baseline			
		n	53	50	103
		Mean	46.70	49.60	48.11
		SD, SE	18.083, 2.484	17.331, 2.451	17.696, 1.744
		Median	46.88	51.56	48.96
		Q1, Q3	37.50, 62.50	38.54, 61.46	38.54, 62.50
		Min, Max	6.3, 92.7	11.5, 87.5	6.3, 92.7
		Observed			
		n	53	51	104
		Mean	42.77	41.85	42.32
		SD, SE	19.934, 2.738	18.056, 2.528	18.950, 1.858
		Median	40.63	42.71	41.67
		Q1, Q3	32.29, 53.13	28.13, 58.33	29.69, 54.69
		Min, Max	8.3, 95.8	5.2, 82.3	5.2, 95.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.12
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Change from Baseline			
		n	53	50	103
		Mean	-3.93	-7.96	-5.89
		SD, SE	11.490, 1.578	10.761, 1.522	11.271, 1.111
		Median	-4.17	-7.81	-5.21
		Q1, Q3	-9.38, 4.17	-15.62, 0.00	-12.50, 3.13
		Min, Max	-28.1, 21.9	-38.5, 10.4	-38.5, 21.9
		GEE Estimates			
		LS Mean (SE)	-1.38 (2.480)	-5.28 (1.949)	
		95% CI	(-6.25, 3.48)	(-9.10, -1.46)	
		LS Mean Difference (SE)		-3.90 (2.173)	
		95% CI		(-8.16, 0.36)	
		p-value		0.0728	
		HedgesG (95% CI)		-0.355 (-0.745, 0.034)	

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Table 2.2.2.5.24.12
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Baseline			
		n	52	50	102
		Mean	46.35	49.60	47.95
		SD, SE	18.084, 2.508	17.331, 2.451	17.706, 1.753
		Median	46.88	51.56	48.96
		Q1, Q3	37.50, 60.42	38.54, 61.46	38.54, 61.46
		Min, Max	6.3, 92.7	11.5, 87.5	6.3, 92.7
		Observed			
		n	52	51	103
		Mean	44.39	42.52	43.47
		SD, SE	21.994, 3.050	17.813, 2.494	19.957, 1.966
		Median	41.67	41.67	41.67
		Q1, Q3	30.21, 56.25	29.17, 57.29	29.17, 57.29
		Min, Max	5.2, 97.9	8.3, 84.4	5.2, 97.9

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Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.12
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Change from Baseline			
		n	52	50	102
		Mean	-1.96	-7.38	-4.62
		SD, SE	13.937, 1.933	15.416, 2.180	14.858, 1.471
		Median	-1.56	-7.29	-5.21
		Q1, Q3	-12.50, 4.69	-15.63, 0.00	-13.54, 2.08
		Min, Max	-28.1, 34.4	-42.7, 54.2	-42.7, 54.2
		GEE Estimates			
		LS Mean (SE)	0.57 (2.773)	-4.70 (2.542)	
		95% CI	(-4.87, 6.00)	(-9.68, 0.28)	
		LS Mean Difference (SE)		-5.27 (2.701)	
		95% CI		(-10.56, 0.03)	
		p-value		0.0513	
		HedgesG (95% CI)		-0.362 (-0.754, 0.029)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.14
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes		N_1	38	32	70
	Baseline	n	38	32	70
		Mean	48.57	52.38	50.31
		SD, SE	15.080, 2.446	19.639, 3.472	17.288, 2.066
		Median	48.44	53.65	51.04
		Q1, Q3	38.54, 62.50	41.15, 62.50	39.58, 62.50
		Min, Max	20.8, 71.9	11.5, 93.8	11.5, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.14
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Baseline			
		n	38	32	70
		Mean	48.57	52.38	50.31
		SD, SE	15.080, 2.446	19.639, 3.472	17.288, 2.066
		Median	48.44	53.65	51.04
		Q1, Q3	38.54, 62.50	41.15, 62.50	39.58, 62.50
		Min, Max	20.8, 71.9	11.5, 93.8	11.5, 93.8
		Observed			
		n	38	32	70
		Mean	44.49	41.93	43.32
		SD, SE	17.315, 2.809	18.210, 3.219	17.647, 2.109
		Median	41.67	39.58	40.63
		Q1, Q3	35.42, 54.17	30.73, 51.56	31.25, 54.17
		Min, Max	17.7, 83.3	12.5, 84.4	12.5, 84.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.14
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Change from Baseline			
		n	38	32	70
		Mean	-4.08	-10.45	-6.99
		SD, SE	13.585, 2.204	10.529, 1.861	12.608, 1.507
		Median	-4.17	-9.38	-6.25
		Q1, Q3	-10.42, 6.25	-16.15, -3.13	-13.54, 0.00
		Min, Max	-39.6, 20.8	-38.5, 11.5	-39.6, 20.8
		GEE Estimates			
		LS Mean (SE)	0.77 (2.792)	-4.81 (2.163)	
		95% CI	(-4.71, 6.24)	(-9.05, -0.57)	
		LS Mean Difference (SE)		-5.58 (2.825)	
		95% CI		(-11.12, -0.04)	
		p-value		0.0482	
		HedgesG (95% CI)		-0.505 (-0.983, -0.027)	

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The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.14
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Baseline			
		n	37	31	68
		Mean	48.14	51.18	49.53
		SD, SE	15.047, 2.474	18.732, 3.364	16.766, 2.033
		Median	47.92	53.13	51.04
		Q1, Q3	38.54, 62.50	39.58, 62.50	39.06, 62.50
		Min, Max	20.8, 71.9	11.5, 93.8	11.5, 93.8
		Observed			
		n	37	31	68
		Mean	46.76	41.40	44.32
		SD, SE	17.244, 2.835	16.636, 2.988	17.057, 2.068
		Median	41.67	36.46	41.15
		Q1, Q3	37.50, 59.38	30.21, 53.13	31.25, 54.69
		Min, Max	16.7, 92.7	11.5, 84.4	11.5, 92.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.14
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Change from Baseline			
		n	37	31	68
		Mean	-1.38	-9.78	-5.21
		SD, SE	14.034, 2.307	17.640, 3.168	16.215, 1.966
		Median	1.04	-8.33	-6.25
		Q1, Q3	-10.42, 5.21	-20.83, -3.13	-15.10, 3.65
		Min, Max	-28.1, 29.2	-42.7, 54.2	-42.7, 54.2
		GEE Estimates			
		LS Mean (SE)	3.41 (2.760)	-4.41 (2.893)	
		95% CI	(-2.00, 8.82)	(-10.08, 1.26)	
		LS Mean Difference (SE)		-7.82 (3.138)	
		95% CI		(-13.97, -1.67)	
		p-value		0.0127	
		HedgesG (95% CI)		-0.519 (-1.004, -0.033)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.14
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No		N_1	28	36	64
	Baseline	n	28	35	63
		Mean	42.97	51.43	47.67
		SD, SE	20.654, 3.903	17.473, 2.953	19.265, 2.427
		Median	43.23	52.08	46.88
		Q1, Q3	30.73, 57.29	38.54, 66.67	34.38, 62.50
		Min, Max	6.3, 92.7	12.5, 77.1	6.3, 92.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.14
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Baseline			
		n	28	35	63
		Mean	42.97	51.43	47.67
		SD, SE	20.654, 3.903	17.473, 2.953	19.265, 2.427
		Median	43.23	52.08	46.88
		Q1, Q3	30.73, 57.29	38.54, 66.67	34.38, 62.50
		Min, Max	6.3, 92.7	12.5, 77.1	6.3, 92.7
		Observed			
		n	28	36	64
		Mean	40.44	46.24	43.70
		SD, SE	21.149, 3.997	20.543, 3.424	20.846, 2.606
		Median	39.58	52.08	45.83
		Q1, Q3	25.52, 50.52	30.21, 63.54	28.65, 59.38
		Min, Max	8.3, 95.8	5.2, 76.0	5.2, 95.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.14
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Change from Baseline			
		n	28	35	63
		Mean	-2.53	-5.36	-4.10
		SD, SE	10.934, 2.066	12.080, 2.042	11.580, 1.459
		Median	-0.52	-1.04	-1.04
		Q1, Q3	-9.38, 4.17	-12.50, 3.13	-10.42, 4.17
		Min, Max	-26.0, 21.9	-43.8, 10.4	-43.8, 21.9
		GEE Estimates			
		LS Mean (SE)	-1.80 (3.348)	-4.14 (2.937)	
		95% CI	(-8.36, 4.77)	(-9.90, 1.61)	
		LS Mean Difference (SE)		-2.35 (2.943)	
		95% CI		(-8.11, 3.42)	
		p-value		0.4251	
		HedgesG (95% CI)		-0.237 (-0.736, 0.262)	

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The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.14
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Baseline			
		n	28	35	63
		Mean	42.97	51.43	47.67
		SD, SE	20.654, 3.903	17.473, 2.953	19.265, 2.427
		Median	43.23	52.08	46.88
		Q1, Q3	30.73, 57.29	38.54, 66.67	34.38, 62.50
		Min, Max	6.3, 92.7	12.5, 77.1	6.3, 92.7
		Observed			
		n	28	36	64
		Mean	41.89	46.09	44.25
		SD, SE	24.737, 4.675	18.671, 3.112	21.456, 2.682
		Median	40.63	47.40	44.27
		Q1, Q3	24.48, 54.17	31.25, 61.98	28.13, 60.42
		Min, Max	5.2, 97.9	8.3, 75.0	5.2, 97.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.14
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Change from Baseline			
		n	28	35	63
		Mean	-1.08	-5.65	-3.62
		SD, SE	13.401, 2.533	12.308, 2.080	12.905, 1.626
		Median	-1.56	-3.13	-2.08
		Q1, Q3	-11.46, 3.65	-11.46, 2.08	-11.46, 2.08
		Min, Max	-28.1, 34.4	-42.7, 17.7	-42.7, 34.4
		GEE Estimates			
		LS Mean (SE)	-0.34 (3.727)	-4.44 (3.039)	
		95% CI	(-7.65, 6.96)	(-10.40, 1.52)	
		LS Mean Difference (SE)		-4.10 (3.273)	
		95% CI		(-10.51, 2.32)	
		p-value		0.2108	
		HedgesG (95% CI)		-0.347 (-0.848, 0.153)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.15
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High		N_1	29	37	66
	Baseline	n	29	37	66
		Mean	53.81	57.71	56.00
		SD, SE	13.943, 2.589	18.174, 2.988	16.447, 2.024
		Median	58.33	59.38	58.33
		Q1, Q3	45.83, 64.58	47.92, 70.83	45.83, 66.67
		Min, Max	22.9, 71.9	11.5, 93.8	11.5, 93.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.15
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Baseline			
		n	29	37	66
		Mean	53.81	57.71	56.00
		SD, SE	13.943, 2.589	18.174, 2.988	16.447, 2.024
		Median	58.33	59.38	58.33
		Q1, Q3	45.83, 64.58	47.92, 70.83	45.83, 66.67
		Min, Max	22.9, 71.9	11.5, 93.8	11.5, 93.8
		Observed			
		n	29	37	66
		Mean	52.26	50.59	51.33
		SD, SE	15.810, 2.936	19.681, 3.236	17.969, 2.212
		Median	47.92	52.08	49.48
		Q1, Q3	40.63, 60.42	34.38, 65.63	36.46, 62.50
		Min, Max	28.1, 88.5	15.6, 84.4	15.6, 88.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.15
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Change from Baseline			
		n	29	37	66
		Mean	-1.54	-7.12	-4.67
		SD, SE	13.449, 2.497	12.977, 2.133	13.378, 1.647
		Median	-2.08	-5.21	-3.65
		Q1, Q3	-8.33, 7.29	-13.54, 3.13	-12.50, 4.17
		Min, Max	-28.1, 21.9	-43.8, 11.5	-43.8, 21.9
		GEE Estimates			
		LS Mean (SE)	1.46 (2.737)	-3.88 (2.152)	
		95% CI	(-3.90, 6.83)	(-8.10, 0.34)	
		LS Mean Difference (SE)		-5.35 (3.173)	
		95% CI		(-11.57, 0.87)	
		p-value		0.0920	
		HedgesG (95% CI)		-0.412 (-0.903, 0.079)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.15
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Baseline			
		n	28	36	64
		Mean	53.42	56.83	55.34
		SD, SE	14.041, 2.653	17.605, 2.934	16.111, 2.014
		Median	57.81	58.85	58.33
		Q1, Q3	44.79, 64.58	46.88, 69.79	45.83, 66.67
		Min, Max	22.9, 71.9	11.5, 93.8	11.5, 93.8
		Observed			
		n	28	36	64
		Mean	52.83	50.55	51.55
		SD, SE	17.831, 3.370	16.221, 2.703	16.844, 2.106
		Median	48.96	53.13	51.04
		Q1, Q3	40.63, 61.46	35.42, 63.54	39.06, 61.98
		Min, Max	16.7, 92.7	22.9, 84.4	16.7, 92.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.15
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-0.60	-6.28	-3.79
		SD, SE	13.497, 2.551	16.589, 2.765	15.461, 1.933
		Median	1.56	-5.73	-2.08
		Q1, Q3	-8.33, 4.69	-13.54, 2.60	-10.94, 4.17
		Min, Max	-28.1, 22.9	-42.7, 54.2	-42.7, 54.2
		GEE Estimates			
		LS Mean (SE)	2.33 (2.794)	-3.27 (2.491)	
		95% CI	(-3.15, 7.80)	(-8.15, 1.61)	
		LS Mean Difference (SE)		-5.60 (3.205)	
		95% CI		(-11.88, 0.68)	
		p-value		0.0807	
		HedgesG (95% CI)		-0.361 (-0.859, 0.137)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.15
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low		N_1	36	30	66
	Baseline	n	36	30	66
		Mean	38.77	44.69	41.46
		SD, SE	16.186, 2.698	16.240, 2.965	16.357, 2.013
		Median	41.15	45.31	41.67
		Q1, Q3	28.13, 50.52	33.33, 56.25	31.25, 53.13
		Min, Max	6.3, 67.7	12.5, 77.1	6.3, 77.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.15
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Baseline			
		n	36	30	66
		Mean	38.77	44.69	41.46
		SD, SE	16.186, 2.698	16.240, 2.965	16.357, 2.013
		Median	41.15	45.31	41.67
		Q1, Q3	28.13, 50.52	33.33, 56.25	31.25, 53.13
		Min, Max	6.3, 67.7	12.5, 77.1	6.3, 77.1
		Observed			
		n	36	30	66
		Mean	33.65	36.08	34.75
		SD, SE	15.132, 2.522	16.471, 3.007	15.678, 1.930
		Median	33.33	36.46	33.85
		Q1, Q3	20.31, 45.31	25.00, 50.00	21.88, 45.83
		Min, Max	8.3, 70.8	5.2, 66.7	5.2, 70.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.15
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Change from Baseline			
		n	36	30	66
		Mean	-5.12	-8.61	-6.71
		SD, SE	11.688, 1.948	9.706, 1.772	10.893, 1.341
		Median	-4.69	-8.85	-6.25
		Q1, Q3	-9.90, 3.13	-13.54, -2.08	-11.46, 0.00
		Min, Max	-39.6, 15.6	-28.1, 9.4	-39.6, 15.6
		GEE Estimates			
		LS Mean (SE)	-9.77 (2.318)	-12.20 (2.346)	
		95% CI	(-14.31, -5.23)	(-16.80, -7.60)	
		LS Mean Difference (SE)		-2.43 (2.600)	
		95% CI		(-7.52, 2.67)	
		p-value		0.3504	
		HedgesG (95% CI)		-0.313 (-0.801, 0.174)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.15
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Baseline			
		n	36	30	66
		Mean	38.77	44.69	41.46
		SD, SE	16.186, 2.698	16.240, 2.965	16.357, 2.013
		Median	41.15	45.31	41.67
		Q1, Q3	28.13, 50.52	33.33, 56.25	31.25, 53.13
		Min, Max	6.3, 67.7	12.5, 77.1	6.3, 77.1
		Observed			
		n	36	30	66
		Mean	36.83	35.52	36.24
		SD, SE	18.603, 3.100	16.384, 2.991	17.508, 2.155
		Median	35.42	32.29	32.29
		Q1, Q3	25.00, 46.35	25.00, 47.92	25.00, 47.92
		Min, Max	5.2, 85.4	8.3, 72.9	5.2, 85.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.2.5.24.15
Subgroup Analysis: Change from baseline to week 24 in the Total score of WOMAC
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Change from Baseline			
		n	36	30	66
		Mean	-1.94	-9.17	-5.22
		SD, SE	14.093, 2.349	13.126, 2.396	14.034, 1.728
		Median	-4.17	-7.81	-5.21
		Q1, Q3	-13.02, 4.17	-16.67, -1.04	-13.54, 1.04
		Min, Max	-28.1, 34.4	-42.7, 14.6	-42.7, 34.4
		GEE Estimates			
		LS Mean (SE)	-6.59 (2.688)	-12.75 (2.722)	
		95% CI	(-11.86, -1.32)	(-18.09, -7.42)	
		LS Mean Difference (SE)		-6.17 (3.210)	
		95% CI		(-12.46, 0.13)	
		p-value		0.0547	
		HedgesG (95% CI)		-0.515 (-1.007, -0.022)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for WOMAC Total Score as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of WOMAC Total Score as a covariate, with compound symmetry covariance structure.
Data source: ADWOMAC_WK96_303.sas7bdat, ADSL.sas7bdat Program source: t-pain-score-SUB.sas

Table 2.2.3.1.3.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6		N_1	27	17	44
	Baseline	n	27	17	44
		Mean	3.76	3.11	3.51
		SD, SE	1.549, 0.298	1.860, 0.451	1.685, 0.254
		Median	3.71	3.43	3.64
		Q1, Q3	2.71, 4.71	1.71, 4.29	2.43, 4.50
		Min, Max	0.0, 7.7	0.1, 6.0	0.0, 7.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Baseline			
		n	27	17	44
		Mean	3.76	3.11	3.51
		SD, SE	1.549, 0.298	1.860, 0.451	1.685, 0.254
		Median	3.71	3.43	3.64
		Q1, Q3	2.71, 4.71	1.71, 4.29	2.43, 4.50
		Min, Max	0.0, 7.7	0.1, 6.0	0.0, 7.7
		Observed			
		n	27	17	44
		Mean	2.72	2.79	2.75
		SD, SE	1.489, 0.287	1.414, 0.343	1.444, 0.218
		Median	2.71	3.29	2.79
		Q1, Q3	1.71, 3.57	1.86, 3.57	1.79, 3.57
		Min, Max	0.6, 6.7	0.4, 5.4	0.4, 6.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Change from Baseline			
		n	27	17	44
		Mean	-1.04	-0.32	-0.76
		SD, SE	1.708, 0.329	1.606, 0.390	1.688, 0.254
		Median	-0.43	-0.29	-0.43
		Q1, Q3	-2.14, 0.57	-1.00, 0.29	-1.64, 0.36
		Min, Max	-5.9, 1.1	-4.0, 2.6	-5.9, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.98 (0.265)	-0.66 (0.331)	
		95% CI	(-1.50, -0.46)	(-1.31, -0.02)	
		LS Mean Difference (SE)		0.32 (0.376)	
		95% CI		(-0.42, 1.06)	
		p-value		0.3957	
		HedgesG (95% CI)		0.412 (-0.201, 1.025)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Baseline			
		n	27	17	44
		Mean	3.76	3.11	3.51
		SD, SE	1.549, 0.298	1.860, 0.451	1.685, 0.254
		Median	3.71	3.43	3.64
		Q1, Q3	2.71, 4.71	1.71, 4.29	2.43, 4.50
		Min, Max	0.0, 7.7	0.1, 6.0	0.0, 7.7
		Observed			
		n	27	17	44
		Mean	3.06	2.74	2.94
		SD, SE	1.775, 0.342	1.468, 0.356	1.653, 0.249
		Median	2.57	3.29	3.07
		Q1, Q3	1.57, 4.57	1.57, 3.86	1.57, 3.93
		Min, Max	0.7, 7.1	0.0, 5.0	0.0, 7.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Change from Baseline			
		n	27	17	44
		Mean	-0.70	-0.37	-0.57
		SD, SE	1.796, 0.346	1.245, 0.302	1.598, 0.241
		Median	-0.71	-0.14	-0.57
		Q1, Q3	-2.00, 0.14	-0.86, 0.57	-1.64, 0.50
		Min, Max	-3.9, 3.9	-3.3, 1.4	-3.9, 3.9
		GEE Estimates			
		LS Mean (SE)	-0.64 (0.309)	-0.71 (0.305)	
		95% CI	(-1.25, -0.04)	(-1.31, -0.12)	
		LS Mean Difference (SE)		-0.07 (0.384)	
		95% CI		(-0.82, 0.68)	
		p-value		0.8559	
		HedgesG (95% CI)		0.196 (-0.412, 0.804)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6		N_1	39	51	90
	Baseline	n	39	51	90
		Mean	5.45	5.94	5.73
		SD, SE	2.289, 0.367	1.886, 0.264	2.072, 0.218
		Median	5.29	6.00	5.71
		Q1, Q3	4.14, 7.29	4.14, 7.57	4.14, 7.29
		Min, Max	0.4, 10.0	1.6, 10.0	0.4, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Baseline			
		n	39	51	90
		Mean	5.45	5.94	5.73
		SD, SE	2.289, 0.367	1.886, 0.264	2.072, 0.218
		Median	5.29	6.00	5.71
		Q1, Q3	4.14, 7.29	4.14, 7.57	4.14, 7.29
		Min, Max	0.4, 10.0	1.6, 10.0	0.4, 10.0
		Observed			
		n	39	51	90
		Mean	5.18	4.80	4.96
		SD, SE	2.481, 0.397	2.432, 0.341	2.447, 0.258
		Median	5.29	5.00	5.29
		Q1, Q3	3.00, 7.29	2.86, 6.57	3.00, 6.71
		Min, Max	0.6, 9.4	0.0, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Change from Baseline			
		n	39	51	90
		Mean	-0.27	-1.14	-0.76
		SD, SE	1.475, 0.236	1.610, 0.225	1.603, 0.169
		Median	-0.14	-0.86	-0.64
		Q1, Q3	-0.86, 0.71	-2.14, 0.00	-1.57, 0.14
		Min, Max	-4.1, 2.3	-7.3, 1.4	-7.3, 2.3
		GEE Estimates			
		LS Mean (SE)	0.03 (0.300)	-0.76 (0.248)	
		95% CI	(-0.56, 0.61)	(-1.25, -0.28)	
		LS Mean Difference (SE)		-0.79 (0.312)	
		95% CI		(-1.40, -0.18)	
		p-value		0.0117	
		HedgesG (95% CI)		-0.545 (-0.969, -0.120)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Baseline			
		n	38	50	88
		Mean	5.37	5.88	5.66
		SD, SE	2.261, 0.367	1.863, 0.263	2.048, 0.218
		Median	5.07	5.86	5.64
		Q1, Q3	4.14, 6.57	4.14, 7.29	4.14, 7.14
		Min, Max	0.4, 10.0	1.6, 10.0	0.4, 10.0
		Observed			
		n	38	50	88
		Mean	4.94	4.92	4.93
		SD, SE	2.472, 0.401	2.345, 0.332	2.386, 0.254
		Median	5.43	5.21	5.29
		Q1, Q3	3.00, 6.57	2.71, 6.71	2.86, 6.71
		Min, Max	0.1, 9.7	0.9, 9.7	0.1, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Change from Baseline			
		n	38	50	88
		Mean	-0.42	-0.96	-0.73
		SD, SE	1.655, 0.268	1.954, 0.276	1.840, 0.196
		Median	-0.50	-1.14	-0.86
		Q1, Q3	-1.29, 0.71	-2.14, 0.00	-1.86, 0.29
		Min, Max	-5.3, 3.0	-6.1, 4.1	-6.1, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.17 (0.344)	-0.60 (0.313)	
		95% CI	(-0.84, 0.50)	(-1.21, 0.01)	
		LS Mean Difference (SE)		-0.43 (0.369)	
		95% CI		(-1.15, 0.29)	
		p-value		0.2424	
		HedgesG (95% CI)		-0.288 (-0.712, 0.136)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6		N_1	49	48	97
	Baseline	n	49	48	97
		Mean	4.09	4.51	4.30
		SD, SE	1.880, 0.269	2.101, 0.303	1.993, 0.202
		Median	4.14	4.36	4.29
		Q1, Q3	2.71, 5.00	3.43, 5.79	2.86, 5.57
		Min, Max	0.0, 10.0	0.1, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Baseline			
		n	49	48	97
		Mean	4.09	4.51	4.30
		SD, SE	1.880, 0.269	2.101, 0.303	1.993, 0.202
		Median	4.14	4.36	4.29
		Q1, Q3	2.71, 5.00	3.43, 5.79	2.86, 5.57
		Min, Max	0.0, 10.0	0.1, 10.0	0.0, 10.0
		Observed			
		n	49	48	97
		Mean	3.41	3.70	3.55
		SD, SE	2.101, 0.300	2.212, 0.319	2.151, 0.218
		Median	3.00	3.36	3.29
		Q1, Q3	1.86, 4.57	1.93, 5.14	1.86, 5.00
		Min, Max	0.6, 9.4	0.0, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Change from Baseline			
		n	49	48	97
		Mean	-0.69	-0.81	-0.75
		SD, SE	1.554, 0.222	1.533, 0.221	1.537, 0.156
		Median	-0.43	-0.57	-0.57
		Q1, Q3	-1.43, 0.43	-1.86, 0.14	-1.57, 0.29
		Min, Max	-5.9, 2.1	-4.0, 2.6	-5.9, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.37 (0.264)	-0.44 (0.250)	
		95% CI	(-0.88, 0.15)	(-0.93, 0.05)	
		LS Mean Difference (SE)		-0.07 (0.288)	
		95% CI		(-0.63, 0.49)	
		p-value		0.8059	
		HedgesG (95% CI)		-0.077 (-0.475, 0.321)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Baseline			
		n	49	48	97
		Mean	4.09	4.51	4.30
		SD, SE	1.880, 0.269	2.101, 0.303	1.993, 0.202
		Median	4.14	4.36	4.29
		Q1, Q3	2.71, 5.00	3.43, 5.79	2.86, 5.57
		Min, Max	0.0, 10.0	0.1, 10.0	0.0, 10.0
		Observed			
		n	49	48	97
		Mean	3.42	3.76	3.59
		SD, SE	2.144, 0.306	2.197, 0.317	2.166, 0.220
		Median	3.00	3.50	3.29
		Q1, Q3	1.71, 4.86	1.93, 5.07	1.86, 5.00
		Min, Max	0.1, 9.3	0.0, 9.7	0.0, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Change from Baseline			
		n	49	48	97
		Mean	-0.67	-0.75	-0.71
		SD, SE	1.724, 0.246	1.632, 0.236	1.671, 0.170
		Median	-0.71	-0.86	-0.86
		Q1, Q3	-1.86, 0.29	-1.71, 0.21	-1.71, 0.29
		Min, Max	-5.3, 3.9	-4.4, 4.1	-5.3, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.35 (0.295)	-0.38 (0.269)	
		95% CI	(-0.93, 0.23)	(-0.91, 0.14)	
		LS Mean Difference (SE)		-0.03 (0.308)	
		95% CI		(-0.64, 0.57)	
		p-value		0.9105	
		HedgesG (95% CI)		-0.050 (-0.448, 0.348)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6		N_1	17	20	37
	Baseline	n	17	20	37
		Mean	6.68	6.96	6.83
		SD, SE	1.819, 0.441	1.504, 0.336	1.638, 0.269
		Median	6.14	7.00	6.86
		Q1, Q3	5.86, 8.57	6.36, 8.29	5.86, 8.29
		Min, Max	4.0, 9.3	3.7, 8.9	3.7, 9.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Baseline			
		n	17	20	37
		Mean	6.68	6.96	6.83
		SD, SE	1.819, 0.441	1.504, 0.336	1.638, 0.269
		Median	6.14	7.00	6.86
		Q1, Q3	5.86, 8.57	6.36, 8.29	5.86, 8.29
		Min, Max	4.0, 9.3	3.7, 8.9	3.7, 9.3
		Observed			
		n	17	20	37
		Mean	6.38	5.72	6.02
		SD, SE	2.004, 0.486	2.198, 0.491	2.108, 0.347
		Median	6.71	6.29	6.43
		Q1, Q3	5.29, 8.00	4.14, 7.21	5.29, 7.86
		Min, Max	2.0, 8.7	1.4, 9.0	1.4, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Change from Baseline			
		n	17	20	37
		Mean	-0.30	-1.24	-0.81
		SD, SE	1.768, 0.429	1.868, 0.418	1.858, 0.305
		Median	0.00	-0.57	-0.43
		Q1, Q3	-0.86, 0.57	-1.93, -0.14	-1.43, 0.29
		Min, Max	-4.1, 2.3	-7.3, 0.9	-7.3, 2.3
		GEE Estimates			
		LS Mean (SE)	0.08 (0.446)	-0.67 (0.262)	
		95% CI	(-0.79, 0.96)	(-1.19, -0.16)	
		LS Mean Difference (SE)		-0.76 (0.582)	
		95% CI		(-1.90, 0.38)	
		p-value		0.1931	
		HedgesG (95% CI)		-0.487 (-1.143, 0.169)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Baseline			
		n	16	19	35
		Mean	6.56	6.86	6.73
		SD, SE	1.810, 0.453	1.486, 0.341	1.624, 0.275
		Median	6.14	7.00	6.86
		Q1, Q3	5.21, 8.36	6.29, 8.29	5.86, 8.29
		Min, Max	4.0, 9.3	3.7, 8.9	3.7, 9.3
		Observed			
		n	16	19	35
		Mean	6.42	5.90	6.14
		SD, SE	1.528, 0.382	2.033, 0.466	1.813, 0.306
		Median	6.29	6.57	6.57
		Q1, Q3	5.43, 7.50	3.43, 7.71	5.29, 7.71
		Min, Max	3.4, 9.7	2.6, 8.4	2.6, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Change from Baseline			
		n	16	19	35
		Mean	-0.14	-0.96	-0.59
		SD, SE	1.642, 0.411	2.243, 0.515	2.006, 0.339
		Median	-0.29	-1.00	-0.43
		Q1, Q3	-0.86, 0.79	-2.29, 0.29	-2.14, 0.71
		Min, Max	-3.6, 3.0	-6.1, 3.7	-6.1, 3.7
		GEE Estimates			
		LS Mean (SE)	0.10 (0.395)	-0.44 (0.326)	
		95% CI	(-0.68, 0.87)	(-1.08, 0.20)	
		LS Mean Difference (SE)		-0.54 (0.577)	
		95% CI		(-1.67, 0.59)	
		p-value		0.3488	
		HedgesG (95% CI)		-0.390 (-1.062, 0.281)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU		N_1	58	58	116
	Baseline	n	58	58	116
		Mean	4.92	5.32	5.12
		SD, SE	2.193, 0.288	2.115, 0.278	2.154, 0.200
		Median	4.64	5.57	4.93
		Q1, Q3	3.71, 6.14	3.86, 6.86	3.71, 6.50
		Min, Max	0.0, 10.0	1.0, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Baseline			
		n	58	58	116
		Mean	4.92	5.32	5.12
		SD, SE	2.193, 0.288	2.115, 0.278	2.154, 0.200
		Median	4.64	5.57	4.93
		Q1, Q3	3.71, 6.14	3.86, 6.86	3.71, 6.50
		Min, Max	0.0, 10.0	1.0, 10.0	0.0, 10.0
		Observed			
		n	58	58	116
		Mean	4.27	4.33	4.30
		SD, SE	2.411, 0.317	2.420, 0.318	2.405, 0.223
		Median	3.57	3.86	3.71
		Q1, Q3	2.14, 6.29	2.14, 6.43	2.14, 6.29
		Min, Max	0.6, 9.3	0.0, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Change from Baseline			
		n	58	58	116
		Mean	-0.66	-0.99	-0.82
		SD, SE	1.640, 0.215	1.640, 0.215	1.642, 0.152
		Median	-0.43	-0.50	-0.43
		Q1, Q3	-1.43, 0.57	-2.00, 0.00	-1.71, 0.21
		Min, Max	-5.9, 2.3	-7.3, 2.1	-7.3, 2.3
		GEE Estimates			
		LS Mean (SE)	-0.75 (0.212)	-1.05 (0.217)	
		95% CI	(-1.17, -0.33)	(-1.48, -0.63)	
		LS Mean Difference (SE)		-0.30 (0.287)	
		95% CI		(-0.87, 0.26)	
		p-value		0.2910	
		HedgesG (95% CI)		-0.203 (-0.568, 0.162)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Baseline			
		n	57	57	114
		Mean	4.86	5.26	5.06
		SD, SE	2.157, 0.286	2.084, 0.276	2.121, 0.199
		Median	4.57	5.57	4.86
		Q1, Q3	3.71, 6.14	3.86, 6.86	3.71, 6.43
		Min, Max	0.0, 10.0	1.0, 10.0	0.0, 10.0
		Observed			
		n	57	57	114
		Mean	4.32	4.31	4.32
		SD, SE	2.314, 0.306	2.337, 0.310	2.315, 0.217
		Median	4.57	4.00	4.29
		Q1, Q3	2.43, 5.86	2.43, 6.14	2.43, 6.00
		Min, Max	0.1, 9.7	0.6, 9.7	0.1, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Change from Baseline			
		n	57	57	114
		Mean	-0.54	-0.95	-0.74
		SD, SE	1.742, 0.231	1.737, 0.230	1.744, 0.163
		Median	-0.57	-0.86	-0.71
		Q1, Q3	-1.57, 0.71	-2.14, 0.14	-1.86, 0.29
		Min, Max	-5.3, 3.9	-6.1, 3.7	-6.1, 3.9
		GEE Estimates			
		LS Mean (SE)	-0.66 (0.222)	-1.02 (0.218)	
		95% CI	(-1.10, -0.23)	(-1.45, -0.59)	
		LS Mean Difference (SE)		-0.36 (0.301)	
		95% CI		(-0.95, 0.23)	
		p-value		0.2323	
		HedgesG (95% CI)		-0.231 (-0.600, 0.137)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia		N_1	8	10	18
	Baseline	n	8	10	18
		Mean	3.55	4.70	4.19
		SD, SE	1.688, 0.597	2.925, 0.925	2.459, 0.580
		Median	2.86	4.86	3.71
		Q1, Q3	2.57, 4.07	3.00, 6.29	2.71, 6.29
		Min, Max	2.1, 7.3	0.1, 8.9	0.1, 8.9

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Baseline			
		n	8	10	18
		Mean	3.55	4.70	4.19
		SD, SE	1.688, 0.597	2.925, 0.925	2.459, 0.580
		Median	2.86	4.86	3.71
		Q1, Q3	2.57, 4.07	3.00, 6.29	2.71, 6.29
		Min, Max	2.1, 7.3	0.1, 8.9	0.1, 8.9
		Observed			
		n	8	10	18
		Mean	3.46	4.11	3.83
		SD, SE	2.720, 0.962	2.235, 0.707	2.409, 0.568
		Median	2.71	3.50	3.21
		Q1, Q3	1.71, 4.14	3.14, 5.29	2.57, 5.29
		Min, Max	1.1, 9.4	0.4, 9.0	0.4, 9.4

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Change from Baseline			
		n	8	10	18
		Mean	-0.09	-0.59	-0.37
		SD, SE	1.322, 0.468	1.653, 0.523	1.494, 0.352
		Median	-0.07	-0.64	-0.50
		Q1, Q3	-1.14, 0.71	-1.00, 0.29	-1.00, 0.29
		Min, Max	-1.9, 2.1	-3.6, 2.6	-3.6, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.06 (0.462)	-0.45 (0.424)	
		95% CI	(-0.97, 0.85)	(-1.28, 0.38)	
		LS Mean Difference (SE)		-0.39 (0.660)	
		95% CI		(-1.68, 0.90)	
		p-value		0.5532	
		HedgesG (95% CI)		-0.294 (-1.228, 0.641)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Baseline			
		n	8	10	18
		Mean	3.55	4.70	4.19
		SD, SE	1.688, 0.597	2.925, 0.925	2.459, 0.580
		Median	2.86	4.86	3.71
		Q1, Q3	2.57, 4.07	3.00, 6.29	2.71, 6.29
		Min, Max	2.1, 7.3	0.1, 8.9	0.1, 8.9
		Observed			
		n	8	10	18
		Mean	3.02	4.66	3.93
		SD, SE	2.737, 0.968	2.519, 0.797	2.673, 0.630
		Median	2.29	4.79	3.71
		Q1, Q3	1.14, 3.71	2.86, 7.14	2.00, 5.43
		Min, Max	0.7, 9.1	0.0, 7.9	0.0, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Change from Baseline			
		n	8	10	18
		Mean	-0.54	-0.04	-0.26
		SD, SE	1.536, 0.543	2.118, 0.670	1.847, 0.435
		Median	-1.00	-0.57	-0.86
		Q1, Q3	-1.64, 0.64	-1.57, 1.43	-1.57, 1.43
		Min, Max	-2.1, 1.9	-2.9, 4.1	-2.9, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.51 (0.592)	0.09 (0.437)	
		95% CI	(-1.67, 0.65)	(-0.76, 0.95)	
		LS Mean Difference (SE)		0.60 (0.744)	
		95% CI		(-0.86, 2.06)	
		p-value		0.4218	
		HedgesG (95% CI)		0.235 (-0.698, 1.168)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male		N_1	23	24	47
	Baseline	n	23	24	47
		Mean	3.99	4.78	4.39
		SD, SE	2.019, 0.421	2.221, 0.453	2.139, 0.312
		Median	4.29	4.64	4.43
		Q1, Q3	2.71, 4.86	3.57, 6.29	2.71, 5.57
		Min, Max	0.0, 10.0	1.0, 8.7	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Baseline			
		n	23	24	47
		Mean	3.99	4.78	4.39
		SD, SE	2.019, 0.421	2.221, 0.453	2.139, 0.312
		Median	4.29	4.64	4.43
		Q1, Q3	2.71, 4.86	3.57, 6.29	2.71, 5.57
		Min, Max	0.0, 10.0	1.0, 8.7	0.0, 10.0
		Observed			
		n	23	24	47
		Mean	3.55	3.91	3.74
		SD, SE	2.315, 0.483	2.125, 0.434	2.203, 0.321
		Median	3.00	3.64	3.29
		Q1, Q3	1.86, 4.29	2.64, 5.43	2.00, 5.29
		Min, Max	0.6, 9.4	0.0, 8.1	0.0, 9.4

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Change from Baseline			
		n	23	24	47
		Mean	-0.43	-0.87	-0.66
		SD, SE	1.451, 0.303	1.542, 0.315	1.498, 0.219
		Median	-0.71	-0.64	-0.71
		Q1, Q3	-1.57, 0.71	-2.07, 0.14	-2.00, 0.57
		Min, Max	-3.0, 2.1	-3.9, 2.1	-3.9, 2.1
		GEE Estimates			
		LS Mean (SE)	-0.33 (0.345)	-0.53 (0.313)	
		95% CI	(-1.01, 0.35)	(-1.14, 0.08)	
		LS Mean Difference (SE)		-0.20 (0.420)	
		95% CI		(-1.02, 0.63)	
		p-value		0.6387	
		HedgesG (95% CI)		-0.279 (-0.854, 0.296)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Baseline			
		n	23	23	46
		Mean	3.99	4.61	4.30
		SD, SE	2.019, 0.421	2.103, 0.438	2.062, 0.304
		Median	4.29	4.43	4.36
		Q1, Q3	2.71, 4.86	3.57, 6.29	2.71, 5.57
		Min, Max	0.0, 10.0	1.0, 8.3	0.0, 10.0
		Observed			
		n	23	23	46
		Mean	3.77	3.39	3.58
		SD, SE	2.454, 0.512	1.629, 0.340	2.068, 0.305
		Median	3.00	3.29	3.21
		Q1, Q3	1.71, 5.29	2.14, 4.86	2.14, 5.00
		Min, Max	0.7, 9.3	0.6, 6.6	0.6, 9.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Change from Baseline			
		n	23	23	46
		Mean	-0.22	-1.22	-0.72
		SD, SE	1.961, 0.409	1.248, 0.260	1.703, 0.251
		Median	-0.57	-1.14	-1.00
		Q1, Q3	-1.57, 1.00	-2.29, 0.00	-2.14, 0.43
		Min, Max	-3.9, 3.9	-3.3, 0.6	-3.9, 3.9
		GEE Estimates			
		LS Mean (SE)	-0.11 (0.438)	-0.93 (0.244)	
		95% CI	(-0.97, 0.75)	(-1.41, -0.45)	
		LS Mean Difference (SE)		-0.82 (0.428)	
		95% CI		(-1.66, 0.02)	
		p-value		0.0559	
		HedgesG (95% CI)		-0.589 (-1.179, 0.002)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female		N_1	43	44	87
	Baseline	n	43	44	87
		Mean	5.17	5.47	5.32
		SD, SE	2.164, 0.330	2.232, 0.337	2.191, 0.235
		Median	5.14	5.64	5.29
		Q1, Q3	3.57, 6.43	3.86, 7.00	3.71, 6.86
		Min, Max	0.4, 9.3	0.1, 10.0	0.1, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Baseline			
		n	43	44	87
		Mean	5.17	5.47	5.32
		SD, SE	2.164, 0.330	2.232, 0.337	2.191, 0.235
		Median	5.14	5.64	5.29
		Q1, Q3	3.57, 6.43	3.86, 7.00	3.71, 6.86
		Min, Max	0.4, 9.3	0.1, 10.0	0.1, 10.0
		Observed			
		n	43	44	87
		Mean	4.50	4.51	4.50
		SD, SE	2.471, 0.377	2.505, 0.378	2.474, 0.265
		Median	4.57	4.00	4.14
		Q1, Q3	2.00, 6.43	2.57, 6.43	2.14, 6.43
		Min, Max	0.6, 8.7	0.4, 10.0	0.4, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Change from Baseline			
		n	43	44	87
		Mean	-0.67	-0.97	-0.82
		SD, SE	1.695, 0.258	1.702, 0.257	1.695, 0.182
		Median	-0.43	-0.43	-0.43
		Q1, Q3	-1.43, 0.57	-1.71, 0.00	-1.57, 0.29
		Min, Max	-5.9, 2.3	-7.3, 2.6	-7.3, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.39 (0.319)	-0.79 (0.324)	
		95% CI	(-1.01, 0.24)	(-1.43, -0.16)	
		LS Mean Difference (SE)		-0.41 (0.337)	
		95% CI		(-1.07, 0.25)	
		p-value		0.2256	
		HedgesG (95% CI)		-0.173 (-0.594, 0.248)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Baseline			
		n	42	44	86
		Mean	5.09	5.47	5.29
		SD, SE	2.123, 0.328	2.232, 0.337	2.175, 0.235
		Median	5.07	5.64	5.29
		Q1, Q3	3.57, 6.29	3.86, 7.00	3.71, 6.86
		Min, Max	0.4, 9.3	0.1, 10.0	0.1, 10.0
		Observed			
		n	42	44	86
		Mean	4.37	4.88	4.63
		SD, SE	2.349, 0.362	2.515, 0.379	2.434, 0.262
		Median	4.71	5.00	4.79
		Q1, Q3	2.43, 6.00	2.71, 7.07	2.57, 6.57
		Min, Max	0.1, 9.7	0.0, 9.7	0.0, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Change from Baseline			
		n	42	44	86
		Mean	-0.71	-0.60	-0.65
		SD, SE	1.547, 0.239	2.024, 0.305	1.798, 0.194
		Median	-0.57	-0.64	-0.57
		Q1, Q3	-1.86, 0.14	-1.71, 0.29	-1.71, 0.29
		Min, Max	-5.3, 2.3	-6.1, 4.1	-6.1, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.47 (0.332)	-0.42 (0.344)	
		95% CI	(-1.12, 0.18)	(-1.10, 0.25)	
		LS Mean Difference (SE)		0.05 (0.366)	
		95% CI		(-0.67, 0.76)	
		p-value		0.8991	
		HedgesG (95% CI)		0.063 (-0.360, 0.486)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White		N_1	53	55	108
	Baseline	n	53	55	108
		Mean	4.89	5.31	5.11
		SD, SE	2.193, 0.301	2.102, 0.283	2.148, 0.207
		Median	4.57	5.57	4.93
		Q1, Q3	3.71, 6.14	3.86, 6.86	3.71, 6.50
		Min, Max	0.0, 10.0	1.0, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Baseline			
		n	53	55	108
		Mean	4.89	5.31	5.11
		SD, SE	2.193, 0.301	2.102, 0.283	2.148, 0.207
		Median	4.57	5.57	4.93
		Q1, Q3	3.71, 6.14	3.86, 6.86	3.71, 6.50
		Min, Max	0.0, 10.0	1.0, 10.0	0.0, 10.0
		Observed			
		n	53	55	108
		Mean	4.16	4.36	4.26
		SD, SE	2.465, 0.339	2.429, 0.328	2.437, 0.235
		Median	3.43	3.86	3.57
		Q1, Q3	2.00, 5.86	2.14, 6.43	2.14, 6.21
		Min, Max	0.6, 9.3	0.0, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Change from Baseline			
		n	53	55	108
		Mean	-0.73	-0.96	-0.85
		SD, SE	1.605, 0.220	1.669, 0.225	1.634, 0.157
		Median	-0.57	-0.43	-0.43
		Q1, Q3	-1.43, 0.43	-1.86, 0.00	-1.64, 0.14
		Min, Max	-5.9, 2.3	-7.3, 2.1	-7.3, 2.3
		GEE Estimates			
		LS Mean (SE)	-0.83 (0.218)	-1.04 (0.228)	
		95% CI	(-1.26, -0.41)	(-1.49, -0.60)	
		LS Mean Difference (SE)		-0.21 (0.298)	
		95% CI		(-0.79, 0.38)	
		p-value		0.4840	
		HedgesG (95% CI)		-0.139 (-0.516, 0.239)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Baseline			
		n	53	55	108
		Mean	4.89	5.31	5.11
		SD, SE	2.193, 0.301	2.102, 0.283	2.148, 0.207
		Median	4.57	5.57	4.93
		Q1, Q3	3.71, 6.14	3.86, 6.86	3.71, 6.50
		Min, Max	0.0, 10.0	1.0, 10.0	0.0, 10.0
		Observed			
		n	53	55	108
		Mean	4.26	4.37	4.31
		SD, SE	2.247, 0.309	2.356, 0.318	2.293, 0.221
		Median	4.43	4.14	4.29
		Q1, Q3	2.43, 5.71	2.43, 6.43	2.43, 5.86
		Min, Max	0.7, 9.7	0.6, 9.7	0.6, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Change from Baseline			
		n	53	55	108
		Mean	-0.63	-0.95	-0.79
		SD, SE	1.707, 0.235	1.764, 0.238	1.735, 0.167
		Median	-0.57	-0.86	-0.71
		Q1, Q3	-1.57, 0.29	-2.14, 0.14	-1.93, 0.21
		Min, Max	-5.3, 3.9	-6.1, 3.7	-6.1, 3.9
		GEE Estimates			
		LS Mean (SE)	-0.74 (0.222)	-1.03 (0.226)	
		95% CI	(-1.17, -0.30)	(-1.47, -0.59)	
		LS Mean Difference (SE)		-0.29 (0.305)	
		95% CI		(-0.89, 0.31)	
		p-value		0.3379	
		HedgesG (95% CI)		-0.178 (-0.556, 0.200)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White		N_1	13	13	26
	Baseline	n	13	13	26
		Mean	4.22	4.87	4.54
		SD, SE	2.092, 0.580	2.805, 0.778	2.447, 0.480
		Median	3.57	4.43	4.07
		Q1, Q3	2.71, 5.43	3.71, 6.29	2.71, 6.29
		Min, Max	2.0, 8.6	0.1, 8.9	0.1, 8.9

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Baseline			
		n	13	13	26
		Mean	4.22	4.87	4.54
		SD, SE	2.092, 0.580	2.805, 0.778	2.447, 0.480
		Median	3.57	4.43	4.07
		Q1, Q3	2.71, 5.43	3.71, 6.29	2.71, 6.29
		Min, Max	2.0, 8.6	0.1, 8.9	0.1, 8.9
		Observed			
		n	13	13	26
		Mean	4.21	4.04	4.13
		SD, SE	2.444, 0.678	2.228, 0.618	2.293, 0.450
		Median	3.00	3.29	3.29
		Q1, Q3	2.57, 5.71	3.14, 5.29	2.86, 5.43
		Min, Max	1.1, 9.4	0.4, 9.0	0.4, 9.4

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Change from Baseline			
		n	13	13	26
		Mean	-0.01	-0.82	-0.42
		SD, SE	1.541, 0.427	1.548, 0.429	1.569, 0.308
		Median	0.29	-0.71	-0.50
		Q1, Q3	-0.71, 0.71	-2.00, 0.14	-1.57, 0.57
		Min, Max	-3.3, 2.1	-3.6, 2.6	-3.6, 2.6
		GEE Estimates			
		LS Mean (SE)	0.03 (0.353)	-0.65 (0.377)	
		95% CI	(-0.66, 0.72)	(-1.39, 0.09)	
		LS Mean Difference (SE)		-0.68 (0.522)	
		95% CI		(-1.71, 0.34)	
		p-value		0.1923	
		HedgesG (95% CI)		-0.490 (-1.270, 0.290)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Baseline			
		n	12	12	24
		Mean	3.86	4.55	4.20
		SD, SE	1.706, 0.492	2.670, 0.771	2.219, 0.453
		Median	3.29	4.14	3.86
		Q1, Q3	2.57, 5.00	3.36, 6.29	2.71, 5.79
		Min, Max	2.0, 7.3	0.1, 8.9	0.1, 8.9
		Observed			
		n	12	12	24
		Mean	3.73	4.35	4.04
		SD, SE	2.997, 0.865	2.416, 0.697	2.681, 0.547
		Median	2.79	4.36	3.86
		Q1, Q3	1.14, 6.57	2.43, 6.29	2.00, 6.57
		Min, Max	0.1, 9.1	0.0, 7.9	0.0, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Change from Baseline			
		n	12	12	24
		Mean	-0.13	-0.20	-0.17
		SD, SE	1.716, 0.495	1.975, 0.570	1.810, 0.369
		Median	-0.57	-0.64	-0.57
		Q1, Q3	-1.64, 1.36	-1.64, 0.93	-1.64, 1.21
		Min, Max	-2.1, 3.0	-2.9, 4.1	-2.9, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.28 (0.547)	-0.12 (0.438)	
		95% CI	(-1.35, 0.80)	(-0.98, 0.73)	
		LS Mean Difference (SE)		0.15 (0.694)	
		95% CI		(-1.21, 1.51)	
		p-value		0.8283	
		HedgesG (95% CI)		-0.036 (-0.836, 0.765)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years		N_1	36	31	67
	Baseline	n	36	31	67
		Mean	4.81	5.40	5.08
		SD, SE	2.495, 0.416	2.035, 0.365	2.295, 0.280
		Median	4.36	5.71	4.86
		Q1, Q3	2.71, 6.36	3.86, 7.00	3.00, 6.86
		Min, Max	0.4, 10.0	1.0, 8.4	0.4, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Baseline			
		n	36	31	67
		Mean	4.81	5.40	5.08
		SD, SE	2.495, 0.416	2.035, 0.365	2.295, 0.280
		Median	4.36	5.71	4.86
		Q1, Q3	2.71, 6.36	3.86, 7.00	3.00, 6.86
		Min, Max	0.4, 10.0	1.0, 8.4	0.4, 10.0
		Observed			
		n	36	31	67
		Mean	4.34	4.63	4.47
		SD, SE	2.632, 0.439	2.302, 0.413	2.471, 0.302
		Median	3.36	4.71	3.71
		Q1, Q3	2.29, 6.50	2.86, 6.43	2.57, 6.43
		Min, Max	0.6, 9.4	0.9, 8.6	0.6, 9.4

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Change from Baseline			
		n	36	31	67
		Mean	-0.48	-0.77	-0.61
		SD, SE	1.585, 0.264	1.186, 0.213	1.412, 0.172
		Median	-0.43	-0.43	-0.43
		Q1, Q3	-0.93, 0.57	-1.43, 0.00	-1.29, 0.29
		Min, Max	-5.9, 2.1	-3.6, 1.3	-5.9, 2.1
		GEE Estimates			
		LS Mean (SE)	-0.45 (0.329)	-0.71 (0.289)	
		95% CI	(-1.10, 0.19)	(-1.28, -0.14)	
		LS Mean Difference (SE)		-0.26 (0.333)	
		95% CI		(-0.91, 0.40)	
		p-value		0.4426	
		HedgesG (95% CI)		-0.202 (-0.683, 0.280)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Baseline			
		n	36	31	67
		Mean	4.81	5.40	5.08
		SD, SE	2.495, 0.416	2.035, 0.365	2.295, 0.280
		Median	4.36	5.71	4.86
		Q1, Q3	2.71, 6.36	3.86, 7.00	3.00, 6.86
		Min, Max	0.4, 10.0	1.0, 8.4	0.4, 10.0
		Observed			
		n	36	31	67
		Mean	4.21	4.53	4.36
		SD, SE	2.573, 0.429	2.191, 0.394	2.391, 0.292
		Median	4.00	4.43	4.43
		Q1, Q3	2.14, 6.00	2.71, 6.14	2.29, 6.00
		Min, Max	0.1, 9.3	1.0, 8.4	0.1, 9.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Change from Baseline			
		n	36	31	67
		Mean	-0.60	-0.87	-0.72
		SD, SE	1.388, 0.231	1.716, 0.308	1.543, 0.188
		Median	-0.71	-0.86	-0.71
		Q1, Q3	-1.50, 0.36	-2.14, 0.14	-1.71, 0.14
		Min, Max	-3.6, 3.0	-4.4, 3.7	-4.4, 3.7
		GEE Estimates			
		LS Mean (SE)	-0.58 (0.321)	-0.81 (0.320)	
		95% CI	(-1.20, 0.05)	(-1.44, -0.18)	
		LS Mean Difference (SE)		-0.23 (0.362)	
		95% CI		(-0.94, 0.48)	
		p-value		0.5182	
		HedgesG (95% CI)		-0.171 (-0.652, 0.310)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years		N_1	30	37	67
	Baseline	n	30	37	67
		Mean	4.69	5.09	4.91
		SD, SE	1.753, 0.320	2.411, 0.396	2.136, 0.261
		Median	4.57	5.29	4.57
		Q1, Q3	3.71, 5.57	3.57, 6.86	3.71, 6.29
		Min, Max	0.0, 8.6	0.1, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Baseline			
		n	30	37	67
		Mean	4.69	5.09	4.91
		SD, SE	1.753, 0.320	2.411, 0.396	2.136, 0.261
		Median	4.57	5.29	4.57
		Q1, Q3	3.71, 5.57	3.57, 6.86	3.71, 6.29
		Min, Max	0.0, 8.6	0.1, 10.0	0.0, 10.0
		Observed			
		n	30	37	67
		Mean	3.97	4.02	4.00
		SD, SE	2.221, 0.405	2.438, 0.401	2.326, 0.284
		Median	3.57	3.43	3.43
		Q1, Q3	1.86, 5.43	2.14, 5.86	2.00, 5.71
		Min, Max	0.6, 8.1	0.0, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Change from Baseline			
		n	30	37	67
		Mean	-0.72	-1.07	-0.91
		SD, SE	1.649, 0.301	1.941, 0.319	1.811, 0.221
		Median	-0.57	-1.00	-0.86
		Q1, Q3	-1.86, 0.57	-2.00, 0.14	-2.00, 0.29
		Min, Max	-3.6, 2.3	-7.3, 2.6	-7.3, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.32 (0.365)	-0.74 (0.318)	
		95% CI	(-1.04, 0.39)	(-1.36, -0.12)	
		LS Mean Difference (SE)		-0.41 (0.404)	
		95% CI		(-1.21, 0.38)	
		p-value		0.3044	
		HedgesG (95% CI)		-0.188 (-0.670, 0.295)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Baseline			
		n	29	36	65
		Mean	4.56	4.99	4.80
		SD, SE	1.621, 0.301	2.365, 0.394	2.063, 0.256
		Median	4.57	5.21	4.57
		Q1, Q3	3.71, 5.29	3.50, 6.64	3.71, 6.14
		Min, Max	0.0, 8.0	0.1, 10.0	0.0, 10.0
		Observed			
		n	29	36	65
		Mean	4.09	4.23	4.17
		SD, SE	2.173, 0.404	2.499, 0.416	2.342, 0.290
		Median	3.86	3.93	3.86
		Q1, Q3	2.57, 5.29	2.07, 6.50	2.14, 5.57
		Min, Max	0.9, 9.7	0.0, 9.7	0.0, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Change from Baseline			
		n	29	36	65
		Mean	-0.46	-0.76	-0.63
		SD, SE	2.058, 0.382	1.911, 0.318	1.968, 0.244
		Median	-0.29	-0.93	-0.71
		Q1, Q3	-2.14, 0.71	-1.79, 0.29	-2.00, 0.43
		Min, Max	-5.3, 3.9	-6.1, 4.1	-6.1, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.13 (0.453)	-0.46 (0.327)	
		95% CI	(-1.02, 0.75)	(-1.10, 0.18)	
		LS Mean Difference (SE)		-0.33 (0.456)	
		95% CI		(-1.22, 0.57)	
		p-value		0.4739	
		HedgesG (95% CI)		-0.147 (-0.637, 0.343)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5		N_1	41	39	80
	Baseline	n	41	39	80
		Mean	4.29	4.42	4.36
		SD, SE	2.211, 0.345	2.083, 0.334	2.137, 0.239
		Median	4.14	4.29	4.21
		Q1, Q3	2.71, 5.14	3.43, 6.00	2.79, 5.71
		Min, Max	0.0, 10.0	0.1, 8.3	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline			
		n	41	39	80
		Mean	4.29	4.42	4.36
		SD, SE	2.211, 0.345	2.083, 0.334	2.137, 0.239
		Median	4.14	4.29	4.21
		Q1, Q3	2.71, 5.14	3.43, 6.00	2.79, 5.71
		Min, Max	0.0, 10.0	0.1, 8.3	0.0, 10.0
		Observed			
		n	41	39	80
		Mean	3.62	3.81	3.71
		SD, SE	2.295, 0.358	2.080, 0.333	2.181, 0.244
		Median	3.00	3.57	3.29
		Q1, Q3	1.86, 5.29	2.29, 5.71	2.00, 5.43
		Min, Max	0.6, 9.3	0.0, 8.3	0.0, 9.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline			
		n	41	39	80
		Mean	-0.67	-0.62	-0.64
		SD, SE	1.407, 0.220	1.416, 0.227	1.403, 0.157
		Median	-0.43	-0.43	-0.43
		Q1, Q3	-1.43, 0.57	-1.43, 0.29	-1.43, 0.29
		Min, Max	-4.1, 1.1	-3.9, 2.6	-4.1, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.51 (0.239)	-0.46 (0.242)	
		95% CI	(-0.98, -0.05)	(-0.94, 0.01)	
		LS Mean Difference (SE)		0.05 (0.291)	
		95% CI		(-0.52, 0.62)	
		p-value		0.8589	
		HedgesG (95% CI)		0.035 (-0.404, 0.473)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline			
		n	41	39	80
		Mean	4.29	4.42	4.36
		SD, SE	2.211, 0.345	2.083, 0.334	2.137, 0.239
		Median	4.14	4.29	4.21
		Q1, Q3	2.71, 5.14	3.43, 6.00	2.79, 5.71
		Min, Max	0.0, 10.0	0.1, 8.3	0.0, 10.0
		Observed			
		n	41	39	80
		Mean	3.75	3.97	3.86
		SD, SE	2.333, 0.364	2.171, 0.348	2.244, 0.251
		Median	3.29	3.57	3.43
		Q1, Q3	2.14, 5.14	2.14, 5.57	2.14, 5.14
		Min, Max	0.1, 9.7	0.0, 8.7	0.0, 9.7

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Table 2.2.3.1.3.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline			
		n	41	39	80
		Mean	-0.54	-0.45	-0.50
		SD, SE	1.779, 0.278	1.715, 0.275	1.738, 0.194
		Median	-0.71	-0.57	-0.64
		Q1, Q3	-1.57, 0.71	-1.57, 0.43	-1.57, 0.57
		Min, Max	-5.3, 3.9	-3.6, 4.1	-5.3, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.39 (0.290)	-0.30 (0.291)	
		95% CI	(-0.96, 0.18)	(-0.87, 0.27)	
		LS Mean Difference (SE)		0.09 (0.353)	
		95% CI		(-0.60, 0.79)	
		p-value		0.7885	
		HedgesG (95% CI)		0.052 (-0.386, 0.491)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5		N_1	25	29	54
	Baseline	n	25	29	54
		Mean	5.53	6.31	5.95
		SD, SE	1.915, 0.383	1.992, 0.370	1.978, 0.269
		Median	5.57	6.29	5.86
		Q1, Q3	4.29, 6.57	5.14, 8.00	4.29, 7.71
		Min, Max	1.7, 9.0	2.1, 10.0	1.7, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline			
		n	25	29	54
		Mean	5.53	6.31	5.95
		SD, SE	1.915, 0.383	1.992, 0.370	1.978, 0.269
		Median	5.57	6.29	5.86
		Q1, Q3	4.29, 6.57	5.14, 8.00	4.29, 7.71
		Min, Max	1.7, 9.0	2.1, 10.0	1.7, 10.0
		Observed			
		n	25	29	54
		Mean	5.07	4.95	5.01
		SD, SE	2.455, 0.491	2.627, 0.488	2.526, 0.344
		Median	5.29	5.00	5.14
		Q1, Q3	3.00, 7.14	2.86, 7.00	2.86, 7.14
		Min, Max	1.4, 9.4	1.3, 10.0	1.3, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline			
		n	25	29	54
		Mean	-0.46	-1.36	-0.94
		SD, SE	1.914, 0.383	1.832, 0.340	1.907, 0.260
		Median	-0.43	-1.00	-0.57
		Q1, Q3	-1.43, 0.57	-2.14, 0.00	-2.00, 0.14
		Min, Max	-5.9, 2.3	-7.3, 1.0	-7.3, 2.3
		GEE Estimates			
		LS Mean (SE)	-0.42 (0.346)	-1.44 (0.318)	
		95% CI	(-1.10, 0.26)	(-2.06, -0.82)	
		LS Mean Difference (SE)		-1.02 (0.451)	
		95% CI		(-1.90, -0.14)	
		p-value		0.0235	
		HedgesG (95% CI)		-0.467 (-1.009, 0.075)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline			
		n	24	28	52
		Mean	5.40	6.22	5.84
		SD, SE	1.846, 0.377	1.974, 0.373	1.942, 0.269
		Median	5.21	6.29	5.79
		Q1, Q3	4.21, 6.50	5.14, 7.86	4.29, 7.43
		Min, Max	1.7, 9.0	2.1, 10.0	1.7, 10.0
		Observed			
		n	24	28	52
		Mean	4.87	4.91	4.89
		SD, SE	2.353, 0.480	2.514, 0.475	2.417, 0.335
		Median	5.57	5.29	5.36
		Q1, Q3	2.79, 6.36	2.50, 6.93	2.57, 6.64
		Min, Max	0.7, 9.1	1.1, 9.7	0.7, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline			
		n	24	28	52
		Mean	-0.53	-1.32	-0.95
		SD, SE	1.612, 0.329	1.850, 0.350	1.772, 0.246
		Median	-0.43	-1.29	-1.00
		Q1, Q3	-1.71, 0.43	-2.21, -0.07	-2.07, 0.07
		Min, Max	-3.9, 3.0	-6.1, 2.1	-6.1, 3.0
		GEE Estimates			
		LS Mean (SE)	-0.56 (0.298)	-1.42 (0.367)	
		95% CI	(-1.15, 0.02)	(-2.14, -0.70)	
		LS Mean Difference (SE)		-0.85 (0.423)	
		95% CI		(-1.68, -0.02)	
		p-value		0.0438	
		HedgesG (95% CI)		-0.435 (-0.987, 0.116)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	3.57	3.57	3.57
		SD, SE	1.584, 0.260	1.820, 0.332	1.680, 0.205
		Median	3.57	3.71	3.71
		Q1, Q3	2.43, 4.57	2.43, 4.43	2.43, 4.57
		Min, Max	0.0, 7.7	0.1, 8.3	0.0, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline			
		n	37	30	67
		Mean	3.57	3.57	3.57
		SD, SE	1.584, 0.260	1.820, 0.332	1.680, 0.205
		Median	3.57	3.71	3.71
		Q1, Q3	2.43, 4.57	2.43, 4.43	2.43, 4.57
		Min, Max	0.0, 7.7	0.1, 8.3	0.0, 8.3
		Observed			
		n	37	30	67
		Mean	3.19	2.91	3.07
		SD, SE	1.811, 0.298	1.504, 0.275	1.674, 0.205
		Median	2.86	3.21	3.00
		Q1, Q3	1.86, 4.14	1.57, 3.71	1.71, 3.86
		Min, Max	0.6, 8.1	0.4, 6.4	0.4, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-0.37	-0.66	-0.50
		SD, SE	1.158, 0.190	1.329, 0.243	1.236, 0.151
		Median	-0.43	-0.57	-0.43
		Q1, Q3	-1.00, 0.57	-1.57, 0.14	-1.43, 0.29
		Min, Max	-3.0, 1.4	-2.9, 2.6	-3.0, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.16 (0.246)	-0.46 (0.258)	
		95% CI	(-0.64, 0.32)	(-0.96, 0.05)	
		LS Mean Difference (SE)		-0.30 (0.274)	
		95% CI		(-0.84, 0.23)	
		p-value		0.2702	
		HedgesG (95% CI)		-0.226 (-0.709, 0.257)	

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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline			
		n	37	30	67
		Mean	3.57	3.57	3.57
		SD, SE	1.584, 0.260	1.820, 0.332	1.680, 0.205
		Median	3.57	3.71	3.71
		Q1, Q3	2.43, 4.57	2.43, 4.43	2.43, 4.57
		Min, Max	0.0, 7.7	0.1, 8.3	0.0, 8.3
		Observed			
		n	37	30	67
		Mean	2.84	3.10	2.96
		SD, SE	1.684, 0.277	2.047, 0.374	1.845, 0.225
		Median	2.57	2.64	2.57
		Q1, Q3	1.43, 3.86	1.57, 4.00	1.43, 3.86
		Min, Max	0.1, 6.7	0.0, 7.4	0.0, 7.4

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-0.73	-0.47	-0.61
		SD, SE	1.707, 0.281	1.770, 0.323	1.727, 0.211
		Median	-0.71	-0.43	-0.71
		Q1, Q3	-1.86, 0.14	-1.71, 0.43	-1.71, 0.43
		Min, Max	-5.3, 3.9	-4.4, 4.1	-5.3, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.51 (0.302)	-0.27 (0.353)	
		95% CI	(-1.11, 0.08)	(-0.96, 0.42)	
		LS Mean Difference (SE)		0.24 (0.375)	
		95% CI		(-0.49, 0.98)	
		p-value		0.5156	
		HedgesG (95% CI)		0.145 (-0.337, 0.627)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	6.28	6.54	6.42
		SD, SE	1.868, 0.347	1.573, 0.255	1.699, 0.208
		Median	6.14	6.43	6.29
		Q1, Q3	4.57, 7.71	5.71, 7.71	5.14, 7.71
		Min, Max	3.6, 10.0	3.4, 10.0	3.4, 10.0

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline			
		n	29	38	67
		Mean	6.28	6.54	6.42
		SD, SE	1.868, 0.347	1.573, 0.255	1.699, 0.208
		Median	6.14	6.43	6.29
		Q1, Q3	4.57, 7.71	5.71, 7.71	5.14, 7.71
		Min, Max	3.6, 10.0	3.4, 10.0	3.4, 10.0
		Observed			
		n	29	38	67
		Mean	5.42	5.39	5.40
		SD, SE	2.599, 0.483	2.385, 0.387	2.461, 0.301
		Median	5.57	5.71	5.71
		Q1, Q3	3.14, 8.00	3.29, 7.00	3.29, 7.43
		Min, Max	0.7, 9.4	0.0, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-0.86	-1.15	-1.02
		SD, SE	2.033, 0.377	1.832, 0.297	1.912, 0.234
		Median	-0.71	-0.57	-0.71
		Q1, Q3	-2.43, 0.57	-2.14, 0.00	-2.43, 0.14
		Min, Max	-5.9, 2.3	-7.3, 1.4	-7.3, 2.3
		GEE Estimates			
		LS Mean (SE)	-1.02 (0.465)	-1.52 (0.355)	
		95% CI	(-1.93, -0.11)	(-2.21, -0.82)	
		LS Mean Difference (SE)		-0.50 (0.426)	
		95% CI		(-1.34, 0.34)	
		p-value		0.2408	
		HedgesG (95% CI)		-0.147 (-0.631, 0.337)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline			
		n	28	37	65
		Mean	6.19	6.48	6.36
		SD, SE	1.848, 0.349	1.552, 0.255	1.678, 0.208
		Median	6.00	6.43	6.29
		Q1, Q3	4.57, 7.57	5.71, 7.57	5.14, 7.57
		Min, Max	3.6, 10.0	3.4, 10.0	3.4, 10.0
		Observed			
		n	28	37	65
		Mean	5.91	5.39	5.61
		SD, SE	2.035, 0.385	2.079, 0.342	2.060, 0.256
		Median	5.71	5.29	5.57
		Q1, Q3	5.00, 7.21	4.14, 6.71	4.43, 7.14
		Min, Max	1.1, 9.7	1.7, 9.7	1.1, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline			
		n	28	37	65
		Mean	-0.29	-1.09	-0.74
		SD, SE	1.703, 0.322	1.819, 0.299	1.802, 0.223
		Median	-0.29	-1.14	-0.71
		Q1, Q3	-1.21, 0.86	-2.14, 0.00	-2.00, 0.29
		Min, Max	-3.6, 3.0	-6.1, 2.6	-6.1, 3.0
		GEE Estimates			
		LS Mean (SE)	-0.51 (0.432)	-1.48 (0.377)	
		95% CI	(-1.35, 0.34)	(-2.22, -0.74)	
		LS Mean Difference (SE)		-0.97 (0.385)	
		95% CI		(-1.73, -0.22)	
		p-value		0.0114	
		HedgesG (95% CI)		-0.441 (-0.938, 0.056)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50		N_1	42	32	74
	Baseline	n	42	32	74
		Mean	4.03	3.75	3.91
		SD, SE	1.898, 0.293	1.934, 0.342	1.906, 0.222
		Median	4.07	3.79	3.86
		Q1, Q3	2.71, 4.86	2.50, 4.64	2.71, 4.86
		Min, Max	0.0, 10.0	0.1, 8.3	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Baseline			
		n	42	32	74
		Mean	4.03	3.75	3.91
		SD, SE	1.898, 0.293	1.934, 0.342	1.906, 0.222
		Median	4.07	3.79	3.86
		Q1, Q3	2.71, 4.86	2.50, 4.64	2.71, 4.86
		Min, Max	0.0, 10.0	0.1, 8.3	0.0, 10.0
		Observed			
		n	42	32	74
		Mean	3.53	3.18	3.38
		SD, SE	2.126, 0.328	1.895, 0.335	2.024, 0.235
		Median	3.07	3.29	3.14
		Q1, Q3	2.00, 4.57	1.71, 3.79	1.86, 3.86
		Min, Max	0.6, 9.3	0.0, 7.9	0.0, 9.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Change from Baseline			
		n	42	32	74
		Mean	-0.50	-0.57	-0.53
		SD, SE	1.216, 0.188	1.399, 0.247	1.290, 0.150
		Median	-0.43	-0.36	-0.43
		Q1, Q3	-1.43, 0.57	-1.29, 0.21	-1.29, 0.29
		Min, Max	-3.3, 1.4	-4.0, 2.6	-4.0, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.25 (0.257)	-0.45 (0.271)	
		95% CI	(-0.75, 0.25)	(-0.99, 0.08)	
		LS Mean Difference (SE)		-0.20 (0.302)	
		95% CI		(-0.79, 0.39)	
		p-value		0.5002	
		HedgesG (95% CI)		-0.048 (-0.508, 0.412)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Baseline			
		n	42	32	74
		Mean	4.03	3.75	3.91
		SD, SE	1.898, 0.293	1.934, 0.342	1.906, 0.222
		Median	4.07	3.79	3.86
		Q1, Q3	2.71, 4.86	2.50, 4.64	2.71, 4.86
		Min, Max	0.0, 10.0	0.1, 8.3	0.0, 10.0
		Observed			
		n	42	32	74
		Mean	3.54	3.21	3.40
		SD, SE	2.209, 0.341	2.027, 0.358	2.125, 0.247
		Median	3.07	3.00	3.07
		Q1, Q3	1.86, 4.86	1.71, 4.21	1.71, 4.57
		Min, Max	0.7, 9.7	0.0, 7.7	0.0, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Change from Baseline			
		n	42	32	74
		Mean	-0.49	-0.54	-0.51
		SD, SE	1.697, 0.262	1.634, 0.289	1.659, 0.193
		Median	-0.57	-0.79	-0.64
		Q1, Q3	-1.57, 0.71	-1.71, 0.43	-1.71, 0.57
		Min, Max	-5.3, 3.9	-3.3, 4.1	-5.3, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.24 (0.315)	-0.43 (0.324)	
		95% CI	(-0.86, 0.38)	(-1.06, 0.21)	
		LS Mean Difference (SE)		-0.19 (0.351)	
		95% CI		(-0.87, 0.50)	
		p-value		0.5943	
		HedgesG (95% CI)		-0.027 (-0.487, 0.432)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50		N_1	24	35	59
	Baseline	n	24	35	59
		Mean	6.02	6.57	6.35
		SD, SE	2.076, 0.424	1.586, 0.268	1.805, 0.235
		Median	6.00	6.71	6.43
		Q1, Q3	4.43, 7.86	5.29, 7.71	5.14, 7.71
		Min, Max	2.0, 9.3	3.6, 10.0	2.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Baseline			
		n	24	35	59
		Mean	6.02	6.57	6.35
		SD, SE	2.076, 0.424	1.586, 0.268	1.805, 0.235
		Median	6.00	6.71	6.43
		Q1, Q3	4.43, 7.86	5.29, 7.71	5.14, 7.71
		Min, Max	2.0, 9.3	3.6, 10.0	2.0, 10.0
		Observed			
		n	24	35	59
		Mean	5.29	5.29	5.29
		SD, SE	2.596, 0.530	2.379, 0.402	2.447, 0.319
		Median	5.43	5.71	5.57
		Q1, Q3	2.57, 7.57	3.29, 6.86	3.00, 7.00
		Min, Max	0.7, 9.4	0.9, 10.0	0.7, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Change from Baseline			
		n	24	35	59
		Mean	-0.73	-1.29	-1.06
		SD, SE	2.150, 0.439	1.796, 0.304	1.949, 0.254
		Median	-0.29	-1.00	-0.71
		Q1, Q3	-2.14, 0.64	-2.57, 0.00	-2.57, 0.14
		Min, Max	-5.9, 2.3	-7.3, 1.4	-7.3, 2.3
		GEE Estimates			
		LS Mean (SE)	-1.12 (0.521)	-1.71 (0.467)	
		95% CI	(-2.14, -0.10)	(-2.63, -0.80)	
		LS Mean Difference (SE)		-0.59 (0.453)	
		95% CI		(-1.48, 0.30)	
		p-value		0.1911	
		HedgesG (95% CI)		-0.276 (-0.798, 0.246)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Baseline			
		n	23	34	57
		Mean	5.91	6.51	6.27
		SD, SE	2.049, 0.427	1.565, 0.268	1.783, 0.236
		Median	5.86	6.57	6.29
		Q1, Q3	4.29, 7.71	5.29, 7.57	5.14, 7.57
		Min, Max	2.0, 9.3	3.6, 10.0	2.0, 10.0
		Observed			
		n	23	34	57
		Mean	5.29	5.44	5.38
		SD, SE	2.320, 0.484	2.161, 0.371	2.207, 0.292
		Median	5.71	5.43	5.57
		Q1, Q3	3.29, 6.57	3.43, 7.00	3.43, 6.71
		Min, Max	0.1, 9.1	1.1, 9.7	0.1, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Change from Baseline			
		n	23	34	57
		Mean	-0.62	-1.07	-0.89
		SD, SE	1.758, 0.367	1.977, 0.339	1.889, 0.250
		Median	-0.57	-1.00	-1.00
		Q1, Q3	-1.86, 0.71	-2.57, 0.14	-2.00, 0.14
		Min, Max	-3.6, 3.0	-6.1, 2.6	-6.1, 3.0
		GEE Estimates			
		LS Mean (SE)	-1.09 (0.544)	-1.52 (0.497)	
		95% CI	(-2.15, -0.02)	(-2.49, -0.54)	
		LS Mean Difference (SE)		-0.43 (0.454)	
		95% CI		(-1.32, 0.46)	
		p-value		0.3417	
		HedgesG (95% CI)		-0.231 (-0.761, 0.300)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	3.57	3.57	3.57
		SD, SE	1.584, 0.260	1.723, 0.315	1.635, 0.200
		Median	3.57	3.71	3.71
		Q1, Q3	2.43, 4.57	2.43, 4.86	2.43, 4.71
		Min, Max	0.0, 7.7	0.1, 6.9	0.0, 7.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Baseline			
		n	37	30	67
		Mean	3.57	3.57	3.57
		SD, SE	1.584, 0.260	1.723, 0.315	1.635, 0.200
		Median	3.57	3.71	3.71
		Q1, Q3	2.43, 4.57	2.43, 4.86	2.43, 4.71
		Min, Max	0.0, 7.7	0.1, 6.9	0.0, 7.7
		Observed			
		n	37	30	67
		Mean	3.19	3.14	3.17
		SD, SE	1.811, 0.298	1.657, 0.303	1.731, 0.211
		Median	2.86	3.29	3.00
		Q1, Q3	1.86, 4.14	1.57, 3.86	1.86, 4.14
		Min, Max	0.6, 8.1	0.4, 6.4	0.4, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-0.37	-0.42	-0.40
		SD, SE	1.158, 0.190	1.209, 0.221	1.172, 0.143
		Median	-0.43	-0.29	-0.43
		Q1, Q3	-1.00, 0.57	-1.29, 0.29	-1.29, 0.43
		Min, Max	-3.0, 1.4	-2.7, 2.6	-3.0, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.18 (0.239)	-0.25 (0.256)	
		95% CI	(-0.65, 0.29)	(-0.75, 0.26)	
		LS Mean Difference (SE)		-0.07 (0.277)	
		95% CI		(-0.61, 0.48)	
		p-value		0.8092	
		HedgesG (95% CI)		-0.041 (-0.522, 0.441)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Baseline			
		n	37	30	67
		Mean	3.57	3.57	3.57
		SD, SE	1.584, 0.260	1.723, 0.315	1.635, 0.200
		Median	3.57	3.71	3.71
		Q1, Q3	2.43, 4.57	2.43, 4.86	2.43, 4.71
		Min, Max	0.0, 7.7	0.1, 6.9	0.0, 7.7
		Observed			
		n	37	30	67
		Mean	2.84	3.11	2.96
		SD, SE	1.684, 0.277	1.977, 0.361	1.812, 0.221
		Median	2.57	2.79	2.57
		Q1, Q3	1.43, 3.86	1.57, 4.29	1.43, 4.00
		Min, Max	0.1, 6.7	0.0, 7.4	0.0, 7.4

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Table 2.2.3.1.3.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-0.73	-0.45	-0.61
		SD, SE	1.707, 0.281	1.759, 0.321	1.723, 0.211
		Median	-0.71	-0.43	-0.71
		Q1, Q3	-1.86, 0.14	-1.57, 0.43	-1.71, 0.43
		Min, Max	-5.3, 3.9	-4.4, 4.1	-5.3, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.53 (0.296)	-0.27 (0.350)	
		95% CI	(-1.11, 0.05)	(-0.96, 0.41)	
		LS Mean Difference (SE)		0.26 (0.376)	
		95% CI		(-0.48, 1.00)	
		p-value		0.4900	
		HedgesG (95% CI)		0.156 (-0.326, 0.638)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.1.3.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	6.28	6.54	6.43
		SD, SE	1.868, 0.347	1.649, 0.268	1.739, 0.212
		Median	6.14	6.57	6.29
		Q1, Q3	4.57, 7.71	5.29, 7.71	5.14, 7.71
		Min, Max	3.6, 10.0	3.4, 10.0	3.4, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Baseline			
		n	29	38	67
		Mean	6.28	6.54	6.43
		SD, SE	1.868, 0.347	1.649, 0.268	1.739, 0.212
		Median	6.14	6.57	6.29
		Q1, Q3	4.57, 7.71	5.29, 7.71	5.14, 7.71
		Min, Max	3.6, 10.0	3.4, 10.0	3.4, 10.0
		Observed			
		n	29	38	67
		Mean	5.42	5.21	5.30
		SD, SE	2.599, 0.483	2.484, 0.403	2.517, 0.308
		Median	5.57	5.64	5.57
		Q1, Q3	3.14, 8.00	3.29, 7.00	3.14, 7.43
		Min, Max	0.7, 9.4	0.0, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-0.86	-1.33	-1.13
		SD, SE	2.033, 0.377	1.824, 0.296	1.917, 0.234
		Median	-0.71	-1.00	-0.71
		Q1, Q3	-2.43, 0.57	-2.57, 0.00	-2.57, 0.14
		Min, Max	-5.9, 2.3	-7.3, 1.4	-7.3, 2.3
		GEE Estimates			
		LS Mean (SE)	-0.97 (0.455)	-1.74 (0.350)	
		95% CI	(-1.86, -0.08)	(-2.43, -1.06)	
		LS Mean Difference (SE)		-0.77 (0.422)	
		95% CI		(-1.60, 0.05)	
		p-value		0.0672	
		HedgesG (95% CI)		-0.243 (-0.728, 0.243)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Baseline			
		n	28	37	65
		Mean	6.19	6.48	6.36
		SD, SE	1.848, 0.349	1.631, 0.268	1.720, 0.213
		Median	6.00	6.43	6.29
		Q1, Q3	4.57, 7.57	5.29, 7.71	5.14, 7.71
		Min, Max	3.6, 10.0	3.4, 10.0	3.4, 10.0
		Observed			
		n	28	37	65
		Mean	5.91	5.38	5.61
		SD, SE	2.035, 0.385	2.145, 0.353	2.099, 0.260
		Median	5.71	5.43	5.57
		Q1, Q3	5.00, 7.21	3.43, 7.00	4.43, 7.14
		Min, Max	1.1, 9.7	1.7, 9.7	1.1, 9.7

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Change from Baseline			
		n	28	37	65
		Mean	-0.29	-1.10	-0.75
		SD, SE	1.703, 0.322	1.823, 0.300	1.805, 0.224
		Median	-0.29	-1.14	-0.86
		Q1, Q3	-1.21, 0.86	-2.14, 0.00	-2.00, 0.29
		Min, Max	-3.6, 3.0	-6.1, 2.6	-6.1, 3.0
		GEE Estimates			
		LS Mean (SE)	-0.46 (0.427)	-1.53 (0.379)	
		95% CI	(-1.29, 0.38)	(-2.27, -0.79)	
		LS Mean Difference (SE)		-1.07 (0.384)	
		95% CI		(-1.83, -0.32)	
		p-value		0.0053	
		HedgesG (95% CI)		-0.449 (-0.946, 0.048)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes		N_1	44	47	91
	Baseline	n	44	47	91
		Mean	5.00	5.67	5.35
		SD, SE	2.016, 0.304	2.114, 0.308	2.083, 0.218
		Median	4.64	5.71	5.29
		Q1, Q3	3.86, 6.00	3.86, 7.57	3.86, 6.86
		Min, Max	0.4, 9.3	1.0, 10.0	0.4, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	44	47	91
		Mean	5.00	5.67	5.35
		SD, SE	2.016, 0.304	2.114, 0.308	2.083, 0.218
		Median	4.64	5.71	5.29
		Q1, Q3	3.86, 6.00	3.86, 7.57	3.86, 6.86
		Min, Max	0.4, 9.3	1.0, 10.0	0.4, 10.0
		Observed			
		n	44	47	91
		Mean	4.15	4.54	4.35
		SD, SE	2.311, 0.348	2.492, 0.364	2.401, 0.252
		Median	3.50	4.29	3.86
		Q1, Q3	2.00, 5.79	2.86, 6.57	2.14, 6.29
		Min, Max	0.6, 8.7	0.0, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	44	47	91
		Mean	-0.85	-1.12	-0.99
		SD, SE	1.764, 0.266	1.785, 0.260	1.770, 0.186
		Median	-0.71	-0.71	-0.71
		Q1, Q3	-1.86, 0.29	-2.14, 0.00	-2.14, 0.14
		Min, Max	-5.9, 2.3	-7.3, 2.1	-7.3, 2.3
		GEE Estimates			
		LS Mean (SE)	-1.20 (0.485)	-1.39 (0.417)	
		95% CI	(-2.15, -0.25)	(-2.21, -0.58)	
		LS Mean Difference (SE)		-0.19 (0.354)	
		95% CI		(-0.89, 0.50)	
		p-value		0.5849	
		HedgesG (95% CI)		-0.150 (-0.561, 0.262)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	43	46	89
		Mean	4.92	5.60	5.27
		SD, SE	1.963, 0.299	2.087, 0.308	2.046, 0.217
		Median	4.57	5.64	5.14
		Q1, Q3	3.71, 5.86	3.86, 7.29	3.86, 6.43
		Min, Max	0.4, 9.3	1.0, 10.0	0.4, 10.0
		Observed			
		n	43	46	89
		Mean	4.23	4.56	4.40
		SD, SE	2.054, 0.313	2.375, 0.350	2.219, 0.235
		Median	4.86	4.64	4.71
		Q1, Q3	2.14, 5.71	2.43, 6.43	2.43, 5.86
		Min, Max	0.7, 8.0	0.6, 9.7	0.6, 9.7

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Table 2.2.3.1.3.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	43	46	89
		Mean	-0.69	-1.05	-0.87
		SD, SE	1.747, 0.266	1.718, 0.253	1.732, 0.184
		Median	-0.57	-0.93	-0.71
		Q1, Q3	-2.00, 0.57	-2.14, 0.14	-2.14, 0.14
		Min, Max	-5.3, 3.0	-6.1, 2.6	-6.1, 3.0
		GEE Estimates			
		LS Mean (SE)	-1.07 (0.484)	-1.33 (0.463)	
		95% CI	(-2.02, -0.12)	(-2.24, -0.43)	
		LS Mean Difference (SE)		-0.26 (0.338)	
		95% CI		(-0.92, 0.40)	
		p-value		0.4413	
		HedgesG (95% CI)		-0.203 (-0.620, 0.214)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.1.3.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No		N_1	22	21	43
	Baseline	n	22	21	43
		Mean	4.27	4.24	4.26
		SD, SE	2.437, 0.520	2.238, 0.488	2.314, 0.353
		Median	3.79	4.00	4.00
		Q1, Q3	2.71, 6.14	3.00, 6.00	2.71, 6.14
		Min, Max	0.0, 10.0	0.1, 8.9	0.0, 10.0

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Table 2.2.3.1.3.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Baseline			
		n	22	21	43
		Mean	4.27	4.24	4.26
		SD, SE	2.437, 0.520	2.238, 0.488	2.314, 0.353
		Median	3.79	4.00	4.00
		Q1, Q3	2.71, 6.14	3.00, 6.00	2.71, 6.14
		Min, Max	0.0, 10.0	0.1, 8.9	0.0, 10.0
		Observed			
		n	22	21	43
		Mean	4.22	3.74	3.99
		SD, SE	2.744, 0.585	2.052, 0.448	2.414, 0.368
		Median	3.14	3.29	3.29
		Q1, Q3	2.57, 6.71	2.29, 5.29	2.29, 5.43
		Min, Max	0.6, 9.4	0.4, 9.0	0.4, 9.4

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Table 2.2.3.1.3.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Change from Baseline			
		n	22	21	43
		Mean	-0.05	-0.50	-0.27
		SD, SE	1.079, 0.230	1.166, 0.254	1.132, 0.173
		Median	0.21	-0.57	-0.43
		Q1, Q3	-0.71, 0.57	-1.00, 0.14	-1.00, 0.57
		Min, Max	-2.1, 2.1	-2.7, 2.6	-2.7, 2.6
		GEE Estimates			
		LS Mean (SE)	0.04 (0.248)	-0.48 (0.265)	
		95% CI	(-0.44, 0.53)	(-1.00, 0.04)	
		LS Mean Difference (SE)		-0.52 (0.325)	
		95% CI		(-1.16, 0.11)	
		p-value		0.1082	
		HedgesG (95% CI)		-0.386 (-0.989, 0.218)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Baseline			
		n	22	21	43
		Mean	4.27	4.24	4.26
		SD, SE	2.437, 0.520	2.238, 0.488	2.314, 0.353
		Median	3.79	4.00	4.00
		Q1, Q3	2.71, 6.14	3.00, 6.00	2.71, 6.14
		Min, Max	0.0, 10.0	0.1, 8.9	0.0, 10.0
		Observed			
		n	22	21	43
		Mean	4.03	3.95	3.99
		SD, SE	2.978, 0.635	2.290, 0.500	2.633, 0.402
		Median	3.00	3.43	3.29
		Q1, Q3	2.14, 6.00	2.57, 5.14	2.14, 6.00
		Min, Max	0.1, 9.7	0.0, 7.9	0.0, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Change from Baseline			
		n	22	21	43
		Mean	-0.25	-0.30	-0.27
		SD, SE	1.624, 0.346	1.942, 0.424	1.765, 0.269
		Median	-0.64	-0.86	-0.71
		Q1, Q3	-1.57, 1.00	-1.57, 0.57	-1.57, 0.86
		Min, Max	-2.1, 3.9	-3.6, 4.1	-3.6, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.15 (0.367)	-0.28 (0.365)	
		95% CI	(-0.87, 0.57)	(-0.99, 0.44)	
		LS Mean Difference (SE)		-0.12 (0.506)	
		95% CI		(-1.11, 0.87)	
		p-value		0.8078	
		HedgesG (95% CI)		-0.028 (-0.626, 0.570)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes		N_1	13	17	30
	Baseline	n	13	17	30
		Mean	4.91	5.85	5.44
		SD, SE	1.559, 0.432	2.545, 0.617	2.191, 0.400
		Median	5.14	6.86	5.71
		Q1, Q3	4.00, 5.86	3.86, 8.29	3.86, 7.00
		Min, Max	2.4, 7.7	1.0, 8.7	1.0, 8.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	13	17	30
		Mean	4.91	5.85	5.44
		SD, SE	1.559, 0.432	2.545, 0.617	2.191, 0.400
		Median	5.14	6.86	5.71
		Q1, Q3	4.00, 5.86	3.86, 8.29	3.86, 7.00
		Min, Max	2.4, 7.7	1.0, 8.7	1.0, 8.7
		Observed			
		n	13	17	30
		Mean	4.26	4.55	4.43
		SD, SE	2.300, 0.638	2.858, 0.693	2.592, 0.473
		Median	3.57	5.00	4.43
		Q1, Q3	2.00, 6.29	1.57, 6.71	1.86, 6.57
		Min, Max	1.7, 8.1	0.7, 8.6	0.7, 8.6

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	13	17	30
		Mean	-0.65	-1.29	-1.01
		SD, SE	2.235, 0.620	2.102, 0.510	2.147, 0.392
		Median	-0.43	-0.71	-0.57
		Q1, Q3	-1.43, 1.00	-2.14, 0.00	-2.14, 0.29
		Min, Max	-5.9, 2.3	-7.3, 1.4	-7.3, 2.3
		GEE Estimates			
		LS Mean (SE)	-0.94 (0.451)	-1.64 (0.435)	
		95% CI	(-1.82, -0.05)	(-2.50, -0.79)	
		LS Mean Difference (SE)		-0.71 (0.610)	
		95% CI		(-1.90, 0.49)	
		p-value		0.2458	
		HedgesG (95% CI)		-0.281 (-1.007, 0.445)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	13	16	29
		Mean	4.91	5.67	5.33
		SD, SE	1.559, 0.432	2.515, 0.629	2.139, 0.397
		Median	5.14	6.36	5.57
		Q1, Q3	4.00, 5.86	3.71, 7.79	3.86, 6.86
		Min, Max	2.4, 7.7	1.0, 8.7	1.0, 8.7
		Observed			
		n	13	16	29
		Mean	3.71	5.06	4.46
		SD, SE	1.749, 0.485	2.588, 0.647	2.316, 0.430
		Median	3.14	5.43	4.14
		Q1, Q3	2.57, 5.29	3.00, 7.07	2.71, 6.14
		Min, Max	1.0, 6.6	0.9, 8.7	0.9, 8.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	13	16	29
		Mean	-1.20	-0.61	-0.87
		SD, SE	1.723, 0.478	2.033, 0.508	1.891, 0.351
		Median	-0.71	-0.43	-0.71
		Q1, Q3	-2.29, -0.14	-1.50, 0.50	-2.00, 0.14
		Min, Max	-5.3, 0.7	-6.1, 2.6	-6.1, 2.6
		GEE Estimates			
		LS Mean (SE)	-1.49 (0.416)	-1.01 (0.415)	
		95% CI	(-2.30, -0.67)	(-1.82, -0.20)	
		LS Mean Difference (SE)		0.48 (0.618)	
		95% CI		(-0.73, 1.69)	
		p-value		0.4390	
		HedgesG (95% CI)		0.291 (-0.444, 1.027)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No		N_1	53	51	104
	Baseline	n	53	51	104
		Mean	4.72	5.02	4.87
		SD, SE	2.311, 0.317	2.111, 0.296	2.210, 0.217
		Median	4.43	5.14	4.57
		Q1, Q3	2.86, 6.14	3.71, 6.43	3.57, 6.29
		Min, Max	0.0, 10.0	0.1, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Baseline			
		n	53	51	104
		Mean	4.72	5.02	4.87
		SD, SE	2.311, 0.317	2.111, 0.296	2.210, 0.217
		Median	4.43	5.14	4.57
		Q1, Q3	2.86, 6.14	3.71, 6.43	3.57, 6.29
		Min, Max	0.0, 10.0	0.1, 10.0	0.0, 10.0
		Observed			
		n	53	51	104
		Mean	4.15	4.21	4.18
		SD, SE	2.496, 0.343	2.223, 0.311	2.355, 0.231
		Median	3.29	3.57	3.57
		Q1, Q3	2.14, 5.71	2.86, 5.71	2.64, 5.71
		Min, Max	0.6, 9.4	0.0, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Change from Baseline			
		n	53	51	104
		Mean	-0.57	-0.81	-0.69
		SD, SE	1.440, 0.198	1.454, 0.204	1.445, 0.142
		Median	-0.43	-0.57	-0.43
		Q1, Q3	-1.43, 0.57	-1.71, 0.14	-1.57, 0.29
		Min, Max	-4.1, 2.1	-3.9, 2.6	-4.1, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.36 (0.242)	-0.58 (0.234)	
		95% CI	(-0.84, 0.11)	(-1.04, -0.13)	
		LS Mean Difference (SE)		-0.22 (0.270)	
		95% CI		(-0.75, 0.31)	
		p-value		0.4165	
		HedgesG (95% CI)		-0.164 (-0.549, 0.221)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Baseline			
		n	52	51	103
		Mean	4.65	5.02	4.83
		SD, SE	2.269, 0.315	2.111, 0.296	2.190, 0.216
		Median	4.36	5.14	4.57
		Q1, Q3	2.86, 5.93	3.71, 6.43	3.57, 6.29
		Min, Max	0.0, 10.0	0.1, 10.0	0.0, 10.0
		Observed			
		n	52	51	103
		Mean	4.27	4.15	4.21
		SD, SE	2.521, 0.350	2.251, 0.315	2.380, 0.235
		Median	4.29	4.00	4.14
		Q1, Q3	2.14, 6.00	2.14, 5.43	2.14, 5.86
		Min, Max	0.1, 9.7	0.0, 9.7	0.0, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Change from Baseline			
		n	52	51	103
		Mean	-0.37	-0.88	-0.62
		SD, SE	1.679, 0.233	1.752, 0.245	1.726, 0.170
		Median	-0.50	-1.00	-0.71
		Q1, Q3	-1.50, 0.79	-2.14, 0.29	-1.71, 0.29
		Min, Max	-3.9, 3.9	-4.4, 4.1	-4.4, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.20 (0.281)	-0.65 (0.264)	
		95% CI	(-0.75, 0.35)	(-1.17, -0.13)	
		LS Mean Difference (SE)		-0.45 (0.313)	
		95% CI		(-1.06, 0.16)	
		p-value		0.1493	
		HedgesG (95% CI)		-0.288 (-0.677, 0.100)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes		N_1	38	32	70
	Baseline	n	38	32	70
		Mean	5.38	5.08	5.24
		SD, SE	2.157, 0.350	2.353, 0.416	2.237, 0.267
		Median	4.86	5.29	5.07
		Q1, Q3	4.00, 6.57	3.43, 6.93	3.71, 6.86
		Min, Max	1.7, 10.0	0.6, 8.9	0.6, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Baseline			
		n	38	32	70
		Mean	5.38	5.08	5.24
		SD, SE	2.157, 0.350	2.353, 0.416	2.237, 0.267
		Median	4.86	5.29	5.07
		Q1, Q3	4.00, 6.57	3.43, 6.93	3.71, 6.86
		Min, Max	1.7, 10.0	0.6, 8.9	0.6, 10.0
		Observed			
		n	38	32	70
		Mean	4.53	3.87	4.23
		SD, SE	2.556, 0.415	2.304, 0.407	2.449, 0.293
		Median	3.71	3.36	3.43
		Q1, Q3	2.00, 6.29	1.93, 5.86	2.00, 6.00
		Min, Max	1.1, 9.4	0.0, 9.0	0.0, 9.4

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Change from Baseline			
		n	38	32	70
		Mean	-0.85	-1.21	-1.02
		SD, SE	1.706, 0.277	1.610, 0.285	1.661, 0.198
		Median	-0.71	-1.43	-0.71
		Q1, Q3	-1.57, 0.29	-2.36, 0.07	-2.14, 0.14
		Min, Max	-5.9, 2.3	-4.0, 2.6	-5.9, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.34 (0.374)	-0.81 (0.322)	
		95% CI	(-1.08, 0.39)	(-1.44, -0.18)	
		LS Mean Difference (SE)		-0.47 (0.354)	
		95% CI		(-1.16, 0.23)	
		p-value		0.1854	
		HedgesG (95% CI)		-0.214 (-0.685, 0.258)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Baseline			
		n	37	31	68
		Mean	5.29	4.97	5.14
		SD, SE	2.119, 0.348	2.295, 0.412	2.190, 0.266
		Median	4.86	5.29	4.93
		Q1, Q3	4.00, 6.43	3.43, 6.86	3.71, 6.64
		Min, Max	1.7, 10.0	0.6, 8.9	0.6, 10.0
		Observed			
		n	37	31	68
		Mean	4.76	4.22	4.51
		SD, SE	2.092, 0.344	2.118, 0.380	2.106, 0.255
		Median	4.86	4.00	4.43
		Q1, Q3	3.14, 6.00	2.00, 6.57	2.79, 6.07
		Min, Max	1.4, 9.3	1.0, 7.9	1.0, 9.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Change from Baseline			
		n	37	31	68
		Mean	-0.53	-0.75	-0.63
		SD, SE	1.463, 0.241	1.676, 0.301	1.556, 0.189
		Median	-0.71	-1.00	-0.71
		Q1, Q3	-1.43, 0.71	-1.86, 0.29	-1.71, 0.57
		Min, Max	-3.6, 3.0	-3.6, 4.1	-3.6, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.07 (0.380)	-0.38 (0.327)	
		95% CI	(-0.81, 0.68)	(-1.02, 0.26)	
		LS Mean Difference (SE)		-0.31 (0.323)	
		95% CI		(-0.94, 0.32)	
		p-value		0.3388	
		HedgesG (95% CI)		-0.136 (-0.614, 0.342)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No		N_1	28	36	64
	Baseline	n	28	36	64
		Mean	3.91	5.36	4.73
		SD, SE	1.929, 0.365	2.153, 0.359	2.166, 0.271
		Median	4.00	5.57	4.43
		Q1, Q3	2.71, 5.21	3.86, 6.86	3.36, 6.21
		Min, Max	0.0, 8.0	0.1, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.1.3.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Baseline			
		n	28	36	64
		Mean	3.91	5.36	4.73
		SD, SE	1.929, 0.365	2.153, 0.359	2.166, 0.271
		Median	4.00	5.57	4.43
		Q1, Q3	2.71, 5.21	3.86, 6.86	3.36, 6.21
		Min, Max	0.0, 8.0	0.1, 10.0	0.0, 10.0
		Observed			
		n	28	36	64
		Mean	3.68	4.67	4.24
		SD, SE	2.232, 0.422	2.412, 0.402	2.369, 0.296
		Median	3.07	4.21	3.79
		Q1, Q3	2.07, 5.50	3.00, 6.29	2.64, 6.00
		Min, Max	0.6, 8.0	0.4, 10.0	0.4, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Change from Baseline			
		n	28	36	64
		Mean	-0.23	-0.68	-0.48
		SD, SE	1.413, 0.267	1.641, 0.273	1.550, 0.194
		Median	0.14	-0.29	-0.29
		Q1, Q3	-0.93, 0.64	-1.14, 0.07	-1.00, 0.50
		Min, Max	-3.6, 2.0	-7.3, 2.1	-7.3, 2.1
		GEE Estimates			
		LS Mean (SE)	-0.44 (0.287)	-0.75 (0.249)	
		95% CI	(-1.00, 0.13)	(-1.24, -0.26)	
		LS Mean Difference (SE)		-0.32 (0.363)	
		95% CI		(-1.03, 0.40)	
		p-value		0.3837	
		HedgesG (95% CI)		-0.285 (-0.781, 0.211)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Baseline			
		n	28	36	64
		Mean	3.91	5.36	4.73
		SD, SE	1.929, 0.365	2.153, 0.359	2.166, 0.271
		Median	4.00	5.57	4.43
		Q1, Q3	2.71, 5.21	3.86, 6.86	3.36, 6.21
		Min, Max	0.0, 8.0	0.1, 10.0	0.0, 10.0
		Observed			
		n	28	36	64
		Mean	3.37	4.49	4.00
		SD, SE	2.550, 0.482	2.553, 0.426	2.593, 0.324
		Median	2.64	4.50	3.64
		Q1, Q3	1.14, 5.21	2.57, 6.29	2.00, 5.57
		Min, Max	0.1, 9.7	0.0, 9.7	0.0, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

UX023-CL303 Table 2.2.3.1.3.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-0.55	-0.87	-0.73
		SD, SE	2.012, 0.380	1.941, 0.324	1.963, 0.245
		Median	-0.57	-0.86	-0.71
		Q1, Q3	-1.86, 0.43	-1.93, 0.14	-1.86, 0.14
		Min, Max	-5.3, 3.9	-6.1, 3.7	-6.1, 3.9
		GEE Estimates			
		LS Mean (SE)	-0.75 (0.389)	-0.93 (0.280)	
		95% CI	(-1.52, 0.01)	(-1.48, -0.39)	
		LS Mean Difference (SE)		-0.18 (0.501)	
		95% CI		(-1.16, 0.80)	
		p-value		0.7155	
		HedgesG (95% CI)		-0.157 (-0.652, 0.337)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High		N_1	29	37	66
	Baseline	n	29	37	66
		Mean	5.92	5.84	5.87
		SD, SE	2.033, 0.377	2.043, 0.336	2.023, 0.249
		Median	5.57	6.00	5.86
		Q1, Q3	4.57, 7.29	3.86, 7.00	4.29, 7.29
		Min, Max	2.4, 10.0	1.0, 10.0	1.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Baseline			
		n	29	37	66
		Mean	5.92	5.84	5.87
		SD, SE	2.033, 0.377	2.043, 0.336	2.023, 0.249
		Median	5.57	6.00	5.86
		Q1, Q3	4.57, 7.29	3.86, 7.00	4.29, 7.29
		Min, Max	2.4, 10.0	1.0, 10.0	1.0, 10.0
		Observed			
		n	29	37	66
		Mean	5.46	4.79	5.09
		SD, SE	2.442, 0.453	2.604, 0.428	2.537, 0.312
		Median	5.71	4.86	5.29
		Q1, Q3	3.14, 7.29	3.00, 6.71	3.00, 7.14
		Min, Max	1.7, 9.4	0.0, 10.0	0.0, 10.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Change from Baseline			
		n	29	37	66
		Mean	-0.45	-1.05	-0.79
		SD, SE	1.561, 0.290	1.828, 0.301	1.729, 0.213
		Median	-0.71	-0.57	-0.64
		Q1, Q3	-1.00, 0.43	-2.14, 0.14	-1.86, 0.29
		Min, Max	-4.1, 2.3	-7.3, 1.4	-7.3, 2.3
		GEE Estimates			
		LS Mean (SE)	-0.16 (0.355)	-0.81 (0.293)	
		95% CI	(-0.85, 0.54)	(-1.38, -0.23)	
		LS Mean Difference (SE)		0.65 (0.410)	
		95% CI		(-0.15, 1.45)	
		p-value		0.1126	
		HedgesG (95% CI)		0.338 (-.151, 0.828)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Baseline			
		n	28	36	64
		Mean	5.82	5.76	5.79
		SD, SE	2.004, 0.379	2.013, 0.335	1.993, 0.249
		Median	5.50	6.00	5.86
		Q1, Q3	4.43, 6.93	3.86, 6.93	4.21, 6.93
		Min, Max	2.4, 10.0	1.0, 10.0	1.0, 10.0
		Observed			
		n	28	36	64
		Mean	5.38	5.06	5.20
		SD, SE	2.011, 0.380	2.292, 0.382	2.163, 0.270
		Median	5.64	4.64	5.21
		Q1, Q3	4.00, 6.57	3.29, 7.07	3.43, 6.71
		Min, Max	1.4, 9.3	1.0, 9.7	1.0, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-0.44	-0.70	-0.59
		SD, SE	1.414, 0.267	1.902, 0.317	1.698, 0.212
		Median	-0.57	-0.71	-0.57
		Q1, Q3	-1.07, 0.21	-1.79, 0.29	-1.43, 0.29
		Min, Max	-3.6, 3.0	-6.1, 4.1	-6.1, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.22 (0.364)	-0.48 (0.311)	
		95% CI	(-0.93, 0.50)	(-1.09, 0.13)	
		LS Mean Difference (SE)		0.26 (0.386)	
		95% CI		(-0.49, 1.02)	
		p-value		0.4973	
		HedgesG (95% CI)		0.145 (-.350, 0.640)	

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treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.1.3.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low		N_1	36	30	66
	Baseline	n	36	30	66
		Mean	3.73	4.46	4.06
		SD, SE	1.727, 0.288	2.296, 0.419	2.022, 0.249
		Median	3.71	4.36	4.00
		Q1, Q3	2.57, 4.79	3.14, 5.71	2.71, 5.14
		Min, Max	0.0, 7.7	0.1, 8.3	0.0, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Baseline			
		n	36	30	66
		Mean	3.73	4.46	4.06
		SD, SE	1.727, 0.288	2.296, 0.419	2.022, 0.249
		Median	3.71	4.36	4.00
		Q1, Q3	2.57, 4.79	3.14, 5.71	2.71, 5.14
		Min, Max	0.0, 7.7	0.1, 8.3	0.0, 8.3
		Observed			
		n	36	30	66
		Mean	3.02	3.65	3.31
		SD, SE	1.775, 0.296	1.966, 0.359	1.876, 0.231
		Median	2.86	3.57	3.07
		Q1, Q3	1.79, 3.86	2.00, 5.00	1.86, 4.29
		Min, Max	0.6, 8.0	0.4, 7.9	0.4, 8.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Change from Baseline			
		n	36	30	66
		Mean	-0.71	-0.81	-0.76
		SD, SE	1.675, 0.279	1.410, 0.257	1.549, 0.191
		Median	-0.43	-0.57	-0.43
		Q1, Q3	-1.57, 0.57	-1.71, 0.00	-1.57, 0.29
		Min, Max	-5.9, 1.9	-3.6, 2.6	-5.9, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.93 (0.224)	-0.89 (0.259)	
		95% CI	(-1.37, -0.49)	(-1.40, -0.38)	
		LS Mean Difference (SE)		-0.04 (0.344)	
		95% CI		(-0.71, 0.64)	
		p-value		0.9139	
		HedgesG (95% CI)		0.062 (-.423, 0.547)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.3.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Baseline			
		n	36	30	66
		Mean	3.73	4.46	4.06
		SD, SE	1.727, 0.288	2.296, 0.419	2.022, 0.249
		Median	3.71	4.36	4.00
		Q1, Q3	2.57, 4.79	3.14, 5.71	2.71, 5.14
		Min, Max	0.0, 7.7	0.1, 8.3	0.0, 8.3
		Observed			
		n	36	30	66
		Mean	3.11	3.50	3.29
		SD, SE	2.129, 0.355	2.197, 0.401	2.153, 0.265
		Median	2.50	3.07	2.71
		Q1, Q3	1.36, 4.86	1.71, 5.43	1.57, 5.14
		Min, Max	0.1, 9.7	0.0, 7.9	0.0, 9.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.3.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Interference score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Change from Baseline			
		n	36	30	66
		Mean	-0.63	-0.95	-0.77
		SD, SE	1.939, 0.323	1.749, 0.319	1.848, 0.227
		Median	-0.64	-1.00	-0.93
		Q1, Q3	-1.93, 0.79	-2.14, 0.14	-2.00, 0.57
		Min, Max	-5.3, 3.9	-4.4, 3.7	-5.3, 3.9
		GEE Estimates			
		LS Mean (SE)	-0.84 (0.276)	-1.03 (0.295)	
		95% CI	(-1.38, -0.30)	(-1.61, -0.45)	
		LS Mean Difference (SE)		0.19 (0.433)	
		95% CI		(-0.66, 1.04)	
		p-value		0.6623	
		HedgesG (95% CI)		0.171 (-.315, 0.656)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Interference as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Interference as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_inter_SUB.sas

Table 2.2.3.1.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6		N_1	27	17	44
	Baseline	n	27	17	44
		Mean	3.55	3.45	3.51
		SD, SE	1.007, 0.194	0.926, 0.225	0.967, 0.146
		Median	3.53	3.44	3.47
		Q1, Q3	2.69, 4.34	2.97, 3.88	2.80, 4.30
		Min, Max	1.2, 5.7	1.8, 5.3	1.2, 5.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Baseline			
		n	27	17	44
		Mean	3.55	3.45	3.51
		SD, SE	1.007, 0.194	0.926, 0.225	0.967, 0.146
		Median	3.53	3.44	3.47
		Q1, Q3	2.69, 4.34	2.97, 3.88	2.80, 4.30
		Min, Max	1.2, 5.7	1.8, 5.3	1.2, 5.7
		Observed			
		n	27	17	44
		Mean	3.29	3.02	3.19
		SD, SE	1.737, 0.334	1.045, 0.253	1.499, 0.226
		Median	2.97	3.03	3.02
		Q1, Q3	2.09, 4.78	1.91, 3.64	2.08, 4.36
		Min, Max	0.2, 7.3	1.5, 4.7	0.2, 7.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Change from Baseline			
		n	27	17	44
		Mean	-0.26	-0.42	-0.32
		SD, SE	1.366, 0.263	1.139, 0.276	1.272, 0.192
		Median	-0.25	-0.38	-0.27
		Q1, Q3	-0.69, 0.88	-0.86, 0.38	-0.82, 0.69
		Min, Max	-3.8, 1.6	-2.9, 1.8	-3.8, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.25 (0.319)	-0.48 (0.350)	
		95% CI	(-0.88, 0.37)	(-1.17, 0.21)	
		LS Mean Difference (SE)		-0.22 (0.369)	
		95% CI		(-0.95, 0.50)	
		p-value		0.5429	
		HedgesG (95% CI)		-.125 (-.732, 0.483)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Baseline			
		n	27	17	44
		Mean	3.55	3.45	3.51
		SD, SE	1.007, 0.194	0.926, 0.225	0.967, 0.146
		Median	3.53	3.44	3.47
		Q1, Q3	2.69, 4.34	2.97, 3.88	2.80, 4.30
		Min, Max	1.2, 5.7	1.8, 5.3	1.2, 5.7
		Observed			
		n	27	17	44
		Mean	3.40	2.94	3.22
		SD, SE	1.951, 0.375	1.287, 0.312	1.723, 0.260
		Median	3.50	2.69	3.13
		Q1, Q3	1.69, 4.16	1.94, 4.11	1.83, 4.13
		Min, Max	0.3, 8.2	1.2, 5.3	0.3, 8.2

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Change from Baseline			
		n	27	17	44
		Mean	-0.15	-0.51	-0.29
		SD, SE	1.936, 0.373	0.804, 0.195	1.593, 0.240
		Median	-0.53	-0.56	-0.55
		Q1, Q3	-1.25, 0.88	-1.00, 0.03	-1.17, 0.19
		Min, Max	-4.6, 4.7	-1.8, 1.1	-4.6, 4.7
		GEE Estimates			
		LS Mean (SE)	-0.15 (0.334)	-0.56 (0.278)	
		95% CI	(-0.80, 0.51)	(-1.11, -0.02)	
		LS Mean Difference (SE)		-0.41 (0.401)	
		95% CI		(-1.20, 0.37)	
		p-value		0.3030	
		HedgesG (95% CI)		-.213 (-.821, 0.396)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6		N_1	39	51	90
	Baseline	n	39	51	90
		Mean	5.86	5.76	5.81
		SD, SE	1.077, 0.172	1.225, 0.171	1.158, 0.122
		Median	5.56	5.75	5.73
		Q1, Q3	4.88, 6.94	5.03, 6.66	4.91, 6.66
		Min, Max	4.1, 7.9	2.6, 8.3	2.6, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Baseline			
		n	39	51	90
		Mean	5.86	5.76	5.81
		SD, SE	1.077, 0.172	1.225, 0.171	1.158, 0.122
		Median	5.56	5.75	5.73
		Q1, Q3	4.88, 6.94	5.03, 6.66	4.91, 6.66
		Min, Max	4.1, 7.9	2.6, 8.3	2.6, 8.3
		Observed			
		n	39	51	90
		Mean	5.25	5.07	5.15
		SD, SE	1.577, 0.252	1.615, 0.226	1.593, 0.168
		Median	5.13	5.31	5.27
		Q1, Q3	4.09, 6.28	4.03, 6.16	4.09, 6.22
		Min, Max	1.8, 8.1	1.5, 8.1	1.5, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Change from Baseline			
		n	39	51	90
		Mean	-0.61	-0.69	-0.66
		SD, SE	1.236, 0.198	1.248, 0.175	1.237, 0.130
		Median	-0.50	-0.28	-0.34
		Q1, Q3	-1.55, 0.44	-1.44, 0.09	-1.44, 0.15
		Min, Max	-3.3, 1.5	-5.5, 1.2	-5.5, 1.5
		GEE Estimates			
		LS Mean (SE)	-0.40 (0.216)	-0.50 (0.186)	
		95% CI	(-0.83, 0.02)	(-0.86, -0.13)	
		LS Mean Difference (SE)		-0.09 (0.259)	
		95% CI		(-0.60, 0.42)	
		p-value		0.7256	
		HedgesG (95% CI)		-.065 (-.482, 0.352)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Baseline			
		n	38	50	88
		Mean	5.82	5.76	5.79
		SD, SE	1.062, 0.172	1.237, 0.175	1.159, 0.124
		Median	5.56	5.75	5.67
		Q1, Q3	4.88, 6.66	5.03, 6.66	4.89, 6.66
		Min, Max	4.1, 7.9	2.6, 8.3	2.6, 8.3
		Observed			
		n	38	50	88
		Mean	5.54	4.96	5.21
		SD, SE	1.796, 0.291	1.772, 0.251	1.795, 0.191
		Median	5.61	4.86	5.33
		Q1, Q3	4.05, 6.88	3.81, 6.09	3.81, 6.59
		Min, Max	2.2, 9.0	1.4, 8.1	1.4, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Change from Baseline			
		n	38	50	88
		Mean	-0.28	-0.80	-0.58
		SD, SE	1.528, 0.248	1.463, 0.207	1.505, 0.160
		Median	-0.02	-0.50	-0.22
		Q1, Q3	-1.06, 0.72	-1.81, 0.22	-1.58, 0.27
		Min, Max	-3.1, 4.3	-5.0, 1.6	-5.0, 4.3
		GEE Estimates			
		LS Mean (SE)	-0.12 (0.242)	-0.59 (0.206)	
		95% CI	(-0.60, 0.35)	(-1.00, -0.19)	
		LS Mean Difference (SE)		-0.47 (0.314)	
		95% CI		(-1.09, 0.14)	
		p-value		0.1326	
		HedgesG (95% CI)		-.340 (-.765, 0.085)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6		N_1	49	48	97
	Baseline	n	49	48	97
		Mean	4.23	4.45	4.34
		SD, SE	1.119, 0.160	1.133, 0.164	1.125, 0.114
		Median	4.47	4.39	4.44
		Q1, Q3	3.44, 5.13	3.66, 5.42	3.53, 5.28
		Min, Max	1.2, 6.2	1.8, 6.0	1.2, 6.2

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Baseline			
		n	49	48	97
		Mean	4.23	4.45	4.34
		SD, SE	1.119, 0.160	1.133, 0.164	1.125, 0.114
		Median	4.47	4.39	4.44
		Q1, Q3	3.44, 5.13	3.66, 5.42	3.53, 5.28
		Min, Max	1.2, 6.2	1.8, 6.0	1.2, 6.2
		Observed			
		n	49	48	97
		Mean	3.77	3.87	3.82
		SD, SE	1.609, 0.230	1.402, 0.202	1.503, 0.153
		Median	3.69	4.00	3.97
		Q1, Q3	2.66, 5.00	2.89, 5.02	2.66, 5.00
		Min, Max	0.2, 6.9	1.5, 6.2	0.2, 6.9

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Change from Baseline			
		n	49	48	97
		Mean	-0.46	-0.57	-0.52
		SD, SE	1.294, 0.185	1.149, 0.166	1.220, 0.124
		Median	-0.31	-0.44	-0.38
		Q1, Q3	-1.41, 0.66	-0.97, 0.17	-1.28, 0.25
		Min, Max	-3.8, 1.6	-4.4, 1.8	-4.4, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.40 (0.199)	-0.50 (0.202)	
		95% CI	(-0.79, -0.01)	(-0.89, -0.10)	
		LS Mean Difference (SE)		-0.10 (0.237)	
		95% CI		(-0.56, 0.37)	
		p-value		0.6793	
		HedgesG (95% CI)		-.093 (-.492, 0.305)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Baseline			
		n	49	48	97
		Mean	4.23	4.45	4.34
		SD, SE	1.119, 0.160	1.133, 0.164	1.125, 0.114
		Median	4.47	4.39	4.44
		Q1, Q3	3.44, 5.13	3.66, 5.42	3.53, 5.28
		Min, Max	1.2, 6.2	1.8, 6.0	1.2, 6.2
		Observed			
		n	49	48	97
		Mean	3.97	3.76	3.87
		SD, SE	1.843, 0.263	1.506, 0.217	1.679, 0.170
		Median	3.69	3.96	3.81
		Q1, Q3	2.81, 5.34	2.50, 4.98	2.59, 5.25
		Min, Max	0.3, 8.4	1.2, 6.7	0.3, 8.4

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Change from Baseline			
		n	49	48	97
		Mean	-0.26	-0.68	-0.47
		SD, SE	1.760, 0.251	1.208, 0.174	1.519, 0.154
		Median	-0.53	-0.48	-0.53
		Q1, Q3	-1.25, 0.69	-1.43, 0.13	-1.28, 0.19
		Min, Max	-4.6, 4.7	-4.6, 1.6	-4.6, 4.7
		GEE Estimates			
		LS Mean (SE)	-0.21 (0.215)	-0.61 (0.201)	
		95% CI	(-0.63, 0.22)	(-1.00, -0.21)	
		LS Mean Difference (SE)		-0.40 (0.288)	
		95% CI		(-0.96, 0.16)	
		p-value		0.1636	
		HedgesG (95% CI)		-.272 (-.672, 0.128)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6		N_1	17	20	37
	Baseline	n	17	20	37
		Mean	6.89	6.95	6.92
		SD, SE	0.615, 0.149	0.658, 0.147	0.630, 0.104
		Median	7.04	6.84	6.94
		Q1, Q3	6.47, 7.38	6.50, 7.44	6.47, 7.38
		Min, Max	5.7, 7.9	5.8, 8.3	5.7, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Baseline			
		n	17	20	37
		Mean	6.89	6.95	6.92
		SD, SE	0.615, 0.149	0.658, 0.147	0.630, 0.104
		Median	7.04	6.84	6.94
		Q1, Q3	6.47, 7.38	6.50, 7.44	6.47, 7.38
		Min, Max	5.7, 7.9	5.8, 8.3	5.7, 8.3
		Observed			
		n	17	20	37
		Mean	6.40	6.20	6.29
		SD, SE	1.189, 0.288	1.311, 0.293	1.244, 0.204
		Median	6.75	6.38	6.50
		Q1, Q3	5.53, 7.31	5.80, 6.95	5.75, 7.19
		Min, Max	4.1, 8.1	2.4, 8.1	2.4, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Change from Baseline			
		n	17	20	37
		Mean	-0.49	-0.75	-0.63
		SD, SE	1.328, 0.322	1.395, 0.312	1.352, 0.222
		Median	-0.31	-0.27	-0.28
		Q1, Q3	-1.55, 0.22	-1.44, 0.00	-1.44, 0.09
		Min, Max	-2.8, 1.6	-5.5, 0.7	-5.5, 1.6
		GEE Estimates			
		LS Mean (SE)	0.26 (0.388)	0.14 (0.486)	
		95% CI	(-0.50, 1.02)	(-0.81, 1.09)	
		LS Mean Difference (SE)		-0.12 (0.422)	
		95% CI		(-0.95, 0.71)	
		p-value		0.7754	
		HedgesG (95% CI)		-.181 (-.829, 0.467)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Baseline			
		n	16	19	35
		Mean	6.86	7.01	6.95
		SD, SE	0.622, 0.156	0.610, 0.140	0.611, 0.103
		Median	6.99	6.84	6.94
		Q1, Q3	6.47, 7.34	6.63, 7.50	6.47, 7.47
		Min, Max	5.7, 7.9	6.1, 8.3	5.7, 8.3
		Observed			
		n	16	19	35
		Mean	6.74	6.17	6.43
		SD, SE	1.521, 0.380	1.606, 0.368	1.571, 0.266
		Median	7.13	6.75	6.84
		Q1, Q3	6.02, 7.67	4.66, 7.66	5.25, 7.66
		Min, Max	3.3, 9.0	2.9, 8.1	2.9, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Change from Baseline			
		n	16	19	35
		Mean	-0.12	-0.84	-0.51
		SD, SE	1.530, 0.383	1.623, 0.372	1.600, 0.270
		Median	0.08	-0.69	0.00
		Q1, Q3	-1.02, 0.89	-1.81, 0.38	-1.72, 0.59
		Min, Max	-3.1, 2.5	-5.0, 1.4	-5.0, 2.5
		GEE Estimates			
		LS Mean (SE)	0.51 (0.420)	0.09 (0.446)	
		95% CI	(-0.32, 1.33)	(-0.78, 0.97)	
		LS Mean Difference (SE)		-0.42 (0.504)	
		95% CI		(-1.40, 0.57)	
		p-value		0.4101	
		HedgesG (95% CI)		-.429 (-1.10, 0.244)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU		N_1	58	58	116
	Baseline	n	58	58	116
		Mean	5.08	5.37	5.22
		SD, SE	1.535, 0.202	1.443, 0.189	1.490, 0.138
		Median	5.00	5.50	5.30
		Q1, Q3	4.09, 6.38	4.30, 6.38	4.25, 6.38
		Min, Max	1.2, 7.9	2.6, 8.3	1.2, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Baseline			
		n	58	58	116
		Mean	5.08	5.37	5.22
		SD, SE	1.535, 0.202	1.443, 0.189	1.490, 0.138
		Median	5.00	5.50	5.30
		Q1, Q3	4.09, 6.38	4.30, 6.38	4.25, 6.38
		Min, Max	1.2, 7.9	2.6, 8.3	1.2, 8.3
		Observed			
		n	58	58	116
		Mean	4.59	4.65	4.62
		SD, SE	1.886, 0.248	1.763, 0.232	1.818, 0.169
		Median	4.77	4.59	4.75
		Q1, Q3	3.16, 6.03	3.19, 6.00	3.17, 6.02
		Min, Max	0.2, 8.1	1.5, 8.1	0.2, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Change from Baseline			
		n	58	58	116
		Mean	-0.49	-0.71	-0.60
		SD, SE	1.313, 0.172	1.242, 0.163	1.278, 0.119
		Median	-0.34	-0.44	-0.38
		Q1, Q3	-1.41, 0.66	-1.25, 0.09	-1.41, 0.21
		Min, Max	-3.8, 1.6	-5.5, 1.2	-5.5, 1.6
		GEE Estimates			
		LS Mean (SE)	-0.52 (0.189)	-0.70 (0.180)	
		95% CI	(-0.89, -0.15)	(-1.06, -0.35)	
		LS Mean Difference (SE)		-0.18 (0.229)	
		95% CI		(-0.63, 0.27)	
		p-value		0.4217	
		HedgesG (95% CI)		-.173 (-.538, 0.191)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Baseline			
		n	57	57	114
		Mean	5.04	5.36	5.20
		SD, SE	1.517, 0.201	1.455, 0.193	1.488, 0.139
		Median	4.88	5.41	5.27
		Q1, Q3	4.09, 6.19	4.30, 6.38	4.25, 6.38
		Min, Max	1.2, 7.9	2.6, 8.3	1.2, 8.3
		Observed			
		n	57	57	114
		Mean	4.85	4.55	4.70
		SD, SE	2.075, 0.275	1.854, 0.246	1.964, 0.184
		Median	4.71	4.44	4.50
		Q1, Q3	3.44, 6.50	3.09, 5.94	3.28, 6.16
		Min, Max	0.3, 9.0	1.2, 8.1	0.3, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Change from Baseline			
		n	57	57	114
		Mean	-0.19	-0.80	-0.50
		SD, SE	1.766, 0.234	1.382, 0.183	1.608, 0.151
		Median	-0.13	-0.56	-0.50
		Q1, Q3	-1.09, 0.72	-1.59, 0.19	-1.47, 0.38
		Min, Max	-4.6, 4.7	-5.0, 1.6	-5.0, 4.7
		GEE Estimates			
		LS Mean (SE)	-0.25 (0.236)	-0.78 (0.191)	
		95% CI	(-0.71, 0.21)	(-1.16, -0.41)	
		LS Mean Difference (SE)		-0.53 (0.282)	
		95% CI		(-1.09, 0.02)	
		p-value		0.0581	
		HedgesG (95% CI)		-.379 (-.750, -.009)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia		N_1	8	10	18
	Baseline	n	8	10	18
		Mean	3.73	4.12	3.95
		SD, SE	1.096, 0.387	1.676, 0.530	1.422, 0.335
		Median	3.58	3.96	3.96
		Q1, Q3	2.78, 4.81	2.97, 5.44	2.91, 4.88
		Min, Max	2.3, 5.1	1.8, 6.8	1.8, 6.8

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Baseline			
		n	8	10	18
		Mean	3.73	4.12	3.95
		SD, SE	1.096, 0.387	1.676, 0.530	1.422, 0.335
		Median	3.58	3.96	3.96
		Q1, Q3	2.78, 4.81	2.97, 5.44	2.91, 4.88
		Min, Max	2.3, 5.1	1.8, 6.8	1.8, 6.8
		Observed			
		n	8	10	18
		Mean	3.42	4.00	3.74
		SD, SE	1.757, 0.621	1.510, 0.477	1.602, 0.378
		Median	2.67	4.00	3.95
		Q1, Q3	2.20, 5.30	2.31, 4.94	2.31, 5.03
		Min, Max	1.3, 5.8	1.9, 6.5	1.3, 6.5

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Change from Baseline			
		n	8	10	18
		Mean	-0.30	-0.12	-0.20
		SD, SE	1.200, 0.424	0.977, 0.309	1.052, 0.248
		Median	-0.30	-0.05	-0.16
		Q1, Q3	-1.09, 0.41	-0.25, 0.16	-0.53, 0.16
		Min, Max	-2.1, 1.6	-1.8, 1.8	-2.1, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.18 (0.283)	-0.00 (0.331)	
		95% CI	(-0.74, 0.37)	(-0.65, 0.65)	
		LS Mean Difference (SE)		0.18 (0.449)	
		95% CI		(-0.70, 1.06)	
		p-value		0.6821	
		HedgesG (95% CI)		0.153 (-.778, 1.084)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Baseline			
		n	8	10	18
		Mean	3.73	4.12	3.95
		SD, SE	1.096, 0.387	1.676, 0.530	1.422, 0.335
		Median	3.58	3.96	3.96
		Q1, Q3	2.78, 4.81	2.97, 5.44	2.91, 4.88
		Min, Max	2.3, 5.1	1.8, 6.8	1.8, 6.8
		Observed			
		n	8	10	18
		Mean	3.24	3.84	3.57
		SD, SE	2.113, 0.747	1.980, 0.626	2.001, 0.472
		Median	2.86	4.00	3.81
		Q1, Q3	1.22, 5.16	1.97, 4.66	1.88, 5.00
		Min, Max	1.2, 6.3	1.6, 8.0	1.2, 8.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Change from Baseline			
		n	8	10	18
		Mean	-0.48	-0.29	-0.37
		SD, SE	1.126, 0.398	0.892, 0.282	0.976, 0.230
		Median	-0.45	-0.02	-0.11
		Q1, Q3	-1.44, 0.22	-1.00, 0.19	-1.16, 0.19
		Min, Max	-1.9, 1.4	-1.7, 1.2	-1.9, 1.4
		GEE Estimates			
		LS Mean (SE)	-0.36 (0.302)	-0.17 (0.245)	
		95% CI	(-0.96, 0.23)	(-0.65, 0.31)	
		LS Mean Difference (SE)		0.20 (0.398)	
		95% CI		(-0.58, 0.98)	
		p-value		0.6191	
		HedgesG (95% CI)		0.178 (-.754, 1.109)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male		N_1	23	24	47
	Baseline	n	23	24	47
		Mean	4.41	4.44	4.42
		SD, SE	1.297, 0.270	1.516, 0.310	1.398, 0.204
		Median	4.56	4.23	4.41
		Q1, Q3	3.75, 5.25	3.33, 5.52	3.44, 5.44
		Min, Max	1.2, 7.0	2.0, 7.5	1.2, 7.5

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Baseline			
		n	23	24	47
		Mean	4.41	4.44	4.42
		SD, SE	1.297, 0.270	1.516, 0.310	1.398, 0.204
		Median	4.56	4.23	4.41
		Q1, Q3	3.75, 5.25	3.33, 5.52	3.44, 5.44
		Min, Max	1.2, 7.0	2.0, 7.5	1.2, 7.5
		Observed			
		n	23	24	47
		Mean	3.99	3.86	3.93
		SD, SE	1.853, 0.386	1.652, 0.337	1.735, 0.253
		Median	3.96	3.77	3.91
		Q1, Q3	2.34, 5.66	2.05, 5.50	2.19, 5.56
		Min, Max	1.0, 7.2	1.7, 6.7	1.0, 7.2

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Change from Baseline			
		n	23	24	47
		Mean	-0.42	-0.58	-0.50
		SD, SE	1.266, 0.264	0.930, 0.190	1.098, 0.160
		Median	-0.50	-0.64	-0.53
		Q1, Q3	-1.41, 0.91	-1.23, 0.00	-1.41, 0.15
		Min, Max	-2.7, 1.6	-2.6, 1.2	-2.7, 1.6
		GEE Estimates			
		LS Mean (SE)	-0.37 (0.256)	-0.50 (0.190)	
		95% CI	(-0.87, 0.13)	(-0.88, -0.13)	
		LS Mean Difference (SE)		-0.13 (0.301)	
		95% CI		(-0.72, 0.46)	
		p-value		0.6554	
		HedgesG (95% CI)		-.135 (-.708, 0.437)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Baseline			
		n	23	23	46
		Mean	4.41	4.38	4.40
		SD, SE	1.297, 0.270	1.524, 0.318	1.399, 0.206
		Median	4.56	4.16	4.38
		Q1, Q3	3.75, 5.25	3.28, 5.44	3.44, 5.28
		Min, Max	1.2, 7.0	2.0, 7.5	1.2, 7.5
		Observed			
		n	23	23	46
		Mean	4.38	3.55	3.97
		SD, SE	2.187, 0.456	1.732, 0.361	1.995, 0.294
		Median	4.44	3.34	3.67
		Q1, Q3	2.81, 5.91	2.00, 4.66	2.47, 5.59
		Min, Max	0.3, 8.4	1.2, 7.3	0.3, 8.4

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Change from Baseline			
		n	23	23	46
		Mean	-0.03	-0.83	-0.43
		SD, SE	2.008, 0.419	1.049, 0.219	1.635, 0.241
		Median	-0.13	-0.63	-0.59
		Q1, Q3	-1.09, 0.75	-1.56, -0.16	-1.47, 0.09
		Min, Max	-4.6, 4.7	-2.9, 1.6	-4.6, 4.7
		GEE Estimates			
		LS Mean (SE)	0.02 (0.343)	-0.74 (0.206)	
		95% CI	(-0.65, 0.70)	(-1.14, -0.34)	
		LS Mean Difference (SE)		-0.76 (0.442)	
		95% CI		(-1.63, 0.10)	
		p-value		0.0837	
		HedgesG (95% CI)		-.481 (-1.07, 0.106)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female		N_1	43	44	87
	Baseline	n	43	44	87
		Mean	5.19	5.59	5.39
		SD, SE	1.614, 0.246	1.395, 0.210	1.512, 0.162
		Median	5.31	5.73	5.47
		Q1, Q3	3.59, 6.56	4.58, 6.63	4.25, 6.63
		Min, Max	2.3, 7.9	1.8, 8.3	1.8, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Baseline			
		n	43	44	87
		Mean	5.19	5.59	5.39
		SD, SE	1.614, 0.246	1.395, 0.210	1.512, 0.162
		Median	5.31	5.73	5.47
		Q1, Q3	3.59, 6.56	4.58, 6.63	4.25, 6.63
		Min, Max	2.3, 7.9	1.8, 8.3	1.8, 8.3
		Observed			
		n	43	44	87
		Mean	4.70	4.93	4.82
		SD, SE	1.895, 0.289	1.676, 0.253	1.781, 0.191
		Median	4.80	5.02	4.82
		Q1, Q3	3.16, 6.25	4.00, 6.16	3.44, 6.16
		Min, Max	0.2, 8.1	1.5, 8.1	0.2, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Change from Baseline			
		n	43	44	87
		Mean	-0.49	-0.65	-0.57
		SD, SE	1.321, 0.201	1.360, 0.205	1.336, 0.143
		Median	-0.31	-0.25	-0.25
		Q1, Q3	-1.55, 0.66	-1.03, 0.16	-1.38, 0.22
		Min, Max	-3.8, 1.6	-5.5, 1.8	-5.5, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.37 (0.263)	-0.43 (0.309)	
		95% CI	(-0.89, 0.14)	(-1.04, 0.17)	
		LS Mean Difference (SE)		-0.06 (0.287)	
		95% CI		(-0.63, 0.50)	
		p-value		0.8247	
		HedgesG (95% CI)		-.119 (-.540, 0.302)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Baseline			
		n	42	44	86
		Mean	5.14	5.59	5.37
		SD, SE	1.597, 0.246	1.395, 0.210	1.505, 0.162
		Median	5.22	5.73	5.45
		Q1, Q3	3.59, 6.47	4.58, 6.63	4.25, 6.56
		Min, Max	2.3, 7.9	1.8, 8.3	1.8, 8.3
		Observed			
		n	42	44	86
		Mean	4.80	4.91	4.86
		SD, SE	2.111, 0.326	1.793, 0.270	1.944, 0.210
		Median	4.65	4.81	4.70
		Q1, Q3	3.28, 6.50	3.80, 6.16	3.53, 6.47
		Min, Max	1.2, 9.0	1.4, 8.1	1.2, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Change from Baseline			
		n	42	44	86
		Mean	-0.34	-0.67	-0.51
		SD, SE	1.513, 0.234	1.461, 0.220	1.488, 0.160
		Median	-0.19	-0.35	-0.27
		Q1, Q3	-1.25, 0.72	-1.70, 0.25	-1.38, 0.38
		Min, Max	-3.1, 4.1	-5.0, 1.4	-5.0, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.26 (0.289)	-0.45 (0.297)	
		95% CI	(-0.82, 0.31)	(-1.04, 0.13)	
		LS Mean Difference (SE)		-0.20 (0.308)	
		95% CI		(-0.80, 0.41)	
		p-value		0.5216	
		HedgesG (95% CI)		-.220 (-.644, 0.204)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White		N_1	53	55	108
	Baseline	n	53	55	108
		Mean	4.97	5.43	5.20
		SD, SE	1.539, 0.211	1.424, 0.192	1.493, 0.144
		Median	4.81	5.59	5.25
		Q1, Q3	4.00, 6.19	4.35, 6.63	4.25, 6.38
		Min, Max	1.2, 7.9	2.6, 8.3	1.2, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Baseline			
		n	53	55	108
		Mean	4.97	5.43	5.20
		SD, SE	1.539, 0.211	1.424, 0.192	1.493, 0.144
		Median	4.81	5.59	5.25
		Q1, Q3	4.00, 6.19	4.35, 6.63	4.25, 6.38
		Min, Max	1.2, 7.9	2.6, 8.3	1.2, 8.3
		Observed			
		n	53	55	108
		Mean	4.51	4.73	4.62
		SD, SE	1.895, 0.260	1.725, 0.233	1.805, 0.174
		Median	4.75	4.59	4.75
		Q1, Q3	3.09, 5.84	3.44, 6.03	3.17, 6.02
		Min, Max	0.2, 8.1	1.5, 8.1	0.2, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Change from Baseline			
		n	53	55	108
		Mean	-0.46	-0.70	-0.58
		SD, SE	1.285, 0.176	1.255, 0.169	1.269, 0.122
		Median	-0.31	-0.38	-0.36
		Q1, Q3	-1.41, 0.66	-1.25, 0.13	-1.39, 0.23
		Min, Max	-3.8, 1.5	-5.5, 1.2	-5.5, 1.5
		GEE Estimates			
		LS Mean (SE)	-0.55 (0.192)	-0.73 (0.179)	
		95% CI	(-0.92, -0.17)	(-1.08, -0.38)	
		LS Mean Difference (SE)		-0.18 (0.235)	
		95% CI		(-0.64, 0.28)	
		p-value		0.4407	
		HedgesG (95% CI)		-.187 (-.565, 0.191)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Baseline			
		n	53	55	108
		Mean	4.97	5.43	5.20
		SD, SE	1.539, 0.211	1.424, 0.192	1.493, 0.144
		Median	4.81	5.59	5.25
		Q1, Q3	4.00, 6.19	4.35, 6.63	4.25, 6.38
		Min, Max	1.2, 7.9	2.6, 8.3	1.2, 8.3
		Observed			
		n	53	55	108
		Mean	4.75	4.64	4.70
		SD, SE	2.033, 0.279	1.828, 0.246	1.923, 0.185
		Median	4.59	4.44	4.50
		Q1, Q3	3.44, 6.47	3.28, 5.94	3.31, 6.13
		Min, Max	0.3, 9.0	1.2, 8.1	0.3, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Change from Baseline			
		n	53	55	108
		Mean	-0.21	-0.79	-0.51
		SD, SE	1.752, 0.241	1.398, 0.189	1.601, 0.154
		Median	-0.25	-0.56	-0.50
		Q1, Q3	-1.09, 0.72	-1.59, 0.22	-1.42, 0.33
		Min, Max	-4.6, 4.7	-5.0, 1.6	-5.0, 4.7
		GEE Estimates			
		LS Mean (SE)	-0.30 (0.236)	-0.82 (0.194)	
		95% CI	(-0.76, 0.16)	(-1.20, -0.44)	
		LS Mean Difference (SE)		-0.51 (0.287)	
		95% CI		(-1.08, 0.05)	
		p-value		0.0728	
		HedgesG (95% CI)		-.357 (-.737, 0.023)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White		N_1	13	13	26
	Baseline	n	13	13	26
		Mean	4.72	4.14	4.43
		SD, SE	1.628, 0.451	1.586, 0.440	1.602, 0.314
		Median	4.88	3.97	4.20
		Q1, Q3	3.19, 5.69	2.97, 5.44	2.97, 5.69
		Min, Max	2.3, 7.4	1.8, 6.8	1.8, 7.4

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Baseline			
		n	13	13	26
		Mean	4.72	4.14	4.43
		SD, SE	1.628, 0.451	1.586, 0.440	1.602, 0.314
		Median	4.88	3.97	4.20
		Q1, Q3	3.19, 5.69	2.97, 5.44	2.97, 5.69
		Min, Max	2.3, 7.4	1.8, 6.8	1.8, 7.4
		Observed			
		n	13	13	26
		Mean	4.21	3.82	4.01
		SD, SE	1.965, 0.545	1.628, 0.451	1.779, 0.349
		Median	4.72	3.97	4.00
		Q1, Q3	2.66, 5.56	2.19, 4.94	2.31, 5.53
		Min, Max	1.3, 7.3	1.8, 6.5	1.3, 7.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Change from Baseline			
		n	13	13	26
		Mean	-0.51	-0.33	-0.42
		SD, SE	1.377, 0.382	1.042, 0.289	1.200, 0.235
		Median	-0.31	-0.09	-0.23
		Q1, Q3	-1.66, 0.15	-0.78, 0.09	-1.44, 0.15
		Min, Max	-2.6, 1.6	-2.3, 1.8	-2.6, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.46 (0.242)	-0.01 (0.314)	
		95% CI	(-0.93, 0.01)	(-0.63, 0.60)	
		LS Mean Difference (SE)		0.45 (0.381)	
		95% CI		(-0.30, 1.19)	
		p-value		0.2425	
		HedgesG (95% CI)		0.138 (-.631, 0.908)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Baseline			
		n	12	12	24
		Mean	4.50	4.01	4.25
		SD, SE	1.482, 0.428	1.578, 0.456	1.518, 0.310
		Median	4.81	3.96	4.06
		Q1, Q3	3.05, 5.56	2.80, 4.84	2.94, 5.44
		Min, Max	2.3, 7.0	1.8, 6.8	1.8, 7.0
		Observed			
		n	12	12	24
		Mean	4.20	3.56	3.88
		SD, SE	2.567, 0.741	1.908, 0.551	2.235, 0.456
		Median	4.42	3.13	3.81
		Q1, Q3	1.56, 6.08	1.98, 4.44	1.95, 5.45
		Min, Max	1.2, 8.2	1.6, 8.0	1.2, 8.2

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Change from Baseline			
		n	12	12	24
		Mean	-0.30	-0.45	-0.38
		SD, SE	1.489, 0.430	0.938, 0.271	1.220, 0.249
		Median	-0.13	-0.27	-0.13
		Q1, Q3	-1.44, 0.50	-1.24, 0.17	-1.32, 0.22
		Min, Max	-2.8, 2.5	-1.9, 1.2	-2.8, 2.5
		GEE Estimates			
		LS Mean (SE)	-0.36 (0.367)	-0.14 (0.273)	
		95% CI	(-1.08, 0.36)	(-0.67, 0.40)	
		LS Mean Difference (SE)		0.22 (0.426)	
		95% CI		(-0.61, 1.05)	
		p-value		0.6062	
		HedgesG (95% CI)		-.111 (-.912, 0.690)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years		N_1	36	31	67
	Baseline	n	36	31	67
		Mean	5.11	5.42	5.25
		SD, SE	1.550, 0.258	1.551, 0.279	1.547, 0.189
		Median	5.06	5.75	5.44
		Q1, Q3	4.19, 6.42	3.96, 6.63	3.97, 6.47
		Min, Max	2.3, 7.6	2.0, 7.9	2.0, 7.9

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Baseline			
		n	36	31	67
		Mean	5.11	5.42	5.25
		SD, SE	1.550, 0.258	1.551, 0.279	1.547, 0.189
		Median	5.06	5.75	5.44
		Q1, Q3	4.19, 6.42	3.96, 6.63	3.97, 6.47
		Min, Max	2.3, 7.6	2.0, 7.9	2.0, 7.9
		Observed			
		n	36	31	67
		Mean	4.65	4.92	4.78
		SD, SE	1.712, 0.285	1.835, 0.330	1.761, 0.215
		Median	4.77	5.53	4.94
		Q1, Q3	3.34, 5.81	3.03, 6.22	3.19, 6.09
		Min, Max	1.3, 7.7	1.8, 7.7	1.3, 7.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Change from Baseline			
		n	36	31	67
		Mean	-0.45	-0.51	-0.48
		SD, SE	1.170, 0.195	0.898, 0.161	1.046, 0.128
		Median	-0.41	-0.34	-0.34
		Q1, Q3	-1.48, 0.48	-1.44, 0.09	-1.44, 0.20
		Min, Max	-2.8, 1.6	-2.3, 0.9	-2.8, 1.6
		GEE Estimates			
		LS Mean (SE)	-0.11 (0.224)	-0.16 (0.199)	
		95% CI	(-0.55, 0.33)	(-0.55, 0.23)	
		LS Mean Difference (SE)		-0.05 (0.229)	
		95% CI		(-0.50, 0.39)	
		p-value		0.8122	
		HedgesG (95% CI)		-.053 (-.533, 0.427)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Baseline			
		n	36	31	67
		Mean	5.11	5.42	5.25
		SD, SE	1.550, 0.258	1.551, 0.279	1.547, 0.189
		Median	5.06	5.75	5.44
		Q1, Q3	4.19, 6.42	3.96, 6.63	3.97, 6.47
		Min, Max	2.3, 7.6	2.0, 7.9	2.0, 7.9
		Observed			
		n	36	31	67
		Mean	4.56	4.60	4.58
		SD, SE	1.972, 0.329	1.980, 0.356	1.961, 0.240
		Median	4.30	4.66	4.56
		Q1, Q3	3.23, 6.02	2.59, 5.94	3.09, 5.94
		Min, Max	1.2, 8.6	1.6, 8.1	1.2, 8.6

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Change from Baseline			
		n	36	31	67
		Mean	-0.55	-0.82	-0.68
		SD, SE	1.225, 0.204	1.080, 0.194	1.160, 0.142
		Median	-0.72	-0.94	-0.78
		Q1, Q3	-1.20, 0.17	-1.72, 0.16	-1.56, 0.16
		Min, Max	-3.1, 2.5	-3.2, 1.4	-3.2, 2.5
		GEE Estimates			
		LS Mean (SE)	-0.20 (0.261)	-0.48 (0.227)	
		95% CI	(-0.71, 0.31)	(-0.92, -0.03)	
		LS Mean Difference (SE)		-0.27 (0.268)	
		95% CI		(-0.80, 0.25)	
		p-value		0.3075	
		HedgesG (95% CI)		-.232 (-.714, 0.250)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years		N_1	30	37	67
	Baseline	n	30	37	67
		Mean	4.69	4.98	4.85
		SD, SE	1.539, 0.281	1.506, 0.248	1.516, 0.185
		Median	4.69	5.03	4.78
		Q1, Q3	3.53, 5.47	4.06, 5.75	3.88, 5.75
		Min, Max	1.2, 7.9	1.8, 8.3	1.2, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Baseline			
		n	30	37	67
		Mean	4.69	4.98	4.85
		SD, SE	1.539, 0.281	1.506, 0.248	1.516, 0.185
		Median	4.69	5.03	4.78
		Q1, Q3	3.53, 5.47	4.06, 5.75	3.88, 5.75
		Min, Max	1.2, 7.9	1.8, 8.3	1.2, 8.3
		Observed			
		n	30	37	67
		Mean	4.21	4.25	4.23
		SD, SE	2.102, 0.384	1.607, 0.264	1.830, 0.224
		Median	4.42	4.25	4.25
		Q1, Q3	2.66, 5.66	3.44, 5.22	2.78, 5.38
		Min, Max	0.2, 8.1	1.5, 8.1	0.2, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Change from Baseline			
		n	30	37	67
		Mean	-0.48	-0.73	-0.62
		SD, SE	1.447, 0.264	1.439, 0.237	1.437, 0.176
		Median	-0.28	-0.25	-0.25
		Q1, Q3	-1.41, 0.81	-1.02, 0.13	-1.25, 0.22
		Min, Max	-3.8, 1.5	-5.5, 1.8	-5.5, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.32 (0.325)	-0.62 (0.283)	
		95% CI	(-0.96, 0.31)	(-1.18, -0.07)	
		LS Mean Difference (SE)		-0.30 (0.345)	
		95% CI		(-0.97, 0.38)	
		p-value		0.3883	
		HedgesG (95% CI)		-.162 (-.645, 0.320)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Baseline			
		n	29	36	65
		Mean	4.60	4.96	4.80
		SD, SE	1.479, 0.275	1.521, 0.254	1.502, 0.186
		Median	4.59	4.89	4.75
		Q1, Q3	3.53, 5.38	4.02, 5.80	3.88, 5.59
		Min, Max	1.2, 7.9	1.8, 8.3	1.2, 8.3
		Observed			
		n	29	36	65
		Mean	4.77	4.32	4.52
		SD, SE	2.343, 0.435	1.798, 0.300	2.054, 0.255
		Median	5.13	4.22	4.25
		Q1, Q3	3.06, 6.75	2.86, 5.41	2.94, 6.09
		Min, Max	0.3, 9.0	1.2, 8.0	0.3, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Change from Baseline			
		n	29	36	65
		Mean	0.17	-0.64	-0.28
		SD, SE	2.098, 0.390	1.520, 0.253	1.831, 0.227
		Median	0.16	-0.22	-0.06
		Q1, Q3	-1.09, 1.03	-1.30, 0.23	-1.22, 0.72
		Min, Max	-4.6, 4.7	-5.0, 1.6	-5.0, 4.7
		GEE Estimates			
		LS Mean (SE)	0.27 (0.395)	-0.53 (0.290)	
		95% CI	(-0.51, 1.04)	(-1.09, 0.04)	
		LS Mean Difference (SE)		-0.79 (0.432)	
		95% CI		(-1.64, 0.05)	
		p-value		0.0659	
		HedgesG (95% CI)		-.438 (-.932, 0.057)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5		N_1	41	39	80
	Baseline	n	41	39	80
		Mean	4.68	4.73	4.71
		SD, SE	1.652, 0.258	1.553, 0.249	1.595, 0.178
		Median	4.72	4.41	4.64
		Q1, Q3	3.38, 5.69	3.53, 5.72	3.48, 5.70
		Min, Max	1.2, 7.9	1.8, 8.3	1.2, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline			
		n	41	39	80
		Mean	4.68	4.73	4.71
		SD, SE	1.652, 0.258	1.553, 0.249	1.595, 0.178
		Median	4.72	4.41	4.64
		Q1, Q3	3.38, 5.69	3.53, 5.72	3.48, 5.70
		Min, Max	1.2, 7.9	1.8, 8.3	1.2, 8.3
		Observed			
		n	41	39	80
		Mean	4.17	4.23	4.20
		SD, SE	1.940, 0.303	1.706, 0.273	1.818, 0.203
		Median	4.09	4.34	4.19
		Q1, Q3	2.75, 5.53	3.00, 5.53	2.86, 5.53
		Min, Max	0.2, 8.1	1.5, 8.1	0.2, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline			
		n	41	39	80
		Mean	-0.52	-0.50	-0.51
		SD, SE	1.365, 0.213	1.025, 0.164	1.204, 0.135
		Median	-0.31	-0.25	-0.30
		Q1, Q3	-1.47, 0.25	-1.25, 0.16	-1.42, 0.17
		Min, Max	-3.8, 1.6	-2.9, 1.8	-3.8, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.43 (0.209)	-0.37 (0.215)	
		95% CI	(-0.84, -0.02)	(-0.79, 0.05)	
		LS Mean Difference (SE)		0.05 (0.253)	
		95% CI		(-0.44, 0.55)	
		p-value		0.8308	
		HedgesG (95% CI)		0.011 (-.427, 0.450)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline			
		n	41	39	80
		Mean	4.68	4.73	4.71
		SD, SE	1.652, 0.258	1.553, 0.249	1.595, 0.178
		Median	4.72	4.41	4.64
		Q1, Q3	3.38, 5.69	3.53, 5.72	3.48, 5.70
		Min, Max	1.2, 7.9	1.8, 8.3	1.2, 8.3
		Observed			
		n	41	39	80
		Mean	4.42	4.12	4.27
		SD, SE	2.062, 0.322	1.806, 0.289	1.935, 0.216
		Median	4.05	4.22	4.14
		Q1, Q3	3.06, 5.88	2.47, 5.56	2.64, 5.73
		Min, Max	1.2, 9.0	1.2, 7.7	1.2, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline			
		n	41	39	80
		Mean	-0.26	-0.61	-0.43
		SD, SE	1.697, 0.265	1.072, 0.172	1.429, 0.160
		Median	-0.47	-0.53	-0.50
		Q1, Q3	-1.16, 0.25	-1.51, 0.19	-1.38, 0.20
		Min, Max	-3.1, 4.7	-2.9, 1.6	-3.1, 4.7
		GEE Estimates			
		LS Mean (SE)	-0.17 (0.232)	-0.48 (0.190)	
		95% CI	(-0.63, 0.29)	(-0.85, -0.11)	
		LS Mean Difference (SE)		-0.31 (0.298)	
		95% CI		(-0.90, 0.27)	
		p-value		0.2931	
		HedgesG (95% CI)		-.242 (-.682, 0.198)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5		N_1	25	29	54
	Baseline	n	25	29	54
		Mean	5.31	5.79	5.56
		SD, SE	1.296, 0.259	1.296, 0.241	1.306, 0.178
		Median	4.88	5.94	5.63
		Q1, Q3	4.47, 6.47	5.13, 6.66	4.59, 6.63
		Min, Max	3.2, 7.6	2.6, 7.9	2.6, 7.9

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline			
		n	25	29	54
		Mean	5.31	5.79	5.56
		SD, SE	1.296, 0.259	1.296, 0.241	1.306, 0.178
		Median	4.88	5.94	5.63
		Q1, Q3	4.47, 6.47	5.13, 6.66	4.59, 6.63
		Min, Max	3.2, 7.6	2.6, 7.9	2.6, 7.9
		Observed			
		n	25	29	54
		Mean	4.92	4.99	4.96
		SD, SE	1.762, 0.352	1.703, 0.316	1.715, 0.233
		Median	5.00	5.13	5.06
		Q1, Q3	3.16, 6.09	3.94, 6.16	3.72, 6.16
		Min, Max	2.1, 7.7	1.5, 7.7	1.5, 7.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline			
		n	25	29	54
		Mean	-0.39	-0.79	-0.61
		SD, SE	1.187, 0.237	1.442, 0.268	1.334, 0.181
		Median	-0.31	-0.34	-0.33
		Q1, Q3	-0.81, 0.66	-1.02, 0.00	-1.02, 0.44
		Min, Max	-2.7, 1.1	-5.5, 0.7	-5.5, 1.1
		GEE Estimates			
		LS Mean (SE)	-0.46 (0.288)	-0.98 (0.342)	
		95% CI	(-1.03, 0.10)	(-1.65, -0.31)	
		LS Mean Difference (SE)		-0.52 (0.328)	
		95% CI		(-1.16, 0.13)	
		p-value		0.1160	
		HedgesG (95% CI)		-.297 (-.835, 0.241)	

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treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline			
		n	24	28	52
		Mean	5.22	5.79	5.53
		SD, SE	1.249, 0.255	1.320, 0.249	1.306, 0.181
		Median	4.88	5.95	5.59
		Q1, Q3	4.45, 6.47	5.02, 6.70	4.55, 6.59
		Min, Max	3.2, 7.6	2.6, 7.9	2.6, 7.9
		Observed			
		n	24	28	52
		Mean	5.04	4.90	4.97
		SD, SE	2.232, 0.456	1.907, 0.360	2.043, 0.283
		Median	5.19	4.35	4.67
		Q1, Q3	3.48, 6.81	3.55, 6.48	3.48, 6.75
		Min, Max	0.3, 8.6	1.4, 8.1	0.3, 8.6

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline			
		n	24	28	52
		Mean	-0.18	-0.88	-0.56
		SD, SE	1.729, 0.353	1.628, 0.308	1.696, 0.235
		Median	0.06	-0.51	-0.35
		Q1, Q3	-1.17, 0.72	-1.83, 0.22	-1.75, 0.53
		Min, Max	-4.6, 4.3	-5.0, 1.4	-5.0, 4.3
		GEE Estimates			
		LS Mean (SE)	-0.33 (0.335)	-1.04 (0.370)	
		95% CI	(-0.99, 0.33)	(-1.77, -0.32)	
		LS Mean Difference (SE)		-0.71 (0.425)	
		95% CI		(-1.55, 0.12)	
		p-value		0.0928	
		HedgesG (95% CI)		-.408 (-.959, 0.142)	

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treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	4.33	4.43	4.38
		SD, SE	1.373, 0.226	1.501, 0.274	1.421, 0.174
		Median	4.50	4.39	4.47
		Q1, Q3	3.19, 5.25	3.28, 5.31	3.19, 5.31
		Min, Max	1.2, 7.1	1.8, 7.5	1.2, 7.5

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline			
		n	37	30	67
		Mean	4.33	4.43	4.38
		SD, SE	1.373, 0.226	1.501, 0.274	1.421, 0.174
		Median	4.50	4.39	4.47
		Q1, Q3	3.19, 5.25	3.28, 5.31	3.19, 5.31
		Min, Max	1.2, 7.1	1.8, 7.5	1.2, 7.5
		Observed			
		n	37	30	67
		Mean	3.89	3.74	3.82
		SD, SE	1.643, 0.270	1.448, 0.264	1.549, 0.189
		Median	4.00	3.81	3.96
		Q1, Q3	2.38, 5.03	2.31, 4.59	2.38, 4.97
		Min, Max	1.0, 7.1	1.5, 6.7	1.0, 7.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-0.44	-0.69	-0.55
		SD, SE	1.274, 0.209	1.073, 0.196	1.186, 0.145
		Median	-0.31	-0.69	-0.50
		Q1, Q3	-1.41, 0.66	-1.66, 0.06	-1.55, 0.44
		Min, Max	-3.3, 1.6	-2.9, 1.8	-3.3, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.44 (0.195)	-0.68 (0.236)	
		95% CI	(-0.82, -0.05)	(-1.14, -0.21)	
		LS Mean Difference (SE)		-0.24 (0.269)	
		95% CI		(-0.77, 0.28)	
		p-value		0.3684	
		HedgesG (95% CI)		-.205 (-.688, 0.278)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline			
		n	37	30	67
		Mean	4.33	4.43	4.38
		SD, SE	1.373, 0.226	1.501, 0.274	1.421, 0.174
		Median	4.50	4.39	4.47
		Q1, Q3	3.19, 5.25	3.28, 5.31	3.19, 5.31
		Min, Max	1.2, 7.1	1.8, 7.5	1.2, 7.5
		Observed			
		n	37	30	67
		Mean	3.89	3.61	3.76
		SD, SE	1.924, 0.316	1.524, 0.278	1.749, 0.214
		Median	3.69	3.45	3.66
		Q1, Q3	2.28, 5.31	2.47, 4.56	2.31, 5.13
		Min, Max	0.3, 8.4	1.2, 7.3	0.3, 8.4

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treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-0.44	-0.82	-0.61
		SD, SE	1.810, 0.298	1.014, 0.185	1.508, 0.184
		Median	-0.66	-0.59	-0.63
		Q1, Q3	-1.28, 0.25	-1.56, -0.09	-1.51, 0.09
		Min, Max	-4.6, 4.7	-3.2, 1.0	-4.6, 4.7
		GEE Estimates			
		LS Mean (SE)	-0.43 (0.238)	-0.81 (0.210)	
		95% CI	(-0.90, 0.03)	(-1.22, -0.40)	
		LS Mean Difference (SE)		-0.37 (0.326)	
		95% CI		(-1.01, 0.27)	
		p-value		0.2522	
		HedgesG (95% CI)		-.247 (-.730, 0.237)	

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treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	5.67	5.78	5.73
		SD, SE	1.447, 0.269	1.289, 0.209	1.350, 0.165
		Median	5.63	5.88	5.75
		Q1, Q3	4.59, 7.04	5.03, 6.66	4.59, 6.84
		Min, Max	3.1, 7.9	3.4, 8.3	3.1, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline			
		n	29	38	67
		Mean	5.67	5.78	5.73
		SD, SE	1.447, 0.269	1.289, 0.209	1.350, 0.165
		Median	5.63	5.88	5.75
		Q1, Q3	4.59, 7.04	5.03, 6.66	4.59, 6.84
		Min, Max	3.1, 7.9	3.4, 8.3	3.1, 8.3
		Observed			
		n	29	38	67
		Mean	5.17	5.20	5.19
		SD, SE	1.984, 0.368	1.683, 0.273	1.805, 0.221
		Median	5.63	5.41	5.47
		Q1, Q3	3.69, 6.75	4.25, 6.25	4.09, 6.50
		Min, Max	0.2, 8.1	1.5, 8.1	0.2, 8.1

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-0.50	-0.58	-0.54
		SD, SE	1.339, 0.249	1.335, 0.217	1.327, 0.162
		Median	-0.31	-0.22	-0.22
		Q1, Q3	-0.97, 0.22	-0.81, 0.16	-0.84, 0.19
		Min, Max	-3.8, 1.6	-5.5, 1.2	-5.5, 1.6
		GEE Estimates			
		LS Mean (SE)	-0.41 (0.408)	-0.60 (0.369)	
		95% CI	(-1.20, 0.39)	(-1.32, 0.12)	
		LS Mean Difference (SE)		-0.19 (0.317)	
		95% CI		(-0.81, 0.43)	
		p-value		0.5400	
		HedgesG (95% CI)		-.056 (-.539, 0.428)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline			
		n	28	37	65
		Mean	5.61	5.78	5.70
		SD, SE	1.435, 0.271	1.307, 0.215	1.355, 0.168
		Median	5.59	5.91	5.75
		Q1, Q3	4.52, 6.99	5.03, 6.66	4.59, 6.75
		Min, Max	3.1, 7.9	3.4, 8.3	3.1, 8.3
		Observed			
		n	28	37	65
		Mean	5.66	5.13	5.35
		SD, SE	1.996, 0.377	1.875, 0.308	1.931, 0.239
		Median	6.08	5.25	5.53
		Q1, Q3	3.75, 7.17	4.22, 6.69	4.03, 6.88
		Min, Max	1.6, 9.0	1.4, 8.1	1.4, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline			
		n	28	37	65
		Mean	0.05	-0.65	-0.35
		SD, SE	1.519, 0.287	1.546, 0.254	1.562, 0.194
		Median	0.03	-0.43	-0.03
		Q1, Q3	-1.08, 0.89	-1.59, 0.38	-1.25, 0.66
		Min, Max	-2.9, 4.1	-5.0, 1.6	-5.0, 4.1
		GEE Estimates			
		LS Mean (SE)	0.08 (0.418)	-0.66 (0.375)	
		95% CI	(-0.74, 0.90)	(-1.40, 0.07)	
		LS Mean Difference (SE)		-0.74 (0.364)	
		95% CI		(-1.45, -0.03)	
		p-value		0.0416	
		HedgesG (95% CI)		-.443 (-.940, 0.054)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50		N_1	42	32	74
	Baseline	n	42	32	74
		Mean	4.41	4.44	4.42
		SD, SE	1.409, 0.217	1.551, 0.274	1.461, 0.170
		Median	4.48	4.30	4.39
		Q1, Q3	3.38, 5.56	3.33, 5.52	3.38, 5.56
		Min, Max	1.2, 7.2	1.8, 7.9	1.2, 7.9

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.1.2.24.9
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Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Baseline			
		n	42	32	74
		Mean	4.41	4.44	4.42
		SD, SE	1.409, 0.217	1.551, 0.274	1.461, 0.170
		Median	4.48	4.30	4.39
		Q1, Q3	3.38, 5.56	3.33, 5.52	3.38, 5.56
		Min, Max	1.2, 7.2	1.8, 7.9	1.2, 7.9
		Observed			
		n	42	32	74
		Mean	4.04	3.84	3.95
		SD, SE	1.765, 0.272	1.613, 0.285	1.692, 0.197
		Median	4.14	3.97	4.06
		Q1, Q3	2.38, 5.13	2.25, 4.84	2.38, 5.13
		Min, Max	1.0, 7.3	1.5, 7.6	1.0, 7.6

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Table 2.2.3.1.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Change from Baseline			
		n	42	32	74
		Mean	-0.37	-0.60	-0.47
		SD, SE	1.284, 0.198	1.051, 0.186	1.187, 0.138
		Median	-0.30	-0.48	-0.34
		Q1, Q3	-1.41, 0.81	-1.23, 0.13	-1.41, 0.38
		Min, Max	-3.3, 1.6	-2.9, 1.8	-3.3, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.30 (0.197)	-0.57 (0.219)	
		95% CI	(-0.69, 0.08)	(-1.00, -0.15)	
		LS Mean Difference (SE)		-0.27 (0.261)	
		95% CI		(-0.78, 0.24)	
		p-value		0.2990	
		HedgesG (95% CI)		-.190 (-.651, 0.271)	

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Table 2.2.3.1.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Baseline			
		n	42	32	74
		Mean	4.41	4.44	4.42
		SD, SE	1.409, 0.217	1.551, 0.274	1.461, 0.170
		Median	4.48	4.30	4.39
		Q1, Q3	3.38, 5.56	3.33, 5.52	3.38, 5.56
		Min, Max	1.2, 7.2	1.8, 7.9	1.2, 7.9
		Observed			
		n	42	32	74
		Mean	4.22	3.65	3.97
		SD, SE	2.096, 0.323	1.691, 0.299	1.939, 0.225
		Median	3.83	3.36	3.73
		Q1, Q3	2.81, 5.88	2.39, 4.98	2.47, 5.38
		Min, Max	0.3, 8.4	1.2, 8.1	0.3, 8.4

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Change from Baseline			
		n	42	32	74
		Mean	-0.19	-0.79	-0.45
		SD, SE	1.778, 0.274	1.119, 0.198	1.547, 0.180
		Median	-0.19	-0.55	-0.45
		Q1, Q3	-1.09, 0.69	-1.58, -0.02	-1.47, 0.19
		Min, Max	-4.6, 4.7	-3.2, 1.1	-4.6, 4.7
		GEE Estimates			
		LS Mean (SE)	-0.13 (0.247)	-0.76 (0.202)	
		95% CI	(-0.61, 0.36)	(-1.16, -0.36)	
		LS Mean Difference (SE)		-0.63 (0.322)	
		95% CI		(-1.27, -0.00)	
		p-value		0.0490	
		HedgesG (95% CI)		-.380 (-.844, 0.084)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50		N_1	24	35	59
	Baseline	n	24	35	59
		Mean	5.81	5.90	5.86
		SD, SE	1.390, 0.284	1.153, 0.195	1.244, 0.162
		Median	5.53	5.94	5.84
		Q1, Q3	4.80, 7.05	5.13, 6.75	4.91, 6.84
		Min, Max	3.1, 7.9	3.4, 8.3	3.1, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Baseline			
		n	24	35	59
		Mean	5.81	5.90	5.86
		SD, SE	1.390, 0.284	1.153, 0.195	1.244, 0.162
		Median	5.53	5.94	5.84
		Q1, Q3	4.80, 7.05	5.13, 6.75	4.91, 6.84
		Min, Max	3.1, 7.9	3.4, 8.3	3.1, 8.3
		Observed			
		n	24	35	59
		Mean	5.17	5.25	5.22
		SD, SE	1.941, 0.396	1.581, 0.267	1.720, 0.224
		Median	5.52	5.34	5.38
		Q1, Q3	3.67, 6.52	4.22, 6.50	3.97, 6.50
		Min, Max	0.2, 8.1	1.5, 8.1	0.2, 8.1

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Table 2.2.3.1.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Change from Baseline			
		n	24	35	59
		Mean	-0.63	-0.64	-0.64
		SD, SE	1.319, 0.269	1.385, 0.234	1.347, 0.175
		Median	-0.36	-0.25	-0.25
		Q1, Q3	-1.59, 0.19	-1.25, 0.13	-1.41, 0.15
		Min, Max	-3.8, 1.1	-5.5, 1.2	-5.5, 1.2
		GEE Estimates			
		LS Mean (SE)	-0.75 (0.423)	-0.83 (0.464)	
		95% CI	(-1.57, 0.08)	(-1.74, 0.08)	
		LS Mean Difference (SE)		-0.09 (0.361)	
		95% CI		(-0.79, 0.62)	
		p-value		0.8121	
		HedgesG (95% CI)		-.008 (-.528, 0.511)	

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treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Baseline			
		n	23	34	57
		Mean	5.74	5.90	5.84
		SD, SE	1.380, 0.288	1.170, 0.201	1.250, 0.166
		Median	5.44	5.95	5.84
		Q1, Q3	4.72, 7.04	5.13, 6.75	4.91, 6.84
		Min, Max	3.1, 7.9	3.4, 8.3	3.1, 8.3
		Observed			
		n	23	34	57
		Mean	5.45	5.25	5.33
		SD, SE	1.998, 0.417	1.724, 0.296	1.825, 0.242
		Median	5.59	5.25	5.31
		Q1, Q3	3.50, 7.13	4.22, 6.75	4.22, 6.75
		Min, Max	1.6, 9.0	1.4, 8.0	1.4, 9.0

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treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Change from Baseline			
		n	23	34	57
		Mean	-0.29	-0.65	-0.51
		SD, SE	1.572, 0.328	1.528, 0.262	1.542, 0.204
		Median	0.00	-0.45	-0.43
		Q1, Q3	-1.28, 0.72	-1.59, 0.38	-1.38, 0.38
		Min, Max	-2.9, 4.1	-5.0, 1.6	-5.0, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.48 (0.446)	-0.83 (0.470)	
		95% CI	(-1.35, 0.39)	(-1.75, 0.10)	
		LS Mean Difference (SE)		-0.35 (0.413)	
		95% CI		(-1.16, 0.46)	
		p-value		0.4011	
		HedgesG (95% CI)		-.227 (-.758, 0.304)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	4.33	4.41	4.37
		SD, SE	1.373, 0.226	1.514, 0.276	1.427, 0.174
		Median	4.50	4.31	4.41
		Q1, Q3	3.19, 5.25	3.28, 5.59	3.19, 5.44
		Min, Max	1.2, 7.1	1.8, 7.5	1.2, 7.5

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Baseline			
		n	37	30	67
		Mean	4.33	4.41	4.37
		SD, SE	1.373, 0.226	1.514, 0.276	1.427, 0.174
		Median	4.50	4.31	4.41
		Q1, Q3	3.19, 5.25	3.28, 5.59	3.19, 5.44
		Min, Max	1.2, 7.1	1.8, 7.5	1.2, 7.5
		Observed			
		n	37	30	67
		Mean	3.89	3.80	3.85
		SD, SE	1.643, 0.270	1.524, 0.278	1.580, 0.193
		Median	4.00	3.77	3.96
		Q1, Q3	2.38, 5.03	2.31, 4.72	2.38, 5.00
		Min, Max	1.0, 7.1	1.5, 6.7	1.0, 7.1

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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-0.44	-0.62	-0.52
		SD, SE	1.274, 0.209	1.038, 0.190	1.169, 0.143
		Median	-0.31	-0.56	-0.38
		Q1, Q3	-1.41, 0.66	-1.44, 0.06	-1.44, 0.44
		Min, Max	-3.3, 1.6	-2.9, 1.8	-3.3, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.43 (0.195)	-0.61 (0.232)	
		95% CI	(-0.81, -0.05)	(-1.07, -0.16)	
		LS Mean Difference (SE)		-0.18 (0.268)	
		95% CI		(-0.71, 0.34)	
		p-value		0.4986	
		HedgesG (95% CI)		-.147 (-.629, 0.335)	

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Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Baseline			
		n	37	30	67
		Mean	4.33	4.41	4.37
		SD, SE	1.373, 0.226	1.514, 0.276	1.427, 0.174
		Median	4.50	4.31	4.41
		Q1, Q3	3.19, 5.25	3.28, 5.59	3.19, 5.44
		Min, Max	1.2, 7.1	1.8, 7.5	1.2, 7.5
		Observed			
		n	37	30	67
		Mean	3.89	3.65	3.78
		SD, SE	1.924, 0.316	1.598, 0.292	1.777, 0.217
		Median	3.69	3.36	3.66
		Q1, Q3	2.28, 5.31	2.47, 4.69	2.31, 5.16
		Min, Max	0.3, 8.4	1.2, 7.3	0.3, 8.4

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treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-0.44	-0.77	-0.59
		SD, SE	1.810, 0.298	0.981, 0.179	1.495, 0.183
		Median	-0.66	-0.56	-0.56
		Q1, Q3	-1.28, 0.25	-1.51, -0.09	-1.49, 0.09
		Min, Max	-4.6, 4.7	-3.2, 0.9	-4.6, 4.7
		GEE Estimates			
		LS Mean (SE)	-0.43 (0.236)	-0.76 (0.208)	
		95% CI	(-0.89, 0.03)	(-1.17, -0.35)	
		LS Mean Difference (SE)		-0.33 (0.327)	
		95% CI		(-0.97, 0.31)	
		p-value		0.3097	
		HedgesG (95% CI)		-.213 (-.696, 0.270)	

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treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.1.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	5.67	5.79	5.74
		SD, SE	1.447, 0.269	1.261, 0.205	1.336, 0.163
		Median	5.63	5.89	5.75
		Q1, Q3	4.59, 7.04	5.03, 6.66	4.75, 6.84
		Min, Max	3.1, 7.9	3.4, 8.3	3.1, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Baseline			
		n	29	38	67
		Mean	5.67	5.79	5.74
		SD, SE	1.447, 0.269	1.261, 0.205	1.336, 0.163
		Median	5.63	5.89	5.75
		Q1, Q3	4.59, 7.04	5.03, 6.66	4.75, 6.84
		Min, Max	3.1, 7.9	3.4, 8.3	3.1, 8.3
		Observed			
		n	29	38	67
		Mean	5.17	5.16	5.16
		SD, SE	1.984, 0.368	1.668, 0.271	1.797, 0.220
		Median	5.63	5.33	5.38
		Q1, Q3	3.69, 6.75	4.22, 6.25	3.97, 6.50
		Min, Max	0.2, 8.1	1.5, 8.1	0.2, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-0.50	-0.63	-0.58
		SD, SE	1.339, 0.249	1.358, 0.220	1.341, 0.164
		Median	-0.31	-0.23	-0.25
		Q1, Q3	-0.97, 0.22	-0.84, 0.13	-0.97, 0.16
		Min, Max	-3.8, 1.6	-5.5, 1.2	-5.5, 1.6
		GEE Estimates			
		LS Mean (SE)	-0.34 (0.399)	-0.60 (0.382)	
		95% CI	(-1.13, 0.44)	(-1.35, 0.15)	
		LS Mean Difference (SE)		-0.26 (0.325)	
		95% CI		(-0.89, 0.38)	
		p-value		0.4263	
		HedgesG (95% CI)		-.097 (-.580, 0.387)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Baseline			
		n	28	37	65
		Mean	5.61	5.79	5.71
		SD, SE	1.435, 0.271	1.278, 0.210	1.341, 0.166
		Median	5.59	5.94	5.72
		Q1, Q3	4.52, 6.99	5.03, 6.66	4.75, 6.75
		Min, Max	3.1, 7.9	3.4, 8.3	3.1, 8.3
		Observed			
		n	28	37	65
		Mean	5.66	5.10	5.34
		SD, SE	1.996, 0.377	1.849, 0.304	1.919, 0.238
		Median	6.08	5.25	5.53
		Q1, Q3	3.75, 7.17	4.03, 6.22	3.94, 6.88
		Min, Max	1.6, 9.0	1.4, 8.1	1.4, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Change from Baseline			
		n	28	37	65
		Mean	0.05	-0.69	-0.37
		SD, SE	1.519, 0.287	1.567, 0.258	1.579, 0.196
		Median	0.03	-0.43	-0.03
		Q1, Q3	-1.08, 0.89	-1.72, 0.38	-1.38, 0.66
		Min, Max	-2.9, 4.1	-5.0, 1.6	-5.0, 4.1
		GEE Estimates			
		LS Mean (SE)	0.14 (0.411)	-0.65 (0.390)	
		95% CI	(-0.66, 0.95)	(-1.41, 0.12)	
		LS Mean Difference (SE)		-0.79 (0.370)	
		95% CI		(-1.52, -0.06)	
		p-value		0.0328	
		HedgesG (95% CI)		-.467 (-.965, 0.030)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes		N_1	44	47	91
	Baseline	n	44	47	91
		Mean	5.14	5.40	5.27
		SD, SE	1.454, 0.219	1.334, 0.195	1.392, 0.146
		Median	5.00	5.59	5.31
		Q1, Q3	4.30, 6.42	4.38, 6.09	4.35, 6.38
		Min, Max	2.3, 7.6	2.6, 8.3	2.3, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	44	47	91
		Mean	5.14	5.40	5.27
		SD, SE	1.454, 0.219	1.334, 0.195	1.392, 0.146
		Median	5.00	5.59	5.31
		Q1, Q3	4.30, 6.42	4.38, 6.09	4.35, 6.38
		Min, Max	2.3, 7.6	2.6, 8.3	2.3, 8.3
		Observed			
		n	44	47	91
		Mean	4.51	4.70	4.61
		SD, SE	1.879, 0.283	1.703, 0.248	1.783, 0.187
		Median	4.75	4.94	4.75
		Q1, Q3	3.03, 5.75	3.44, 6.00	3.13, 6.00
		Min, Max	0.2, 7.7	1.5, 8.1	0.2, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	44	47	91
		Mean	-0.63	-0.70	-0.67
		SD, SE	1.374, 0.207	1.266, 0.185	1.313, 0.138
		Median	-0.39	-0.38	-0.38
		Q1, Q3	-1.57, 0.55	-0.91, 0.06	-1.44, 0.16
		Min, Max	-3.8, 1.5	-5.5, 1.2	-5.5, 1.5
		GEE Estimates			
		LS Mean (SE)	-0.75 (0.326)	-0.84 (0.290)	
		95% CI	(-1.38, -0.11)	(-1.41, -0.27)	
		LS Mean Difference (SE)		-0.09 (0.276)	
		95% CI		(-0.63, 0.45)	
		p-value		0.7348	
		HedgesG (95% CI)		-.055 (-.466, 0.357)	

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treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	43	46	89
		Mean	5.09	5.39	5.25
		SD, SE	1.429, 0.218	1.348, 0.199	1.388, 0.147
		Median	4.88	5.50	5.28
		Q1, Q3	4.25, 6.38	4.38, 6.09	4.35, 6.09
		Min, Max	2.3, 7.6	2.6, 8.3	2.3, 8.3
		Observed			
		n	43	46	89
		Mean	4.74	4.57	4.66
		SD, SE	2.006, 0.306	1.814, 0.267	1.900, 0.201
		Median	4.59	4.44	4.44
		Q1, Q3	3.44, 6.50	3.09, 5.94	3.28, 6.16
		Min, Max	0.3, 8.6	1.2, 8.1	0.3, 8.6

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	43	46	89
		Mean	-0.34	-0.82	-0.59
		SD, SE	1.596, 0.243	1.422, 0.210	1.519, 0.161
		Median	-0.13	-0.55	-0.47
		Q1, Q3	-1.25, 0.72	-1.59, 0.22	-1.38, 0.28
		Min, Max	-4.6, 4.1	-5.0, 1.6	-5.0, 4.1
		GEE Estimates			
		LS Mean (SE)	-0.49 (0.351)	-0.94 (0.296)	
		95% CI	(-1.18, 0.20)	(-1.52, -0.36)	
		LS Mean Difference (SE)		-0.45 (0.309)	
		95% CI		(-1.06, 0.15)	
		p-value		0.1444	
		HedgesG (95% CI)		-.311 (-.730, 0.107)	

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treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No		N_1	22	21	43
	Baseline	n	22	21	43
		Mean	4.48	4.69	4.58
		SD, SE	1.667, 0.355	1.842, 0.402	1.737, 0.265
		Median	4.48	4.16	4.25
		Q1, Q3	3.19, 5.56	3.44, 6.75	3.28, 6.19
		Min, Max	1.2, 7.9	1.8, 7.5	1.2, 7.9

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Baseline			
		n	22	21	43
		Mean	4.48	4.69	4.58
		SD, SE	1.667, 0.355	1.842, 0.402	1.737, 0.265
		Median	4.48	4.16	4.25
		Q1, Q3	3.19, 5.56	3.44, 6.75	3.28, 6.19
		Min, Max	1.2, 7.9	1.8, 7.5	1.2, 7.9
		Observed			
		n	22	21	43
		Mean	4.34	4.24	4.29
		SD, SE	1.972, 0.421	1.801, 0.393	1.869, 0.285
		Median	4.76	4.22	4.25
		Q1, Q3	2.66, 5.78	2.31, 5.84	2.38, 5.84
		Min, Max	1.0, 8.1	1.8, 7.0	1.0, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Change from Baseline			
		n	22	21	43
		Mean	-0.14	-0.45	-0.29
		SD, SE	1.067, 0.227	1.114, 0.243	1.089, 0.166
		Median	-0.27	-0.22	-0.25
		Q1, Q3	-0.72, 0.91	-1.44, 0.16	-0.97, 0.53
		Min, Max	-2.1, 1.6	-2.6, 1.8	-2.6, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.05 (0.214)	-0.40 (0.254)	
		95% CI	(-0.47, 0.37)	(-0.90, 0.10)	
		LS Mean Difference (SE)		-0.35 (0.301)	
		95% CI		(-0.94, 0.24)	
		p-value		0.2442	
		HedgesG (95% CI)		-.277 (-.878, 0.324)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Baseline			
		n	22	21	43
		Mean	4.48	4.69	4.58
		SD, SE	1.667, 0.355	1.842, 0.402	1.737, 0.265
		Median	4.48	4.16	4.25
		Q1, Q3	3.19, 5.56	3.44, 6.75	3.28, 6.19
		Min, Max	1.2, 7.9	1.8, 7.5	1.2, 7.9
		Observed			
		n	22	21	43
		Mean	4.47	4.17	4.32
		SD, SE	2.393, 0.510	2.020, 0.441	2.198, 0.335
		Median	4.61	4.11	4.22
		Q1, Q3	2.59, 5.91	2.31, 5.56	2.31, 5.63
		Min, Max	1.2, 9.0	1.6, 8.0	1.2, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Change from Baseline			
		n	22	21	43
		Mean	-0.01	-0.52	-0.26
		SD, SE	1.897, 0.404	1.098, 0.240	1.562, 0.238
		Median	-0.30	-0.44	-0.44
		Q1, Q3	-1.16, 0.69	-1.56, 0.16	-1.49, 0.25
		Min, Max	-2.8, 4.7	-2.4, 1.4	-2.8, 4.7
		GEE Estimates			
		LS Mean (SE)	0.08 (0.326)	-0.47 (0.240)	
		95% CI	(-0.56, 0.72)	(-0.94, 0.00)	
		LS Mean Difference (SE)		-0.55 (0.430)	
		95% CI		(-1.39, 0.29)	
		p-value		0.2016	
		HedgesG (95% CI)		-.315 (-.917, 0.286)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes		N_1	13	17	30
	Baseline	n	13	17	30
		Mean	4.81	5.79	5.36
		SD, SE	1.541, 0.427	1.521, 0.369	1.582, 0.289
		Median	5.13	5.59	5.28
		Q1, Q3	3.59, 5.79	4.91, 7.00	4.44, 6.47
		Min, Max	2.3, 7.1	3.4, 8.3	2.3, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	13	17	30
		Mean	4.81	5.79	5.36
		SD, SE	1.541, 0.427	1.521, 0.369	1.582, 0.289
		Median	5.13	5.59	5.28
		Q1, Q3	3.59, 5.79	4.91, 7.00	4.44, 6.47
		Min, Max	2.3, 7.1	3.4, 8.3	2.3, 8.3
		Observed			
		n	13	17	30
		Mean	4.59	4.93	4.78
		SD, SE	2.205, 0.611	1.894, 0.459	2.005, 0.366
		Median	4.00	4.59	4.36
		Q1, Q3	2.66, 6.94	3.13, 6.03	3.00, 6.94
		Min, Max	1.8, 7.6	2.4, 8.1	1.8, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	13	17	30
		Mean	-0.22	-0.86	-0.58
		SD, SE	1.496, 0.415	1.408, 0.342	1.458, 0.266
		Median	0.09	-0.38	-0.33
		Q1, Q3	-0.63, 0.84	-0.78, -0.16	-0.78, 0.19
		Min, Max	-3.3, 1.5	-5.5, 0.7	-5.5, 1.5
		GEE Estimates			
		LS Mean (SE)	-0.37 (0.387)	-1.05 (0.362)	
		95% CI	(-1.13, 0.39)	(-1.76, -0.34)	
		LS Mean Difference (SE)		-0.68 (0.484)	
		95% CI		(-1.63, 0.26)	
		p-value		0.1575	
		HedgesG (95% CI)		-.418 (-1.15, 0.312)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	13	16	29
		Mean	4.81	5.79	5.35
		SD, SE	1.541, 0.427	1.571, 0.393	1.608, 0.299
		Median	5.13	5.45	5.25
		Q1, Q3	3.59, 5.79	4.83, 7.28	4.44, 6.47
		Min, Max	2.3, 7.1	3.4, 8.3	2.3, 8.3
		Observed			
		n	13	16	29
		Mean	4.78	4.93	4.86
		SD, SE	1.997, 0.554	2.101, 0.525	2.020, 0.375
		Median	4.16	4.50	4.44
		Q1, Q3	3.19, 6.75	3.02, 6.92	3.09, 6.75
		Min, Max	2.0, 7.4	1.8, 8.1	1.8, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	13	16	29
		Mean	-0.03	-0.86	-0.49
		SD, SE	1.199, 0.333	1.457, 0.364	1.390, 0.258
		Median	0.09	-0.63	-0.25
		Q1, Q3	-0.53, 1.00	-1.41, 0.20	-1.09, 0.38
		Min, Max	-2.8, 1.6	-5.0, 1.0	-5.0, 1.6
		GEE Estimates			
		LS Mean (SE)	-0.18 (0.312)	-1.00 (0.363)	
		95% CI	(-0.79, 0.43)	(-1.71, -0.29)	
		LS Mean Difference (SE)		-0.82 (0.441)	
		95% CI		(-1.68, 0.05)	
		p-value		0.0636	
		HedgesG (95% CI)		-.578 (-1.33, 0.169)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No		N_1	53	51	104
	Baseline	n	53	51	104
		Mean	4.94	4.98	4.96
		SD, SE	1.562, 0.215	1.495, 0.209	1.522, 0.149
		Median	4.81	5.25	4.88
		Q1, Q3	3.97, 6.00	3.88, 6.09	3.92, 6.05
		Min, Max	1.2, 7.9	1.8, 7.5	1.2, 7.9

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Baseline			
		n	53	51	104
		Mean	4.94	4.98	4.96
		SD, SE	1.562, 0.215	1.495, 0.209	1.522, 0.149
		Median	4.81	5.25	4.88
		Q1, Q3	3.97, 6.00	3.88, 6.09	3.92, 6.05
		Min, Max	1.2, 7.9	1.8, 7.5	1.2, 7.9
		Observed			
		n	53	51	104
		Mean	4.42	4.43	4.42
		SD, SE	1.836, 0.252	1.678, 0.235	1.752, 0.172
		Median	4.78	4.50	4.72
		Q1, Q3	3.09, 5.66	3.19, 5.94	3.13, 5.77
		Min, Max	0.2, 8.1	1.5, 7.0	0.2, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Change from Baseline			
		n	53	51	104
		Mean	-0.53	-0.55	-0.54
		SD, SE	1.246, 0.171	1.154, 0.162	1.196, 0.117
		Median	-0.38	-0.22	-0.30
		Q1, Q3	-1.41, 0.25	-1.25, 0.16	-1.41, 0.21
		Min, Max	-3.8, 1.6	-4.4, 1.8	-4.4, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.38 (0.200)	-0.40 (0.199)	
		95% CI	(-0.78, 0.01)	(-0.79, -0.01)	
		LS Mean Difference (SE)		-0.01 (0.218)	
		95% CI		(-0.44, 0.41)	
		p-value		0.9561	
		HedgesG (95% CI)		-.017 (-.402, 0.367)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Baseline			
		n	52	51	103
		Mean	4.90	4.98	4.94
		SD, SE	1.540, 0.213	1.495, 0.209	1.511, 0.149
		Median	4.80	5.25	4.88
		Q1, Q3	3.86, 5.84	3.88, 6.09	3.88, 6.00
		Min, Max	1.2, 7.9	1.8, 7.5	1.2, 7.9
		Observed			
		n	52	51	103
		Mean	4.62	4.30	4.46
		SD, SE	2.180, 0.302	1.794, 0.251	1.995, 0.197
		Median	4.65	4.25	4.43
		Q1, Q3	3.17, 6.22	2.59, 5.56	2.94, 5.88
		Min, Max	0.3, 9.0	1.2, 8.0	0.3, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Change from Baseline			
		n	52	51	103
		Mean	-0.28	-0.68	-0.48
		SD, SE	1.805, 0.250	1.297, 0.182	1.580, 0.156
		Median	-0.55	-0.44	-0.47
		Q1, Q3	-1.33, 0.70	-1.59, 0.19	-1.49, 0.25
		Min, Max	-4.6, 4.7	-4.6, 1.6	-4.6, 4.7
		GEE Estimates			
		LS Mean (SE)	-0.16 (0.240)	-0.53 (0.204)	
		95% CI	(-0.63, 0.31)	(-0.93, -0.13)	
		LS Mean Difference (SE)		-0.37 (0.291)	
		95% CI		(-0.94, 0.20)	
		p-value		0.2030	
		HedgesG (95% CI)		-.253 (-.641, 0.134)	

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treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes		N_1	38	32	70
	Baseline	n	38	32	70
		Mean	5.20	5.01	5.11
		SD, SE	1.408, 0.228	1.438, 0.254	1.414, 0.169
		Median	5.00	5.19	5.13
		Q1, Q3	4.41, 6.47	3.92, 5.96	4.16, 6.38
		Min, Max	2.6, 7.6	1.8, 7.6	1.8, 7.6

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Baseline			
		n	38	32	70
		Mean	5.20	5.01	5.11
		SD, SE	1.408, 0.228	1.438, 0.254	1.414, 0.169
		Median	5.00	5.19	5.13
		Q1, Q3	4.41, 6.47	3.92, 5.96	4.16, 6.38
		Min, Max	2.6, 7.6	1.8, 7.6	1.8, 7.6
		Observed			
		n	38	32	70
		Mean	4.76	4.19	4.50
		SD, SE	1.622, 0.263	1.765, 0.312	1.700, 0.203
		Median	4.81	3.97	4.59
		Q1, Q3	3.44, 5.78	2.89, 5.56	3.19, 5.75
		Min, Max	1.3, 7.7	1.5, 7.4	1.3, 7.7

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.1.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Change from Baseline			
		n	38	32	70
		Mean	-0.43	-0.82	-0.61
		SD, SE	1.249, 0.203	1.155, 0.204	1.214, 0.145
		Median	-0.44	-0.44	-0.44
		Q1, Q3	-1.47, 0.75	-1.52, 0.00	-1.47, 0.16
		Min, Max	-2.8, 1.4	-4.4, 0.9	-4.4, 1.4
		GEE Estimates			
		LS Mean (SE)	-0.12 (0.290)	-0.54 (0.244)	
		95% CI	(-0.69, 0.45)	(-1.02, -0.06)	
		LS Mean Difference (SE)		-0.42 (0.280)	
		95% CI		(-0.97, 0.13)	
		p-value		0.1303	
		HedgesG (95% CI)		-.311 (-.785, 0.162)	

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Table 2.2.3.1.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Baseline			
		n	37	31	68
		Mean	5.14	4.99	5.07
		SD, SE	1.379, 0.227	1.455, 0.261	1.406, 0.170
		Median	4.88	5.13	5.00
		Q1, Q3	4.41, 6.38	3.88, 5.97	4.13, 6.19
		Min, Max	2.6, 7.6	1.8, 7.6	1.8, 7.6
		Observed			
		n	37	31	68
		Mean	4.91	4.20	4.59
		SD, SE	1.848, 0.304	1.889, 0.339	1.887, 0.229
		Median	5.00	4.11	4.33
		Q1, Q3	3.50, 6.28	2.69, 5.56	3.31, 6.00
		Min, Max	1.2, 8.6	1.4, 8.0	1.2, 8.6

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Change from Baseline			
		n	37	31	68
		Mean	-0.23	-0.79	-0.48
		SD, SE	1.451, 0.239	1.299, 0.233	1.402, 0.170
		Median	0.00	-0.56	-0.35
		Q1, Q3	-1.25, 0.47	-1.72, 0.19	-1.42, 0.25
		Min, Max	-3.1, 4.3	-4.6, 1.2	-4.6, 4.3
		GEE Estimates			
		LS Mean (SE)	0.04 (0.287)	-0.50 (0.251)	
		95% CI	(-0.52, 0.61)	(-0.99, -0.00)	
		LS Mean Difference (SE)		-0.54 (0.323)	
		95% CI		(-1.17, 0.09)	
		p-value		0.0953	
		HedgesG (95% CI)		-.393 (-.875, 0.088)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.1.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No		N_1	28	36	64
	Baseline	n	28	36	64
		Mean	4.54	5.34	4.99
		SD, SE	1.670, 0.316	1.614, 0.269	1.674, 0.209
		Median	4.66	5.52	5.11
		Q1, Q3	3.25, 5.52	4.16, 6.50	3.83, 6.14
		Min, Max	1.2, 7.9	2.0, 8.3	1.2, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Baseline			
		n	28	36	64
		Mean	4.54	5.34	4.99
		SD, SE	1.670, 0.316	1.614, 0.269	1.674, 0.209
		Median	4.66	5.52	5.11
		Q1, Q3	3.25, 5.52	4.16, 6.50	3.83, 6.14
		Min, Max	1.2, 7.9	2.0, 8.3	1.2, 8.3
		Observed			
		n	28	36	64
		Mean	4.03	4.88	4.51
		SD, SE	2.176, 0.411	1.663, 0.277	1.936, 0.242
		Median	3.78	5.02	4.72
		Q1, Q3	2.23, 5.80	4.17, 6.00	2.86, 6.00
		Min, Max	0.2, 8.1	1.7, 8.1	0.2, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.3.1.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Change from Baseline			
		n	28	36	64
		Mean	-0.51	-0.46	-0.48
		SD, SE	1.372, 0.259	1.265, 0.211	1.302, 0.163
		Median	-0.30	-0.23	-0.27
		Q1, Q3	-1.17, 0.19	-0.88, 0.31	-0.94, 0.23
		Min, Max	-3.8, 1.6	-5.5, 1.8	-5.5, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.66 (0.297)	-0.49 (0.314)	
		95% CI	(-1.25, -0.08)	(-1.11, 0.12)	
		LS Mean Difference (SE)		0.17 (0.349)	
		95% CI		(-0.51, 0.85)	
		p-value		0.6276	
		HedgesG (95% CI)		0.042 (-.452, 0.536)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Baseline			
		n	28	36	64
		Mean	4.54	5.34	4.99
		SD, SE	1.670, 0.316	1.614, 0.269	1.674, 0.209
		Median	4.66	5.52	5.11
		Q1, Q3	3.25, 5.52	4.16, 6.50	3.83, 6.14
		Min, Max	1.2, 7.9	2.0, 8.3	1.2, 8.3
		Observed			
		n	28	36	64
		Mean	4.31	4.66	4.51
		SD, SE	2.448, 0.463	1.863, 0.310	2.128, 0.266
		Median	3.95	4.50	4.43
		Q1, Q3	2.16, 6.69	3.02, 5.91	2.64, 6.02
		Min, Max	0.3, 9.0	1.2, 8.1	0.3, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-0.23	-0.67	-0.48
		SD, SE	2.003, 0.378	1.369, 0.228	1.676, 0.210
		Median	-0.58	-0.48	-0.53
		Q1, Q3	-1.09, 0.81	-1.50, 0.20	-1.43, 0.30
		Min, Max	-4.6, 4.7	-5.0, 1.6	-5.0, 4.7
		GEE Estimates			
		LS Mean (SE)	-0.38 (0.320)	-0.71 (0.298)	
		95% CI	(-1.01, 0.25)	(-1.30, -0.13)	
		LS Mean Difference (SE)		-0.33 (0.418)	
		95% CI		(-1.15, 0.49)	
		p-value		0.4258	
		HedgesG (95% CI)		-.259 (-.754, 0.237)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High		N_1	29	37	66
	Baseline	n	29	37	66
		Mean	5.66	5.29	5.45
		SD, SE	1.298, 0.241	1.480, 0.243	1.404, 0.173
		Median	5.47	5.44	5.45
		Q1, Q3	4.75, 6.66	4.16, 6.38	4.41, 6.63
		Min, Max	2.6, 7.6	2.0, 8.3	2.0, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Baseline			
		n	29	37	66
		Mean	5.66	5.29	5.45
		SD, SE	1.298, 0.241	1.480, 0.243	1.404, 0.173
		Median	5.47	5.44	5.45
		Q1, Q3	4.75, 6.66	4.16, 6.38	4.41, 6.63
		Min, Max	2.6, 7.6	2.0, 8.3	2.0, 8.3
		Observed			
		n	29	37	66
		Mean	5.20	4.62	4.88
		SD, SE	1.538, 0.286	1.820, 0.299	1.714, 0.211
		Median	5.13	4.59	4.93
		Q1, Q3	4.09, 6.28	3.91, 6.00	3.94, 6.03
		Min, Max	2.2, 7.7	1.5, 8.1	1.5, 8.1

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Change from Baseline			
		n	29	37	66
		Mean	-0.46	-0.67	-0.58
		SD, SE	1.220, 0.227	1.376, 0.226	1.304, 0.161
		Median	-0.31	-0.22	-0.23
		Q1, Q3	-1.41, 0.66	-0.78, 0.09	-1.28, 0.16
		Min, Max	-2.8, 1.5	-5.5, 0.9	-5.5, 1.5
		GEE Estimates			
		LS Mean (SE)	-0.30 (0.372)	-0.61 (0.356)	
		95% CI	(-1.03, 0.43)	(-1.31, 0.09)	
		LS Mean Difference (SE)		-0.31 (0.321)	
		95% CI		(-0.94, 0.32)	
		p-value		0.3369	
		HedgesG (95% CI)		-.158 (-.644, 0.329)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Baseline			
		n	28	36	64
		Mean	5.59	5.28	5.42
		SD, SE	1.278, 0.242	1.499, 0.250	1.404, 0.176
		Median	5.39	5.36	5.38
		Q1, Q3	4.73, 6.61	4.11, 6.50	4.41, 6.59
		Min, Max	2.6, 7.6	2.0, 8.3	2.0, 8.3
		Observed			
		n	28	36	64
		Mean	5.41	4.54	4.92
		SD, SE	1.586, 0.300	1.948, 0.325	1.836, 0.230
		Median	5.42	4.35	5.02
		Q1, Q3	3.88, 6.63	3.14, 5.84	3.58, 6.48
		Min, Max	2.8, 8.6	1.4, 8.0	1.4, 8.6

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-0.19	-0.74	-0.50
		SD, SE	1.232, 0.233	1.475, 0.246	1.391, 0.174
		Median	0.08	-0.43	-0.08
		Q1, Q3	-1.08, 0.73	-1.41, 0.22	-1.16, 0.33
		Min, Max	-3.1, 2.1	-5.0, 1.2	-5.0, 2.1
		GEE Estimates			
		LS Mean (SE)	-0.09 (0.335)	-0.67 (0.358)	
		95% CI	(-0.75, 0.57)	(-1.37, 0.04)	
		LS Mean Difference (SE)		-0.58 (0.333)	
		95% CI		(-1.23, 0.08)	
		p-value		0.0842	
		HedgesG (95% CI)		-.389 (-.888, 0.109)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low		N_1	36	30	66
	Baseline	n	36	30	66
		Mean	4.24	5.10	4.63
		SD, SE	1.388, 0.231	1.615, 0.295	1.544, 0.190
		Median	4.22	5.28	4.55
		Q1, Q3	3.17, 5.41	3.96, 6.34	3.38, 5.63
		Min, Max	1.2, 7.2	1.8, 7.9	1.2, 7.9

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Baseline			
		n	36	30	66
		Mean	4.24	5.10	4.63
		SD, SE	1.388, 0.231	1.615, 0.295	1.544, 0.190
		Median	4.22	5.28	4.55
		Q1, Q3	3.17, 5.41	3.96, 6.34	3.38, 5.63
		Min, Max	1.2, 7.2	1.8, 7.9	1.2, 7.9
		Observed			
		n	36	30	66
		Mean	3.75	4.52	4.10
		SD, SE	1.855, 0.309	1.657, 0.302	1.797, 0.221
		Median	3.30	4.53	4.16
		Q1, Q3	2.36, 5.27	3.19, 5.84	2.66, 5.53
		Min, Max	0.2, 7.3	1.7, 7.6	0.2, 7.6

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Change from Baseline			
		n	36	30	66
		Mean	-0.49	-0.57	-0.53
		SD, SE	1.378, 0.230	1.037, 0.189	1.226, 0.151
		Median	-0.34	-0.64	-0.39
		Q1, Q3	-1.50, 0.59	-1.44, 0.13	-1.44, 0.38
		Min, Max	-3.8, 1.6	-2.3, 1.8	-3.8, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.45 (0.190)	-0.26 (0.227)	
		95% CI	(-0.83, -0.08)	(-0.71, 0.18)	
		LS Mean Difference (SE)		0.19 (0.317)	
		95% CI		(-0.43, 0.81)	
		p-value		0.5470	
		HedgesG (95% CI)		-.061 (-.545, 0.424)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Baseline			
		n	36	30	66
		Mean	4.24	5.10	4.63
		SD, SE	1.388, 0.231	1.615, 0.295	1.544, 0.190
		Median	4.22	5.28	4.55
		Q1, Q3	3.17, 5.41	3.96, 6.34	3.38, 5.63
		Min, Max	1.2, 7.2	1.8, 7.9	1.2, 7.9
		Observed			
		n	36	30	66
		Mean	3.94	4.40	4.15
		SD, SE	2.203, 0.367	1.815, 0.331	2.033, 0.250
		Median	3.61	4.33	3.95
		Q1, Q3	2.13, 5.77	2.69, 5.88	2.47, 5.88
		Min, Max	0.3, 8.4	1.2, 8.1	0.3, 8.4

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.3.1.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Pain Inventory (BPI) Pain Severity score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Change from Baseline			
		n	36	30	66
		Mean	-0.30	-0.70	-0.48
		SD, SE	2.008, 0.335	1.175, 0.214	1.681, 0.207
		Median	-0.73	-0.91	-0.78
		Q1, Q3	-1.36, 0.44	-1.59, 0.19	-1.56, 0.19
		Min, Max	-4.6, 4.7	-3.2, 1.6	-4.6, 4.7
		GEE Estimates			
		LS Mean (SE)	-0.26 (0.236)	-0.39 (0.224)	
		95% CI	(-0.72, 0.20)	(-0.83, 0.05)	
		LS Mean Difference (SE)		-0.13 (0.384)	
		95% CI		(-0.89, 0.62)	
		p-value		0.7295	
		HedgesG (95% CI)		-.232 (-.718, 0.254)	

The GEE Estimates are from the GEE model which includes the change from baseline for the BPI Pain Severity as the dependent variable, region, visit, treatment and visit by
treatment as fixed factors, and baseline of BPI Pain Severity as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_sev_SUB.sas

Table 2.2.2.1.24.1
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6		N_1	27	17	44
	Baseline	n	27	17	44
		Mean	5.18	5.01	5.12
		SD, SE	0.916, 0.176	0.936, 0.227	0.917, 0.138
		Median	5.50	5.13	5.25
		Q1, Q3	4.63, 5.88	4.13, 5.75	4.56, 5.88
		Min, Max	3.1, 6.1	3.0, 6.1	3.0, 6.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.1
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Baseline			
		n	27	17	44
		Mean	5.18	5.01	5.12
		SD, SE	0.916, 0.176	0.936, 0.227	0.917, 0.138
		Median	5.50	5.13	5.25
		Q1, Q3	4.63, 5.88	4.13, 5.75	4.56, 5.88
		Min, Max	3.1, 6.1	3.0, 6.1	3.0, 6.1
		Observed			
		n	27	17	44
		Mean	4.98	4.40	4.76
		SD, SE	1.987, 0.382	1.165, 0.283	1.725, 0.260
		Median	4.75	4.88	4.81
		Q1, Q3	3.63, 6.75	3.63, 5.43	3.63, 6.00
		Min, Max	0.6, 8.3	2.1, 6.0	0.6, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.1
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Change from Baseline			
		n	27	17	44
		Mean	-0.20	-0.61	-0.36
		SD, SE	1.638, 0.315	1.203, 0.292	1.484, 0.224
		Median	-0.13	-0.40	-0.19
		Q1, Q3	-0.96, 0.88	-1.20, 0.13	-1.10, 0.56
		Min, Max	-3.9, 2.4	-3.0, 1.4	-3.9, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.09 (0.342)	-0.59 (0.347)	
		95% CI	(-0.76, 0.58)	(-1.27, 0.09)	
		LS Mean Difference (SE)		-0.50 (0.423)	
		95% CI		(0.33, -1.33)	
		p-value		0.2377	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.1
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Baseline			
		n	27	17	44
		Mean	5.18	5.01	5.12
		SD, SE	0.916, 0.176	0.936, 0.227	0.917, 0.138
		Median	5.50	5.13	5.25
		Q1, Q3	4.63, 5.88	4.13, 5.75	4.56, 5.88
		Min, Max	3.1, 6.1	3.0, 6.1	3.0, 6.1
		Observed			
		n	27	17	44
		Mean	4.89	4.18	4.62
		SD, SE	1.845, 0.355	1.281, 0.311	1.671, 0.252
		Median	4.75	4.13	4.75
		Q1, Q3	3.63, 5.88	3.13, 5.38	3.38, 5.47
		Min, Max	0.4, 8.5	2.5, 6.8	0.4, 8.5

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.1
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Change from Baseline			
		n	27	17	44
		Mean	-0.29	-0.83	-0.50
		SD, SE	2.008, 0.387	0.989, 0.240	1.695, 0.256
		Median	-0.75	-0.75	-0.75
		Q1, Q3	-1.38, 0.25	-1.50, -0.26	-1.38, 0.06
		Min, Max	-4.9, 4.3	-2.6, 1.0	-4.9, 4.3
		GEE Estimates			
		LS Mean (SE)	-0.18 (0.311)	-0.81 (0.318)	
		95% CI	(-0.79, 0.42)	(-1.44, -0.19)	
		LS Mean Difference (SE)		-0.63 (0.435)	
		95% CI		(0.22, -1.48)	
		p-value		0.1485	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
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Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.1
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6		N_1	39	51	90
	Baseline	n	39	51	90
		Mean	7.49	7.40	7.44
		SD, SE	0.844, 0.135	0.742, 0.104	0.785, 0.083
		Median	7.38	7.38	7.38
		Q1, Q3	6.88, 8.25	6.75, 8.00	6.75, 8.00
		Min, Max	6.1, 9.1	6.3, 8.9	6.1, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.1
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Baseline			
		n	39	51	90
		Mean	7.49	7.40	7.44
		SD, SE	0.844, 0.135	0.742, 0.104	0.785, 0.083
		Median	7.38	7.38	7.38
		Q1, Q3	6.88, 8.25	6.75, 8.00	6.75, 8.00
		Min, Max	6.1, 9.1	6.3, 8.9	6.1, 9.1
		Observed			
		n	39	51	90
		Mean	6.75	6.52	6.62
		SD, SE	1.590, 0.255	1.607, 0.225	1.595, 0.168
		Median	6.88	6.88	6.88
		Q1, Q3	5.60, 8.13	5.88, 7.50	5.88, 7.75
		Min, Max	2.9, 9.9	1.9, 9.6	1.9, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.1.24.1
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Change from Baseline			
		n	39	51	90
		Mean	-0.74	-0.89	-0.82
		SD, SE	1.486, 0.238	1.543, 0.216	1.512, 0.159
		Median	-0.38	-0.50	-0.44
		Q1, Q3	-1.75, 0.38	-1.29, 0.00	-1.50, 0.00
		Min, Max	-4.0, 2.1	-6.1, 1.3	-6.1, 2.1
		GEE Estimates			
		LS Mean (SE)	-0.51 (0.298)	-0.68 (0.253)	
		95% CI	(-1.10, 0.07)	(-1.18, -0.19)	
		LS Mean Difference (SE)		-0.17 (0.316)	
		95% CI		(0.45, -0.79)	
		p-value		0.5916	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.1
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Baseline			
		n	38	50	88
		Mean	7.45	7.41	7.43
		SD, SE	0.829, 0.135	0.750, 0.106	0.781, 0.083
		Median	7.31	7.38	7.38
		Q1, Q3	6.88, 8.00	6.75, 8.00	6.75, 8.00
		Min, Max	6.1, 9.1	6.3, 8.9	6.1, 9.1
		Observed			
		n	38	50	88
		Mean	6.94	6.38	6.62
		SD, SE	1.685, 0.273	1.777, 0.251	1.750, 0.187
		Median	6.94	6.75	6.84
		Q1, Q3	6.25, 8.50	5.13, 7.63	5.72, 7.94
		Min, Max	3.1, 9.9	2.1, 9.3	2.1, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.1
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Change from Baseline			
		n	38	50	88
		Mean	-0.52	-1.03	-0.81
		SD, SE	1.580, 0.256	1.722, 0.244	1.672, 0.178
		Median	-0.43	-0.85	-0.56
		Q1, Q3	-1.13, 0.54	-2.13, 0.25	-1.75, 0.44
		Min, Max	-3.8, 2.5	-5.9, 1.6	-5.9, 2.5
		GEE Estimates			
		LS Mean (SE)	-0.36 (0.312)	-0.81 (0.281)	
		95% CI	(-0.97, 0.25)	(-1.36, -0.26)	
		LS Mean Difference (SE)		-0.45 (0.344)	
		95% CI		(0.23, -1.12)	
		p-value		0.1944	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.2
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6		N_1	49	48	97
	Baseline	n	49	48	97
		Mean	5.98	6.32	6.15
		SD, SE	1.158, 0.165	1.211, 0.175	1.190, 0.121
		Median	6.13	6.44	6.25
		Q1, Q3	5.25, 6.88	5.69, 7.13	5.63, 7.13
		Min, Max	3.1, 7.9	3.0, 8.3	3.0, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.2
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Baseline			
		n	49	48	97
		Mean	5.98	6.32	6.15
		SD, SE	1.158, 0.165	1.211, 0.175	1.190, 0.121
		Median	6.13	6.44	6.25
		Q1, Q3	5.25, 6.88	5.69, 7.13	5.63, 7.13
		Min, Max	3.1, 7.9	3.0, 8.3	3.0, 8.3
		Observed			
		n	49	48	97
		Mean	5.52	5.47	5.49
		SD, SE	1.854, 0.265	1.643, 0.237	1.744, 0.177
		Median	6.00	5.63	5.63
		Q1, Q3	4.00, 7.00	4.25, 6.81	4.25, 6.88
		Min, Max	0.6, 8.4	1.9, 8.1	0.6, 8.4

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.2
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Change from Baseline			
		n	49	48	97
		Mean	-0.46	-0.85	-0.65
		SD, SE	1.595, 0.228	1.492, 0.215	1.549, 0.157
		Median	-0.25	-0.50	-0.38
		Q1, Q3	-1.75, 0.50	-1.16, 0.00	-1.25, 0.25
		Min, Max	-4.0, 2.4	-6.1, 1.4	-6.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.33 (0.233)	-0.61 (0.225)	
		95% CI	(-0.78, 0.13)	(-1.05, -0.17)	
		LS Mean Difference (SE)		-0.28 (0.291)	
		95% CI		(0.29, -0.85)	
		p-value		0.3318	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.2.1.24.2
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Baseline			
		n	49	48	97
		Mean	5.98	6.32	6.15
		SD, SE	1.158, 0.165	1.211, 0.175	1.190, 0.121
		Median	6.13	6.44	6.25
		Q1, Q3	5.25, 6.88	5.69, 7.13	5.63, 7.13
		Min, Max	3.1, 7.9	3.0, 8.3	3.0, 8.3
		Observed			
		n	49	48	97
		Mean	5.52	5.32	5.42
		SD, SE	1.846, 0.264	1.808, 0.261	1.820, 0.185
		Median	5.88	5.38	5.38
		Q1, Q3	4.50, 6.88	3.56, 6.81	4.13, 6.88
		Min, Max	0.4, 9.0	2.1, 8.8	0.4, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.1.24.2
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Change from Baseline			
		n	49	48	97
		Mean	-0.46	-0.99	-0.72
		SD, SE	1.862, 0.266	1.573, 0.227	1.737, 0.176
		Median	-0.50	-0.81	-0.63
		Q1, Q3	-1.38, 0.25	-1.63, 0.13	-1.50, 0.25
		Min, Max	-4.9, 4.3	-5.9, 1.6	-5.9, 4.3
		GEE Estimates			
		LS Mean (SE)	-0.33 (0.252)	-0.75 (0.247)	
		95% CI	(-0.82, 0.17)	(-1.24, -0.27)	
		LS Mean Difference (SE)		-0.43 (0.321)	
		95% CI		(0.20, -1.05)	
		p-value		0.1847	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.1.24.2
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6		N_1	17	20	37
	Baseline	n	17	20	37
		Mean	8.17	7.98	8.07
		SD, SE	0.748, 0.181	0.591, 0.132	0.664, 0.109
		Median	8.25	8.00	8.13
		Q1, Q3	7.83, 8.75	7.50, 8.38	7.63, 8.63
		Min, Max	6.1, 9.1	6.5, 8.9	6.1, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.2.1.24.2
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Baseline			
		n	17	20	37
		Mean	8.17	7.98	8.07
		SD, SE	0.748, 0.181	0.591, 0.132	0.664, 0.109
		Median	8.25	8.00	8.13
		Q1, Q3	7.83, 8.75	7.50, 8.38	7.63, 8.63
		Min, Max	6.1, 9.1	6.5, 8.9	6.1, 9.1
		Observed			
		n	17	20	37
		Mean	7.48	7.23	7.35
		SD, SE	1.478, 0.358	1.396, 0.312	1.419, 0.233
		Median	7.88	7.50	7.57
		Q1, Q3	6.43, 8.63	6.81, 8.00	6.75, 8.25
		Min, Max	4.8, 9.9	2.9, 9.6	2.9, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.2.1.24.2
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Change from Baseline			
		n	17	20	37
		Mean	-0.69	-0.75	-0.72
		SD, SE	1.493, 0.362	1.420, 0.318	1.434, 0.236
		Median	-0.38	-0.31	-0.38
		Q1, Q3	-1.25, 0.04	-1.38, -0.06	-1.29, 0.00
		Min, Max	-4.0, 1.5	-5.1, 1.3	-5.1, 1.5
		GEE Estimates			
		LS Mean (SE)	-0.59 (0.408)	-0.74 (0.133)	
		95% CI	(-1.39, 0.21)	(-1.00, -0.48)	
		LS Mean Difference (SE)		-0.15 (0.477)	
		95% CI		(0.79, -1.09)	
		p-value		0.7536	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
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Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.2
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Baseline			
		n	16	19	35
		Mean	8.13	8.01	8.07
		SD, SE	0.756, 0.189	0.589, 0.135	0.663, 0.112
		Median	8.25	8.00	8.13
		Q1, Q3	7.73, 8.69	7.50, 8.38	7.63, 8.63
		Min, Max	6.1, 9.1	6.5, 8.9	6.1, 9.1
		Observed			
		n	16	19	35
		Mean	7.82	7.08	7.42
		SD, SE	1.463, 0.366	1.614, 0.370	1.570, 0.265
		Median	8.44	7.63	7.63
		Q1, Q3	6.88, 8.75	6.25, 8.13	6.25, 8.63
		Min, Max	4.6, 9.9	3.4, 9.3	3.4, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.2
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Change from Baseline			
		n	16	19	35
		Mean	-0.31	-0.94	-0.65
		SD, SE	1.444, 0.361	1.585, 0.364	1.533, 0.259
		Median	-0.06	-0.75	-0.50
		Q1, Q3	-0.81, 0.58	-2.13, 0.38	-1.75, 0.54
		Min, Max	-3.3, 2.4	-4.6, 1.3	-4.6, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.40 (0.430)	-0.91 (0.155)	
		95% CI	(-1.24, 0.45)	(-1.22, -0.61)	
		LS Mean Difference (SE)		-0.52 (0.506)	
		95% CI		(0.47, -1.51)	
		p-value		0.3070	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.3
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU		N_1	58	58	116
	Baseline	n	58	58	116
		Mean	6.63	6.90	6.76
		SD, SE	1.435, 0.188	1.152, 0.151	1.302, 0.121
		Median	6.63	7.13	6.85
		Q1, Q3	5.88, 7.63	6.25, 7.88	6.00, 7.79
		Min, Max	3.4, 9.1	3.9, 8.8	3.4, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.3
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Baseline			
		n	58	58	116
		Mean	6.63	6.90	6.76
		SD, SE	1.435, 0.188	1.152, 0.151	1.302, 0.121
		Median	6.63	7.13	6.85
		Q1, Q3	5.88, 7.63	6.25, 7.88	6.00, 7.79
		Min, Max	3.4, 9.1	3.9, 8.8	3.4, 9.1
		Observed			
		n	58	58	116
		Mean	6.08	6.00	6.04
		SD, SE	1.961, 0.258	1.814, 0.238	1.881, 0.175
		Median	6.46	6.38	6.38
		Q1, Q3	4.75, 7.25	5.00, 7.38	4.75, 7.38
		Min, Max	0.6, 9.9	1.9, 9.6	0.6, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.3
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Change from Baseline			
		n	58	58	116
		Mean	-0.55	-0.89	-0.72
		SD, SE	1.560, 0.205	1.482, 0.195	1.525, 0.142
		Median	-0.31	-0.50	-0.39
		Q1, Q3	-1.75, 0.50	-1.25, 0.00	-1.38, 0.08
		Min, Max	-4.0, 2.4	-6.1, 1.3	-6.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.58 (0.201)	-0.86 (0.190)	
		95% CI	(-0.97, -0.18)	(-1.24, -0.49)	
		LS Mean Difference (SE)		-0.29 (0.275)	
		95% CI		(0.25, -0.83)	
		p-value		0.2947	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.3
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Baseline			
		n	57	57	114
		Mean	6.59	6.89	6.74
		SD, SE	1.419, 0.188	1.160, 0.154	1.299, 0.122
		Median	6.50	7.13	6.79
		Q1, Q3	5.88, 7.63	6.25, 7.88	6.00, 7.75
		Min, Max	3.4, 9.1	3.9, 8.8	3.4, 9.1
		Observed			
		n	57	57	114
		Mean	6.23	5.83	6.03
		SD, SE	1.945, 0.258	1.856, 0.246	1.903, 0.178
		Median	6.25	6.00	6.19
		Q1, Q3	4.75, 7.63	4.50, 7.38	4.63, 7.63
		Min, Max	0.4, 9.9	2.1, 9.3	0.4, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.3
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Change from Baseline			
		n	57	57	114
		Mean	-0.36	-1.06	-0.71
		SD, SE	1.796, 0.238	1.582, 0.209	1.721, 0.161
		Median	-0.37	-0.88	-0.63
		Q1, Q3	-1.21, 0.54	-1.75, 0.13	-1.63, 0.25
		Min, Max	-4.9, 4.3	-5.9, 1.6	-5.9, 4.3
		GEE Estimates			
		LS Mean (SE)	-0.43 (0.228)	-1.02 (0.202)	
		95% CI	(-0.88, 0.01)	(-1.42, -0.63)	
		LS Mean Difference (SE)		-0.59 (0.302)	
		95% CI		(0.00, -1.18)	
		p-value		0.0509	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.3
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia		N_1	8	10	18
	Baseline	n	8	10	18
		Mean	5.92	6.27	6.12
		SD, SE	1.346, 0.476	1.993, 0.630	1.697, 0.400
		Median	5.94	6.75	6.38
		Q1, Q3	5.50, 7.06	4.13, 7.50	5.25, 7.25
		Min, Max	3.1, 7.3	3.0, 8.9	3.0, 8.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.3
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Baseline			
		n	8	10	18
		Mean	5.92	6.27	6.12
		SD, SE	1.346, 0.476	1.993, 0.630	1.697, 0.400
		Median	5.94	6.75	6.38
		Q1, Q3	5.50, 7.06	4.13, 7.50	5.25, 7.25
		Min, Max	3.1, 7.3	3.0, 8.9	3.0, 8.9
		Observed			
		n	8	10	18
		Mean	5.63	5.89	5.77
		SD, SE	1.988, 0.703	1.499, 0.474	1.684, 0.397
		Median	6.19	6.44	6.25
		Q1, Q3	4.00, 7.19	4.25, 7.00	4.25, 7.00
		Min, Max	2.4, 7.9	3.6, 7.6	2.4, 7.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.3
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Change from Baseline			
		n	8	10	18
		Mean	-0.30	-0.38	-0.34
		SD, SE	1.654, 0.585	1.320, 0.418	1.432, 0.338
		Median	-0.13	-0.03	-0.03
		Q1, Q3	-1.56, 0.63	-0.75, 0.38	-0.75, 0.50
		Min, Max	-2.6, 2.4	-3.1, 1.4	-3.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.16 (0.434)	-0.21 (0.312)	
		95% CI	(-1.02, 0.69)	(-0.83, 0.40)	
		LS Mean Difference (SE)		-0.05 (0.545)	
		95% CI		(1.02, -1.12)	
		p-value		0.9275	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.3
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Baseline			
		n	8	10	18
		Mean	5.92	6.27	6.12
		SD, SE	1.346, 0.476	1.993, 0.630	1.697, 0.400
		Median	5.94	6.75	6.38
		Q1, Q3	5.50, 7.06	4.13, 7.50	5.25, 7.25
		Min, Max	3.1, 7.3	3.0, 8.9	3.0, 8.9
		Observed			
		n	8	10	18
		Mean	5.06	5.78	5.46
		SD, SE	2.330, 0.824	2.341, 0.740	2.295, 0.541
		Median	4.88	6.06	5.44
		Q1, Q3	3.06, 7.00	3.38, 7.50	3.38, 7.38
		Min, Max	2.0, 8.6	2.5, 8.8	2.0, 8.8

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.3
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Change from Baseline			
		n	8	10	18
		Mean	-0.86	-0.50	-0.66
		SD, SE	1.495, 0.528	1.442, 0.456	1.434, 0.338
		Median	-0.75	-0.44	-0.50
		Q1, Q3	-1.88, 0.00	-1.00, 0.50	-1.13, 0.25
		Min, Max	-3.1, 1.5	-3.1, 1.3	-3.1, 1.5
		GEE Estimates			
		LS Mean (SE)	-0.73 (0.427)	-0.33 (0.394)	
		95% CI	(-1.56, 0.11)	(-1.11, 0.44)	
		LS Mean Difference (SE)		0.39 (0.588)	
		95% CI		(1.55, -0.76)	
		p-value		0.5036	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.4
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male		N_1	23	24	47
	Baseline	n	23	24	47
		Mean	6.35	6.50	6.43
		SD, SE	1.217, 0.254	1.597, 0.326	1.411, 0.206
		Median	6.50	6.73	6.50
		Q1, Q3	5.25, 7.13	5.41, 7.81	5.25, 7.50
		Min, Max	3.4, 8.3	3.0, 8.9	3.0, 8.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.4
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Baseline			
		n	23	24	47
		Mean	6.35	6.50	6.43
		SD, SE	1.217, 0.254	1.597, 0.326	1.411, 0.206
		Median	6.50	6.73	6.50
		Q1, Q3	5.25, 7.13	5.41, 7.81	5.25, 7.50
		Min, Max	3.4, 8.3	3.0, 8.9	3.0, 8.9
		Observed			
		n	23	24	47
		Mean	5.86	5.62	5.74
		SD, SE	1.975, 0.412	1.777, 0.363	1.860, 0.271
		Median	6.50	5.34	6.00
		Q1, Q3	4.00, 7.63	4.56, 7.19	4.25, 7.25
		Min, Max	2.3, 8.4	1.9, 8.1	1.9, 8.4

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.4
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Change from Baseline			
		n	23	24	47
		Mean	-0.49	-0.89	-0.69
		SD, SE	1.560, 0.325	1.436, 0.293	1.495, 0.218
		Median	-0.25	-0.63	-0.50
		Q1, Q3	-1.75, 0.75	-1.23, -0.06	-1.50, 0.25
		Min, Max	-3.5, 2.4	-6.1, 0.8	-6.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.28 (0.278)	-0.64 (0.256)	
		95% CI	(-0.83, 0.26)	(-1.14, -0.14)	
		LS Mean Difference (SE)		-0.36 (0.389)	
		95% CI		(0.40, -1.12)	
		p-value		0.3569	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.4
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Baseline			
		n	23	23	46
		Mean	6.35	6.47	6.41
		SD, SE	1.217, 0.254	1.622, 0.338	1.419, 0.209
		Median	6.50	6.71	6.50
		Q1, Q3	5.25, 7.13	5.20, 7.88	5.25, 7.50
		Min, Max	3.4, 8.3	3.0, 8.9	3.0, 8.9
		Observed			
		n	23	23	46
		Mean	6.00	5.23	5.61
		SD, SE	2.154, 0.449	2.039, 0.425	2.111, 0.311
		Median	6.25	5.38	5.94
		Q1, Q3	4.75, 7.50	3.25, 7.13	4.13, 7.38
		Min, Max	0.4, 9.0	2.1, 8.8	0.4, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.4
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Change from Baseline			
		n	23	23	46
		Mean	-0.35	-1.24	-0.79
		SD, SE	2.003, 0.418	1.551, 0.323	1.828, 0.270
		Median	-0.25	-0.88	-0.69
		Q1, Q3	-1.38, 0.71	-2.00, -0.25	-1.75, 0.25
		Min, Max	-4.9, 4.0	-5.9, 0.9	-5.9, 4.0
		GEE Estimates			
		LS Mean (SE)	-0.14 (0.354)	-0.98 (0.304)	
		95% CI	(-0.84, 0.55)	(-1.58, -0.38)	
		LS Mean Difference (SE)		-0.84 (0.489)	
		95% CI		(0.12, -1.80)	
		p-value		0.0865	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.4
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female		N_1	43	44	87
	Baseline	n	43	44	87
		Mean	6.65	6.97	6.81
		SD, SE	1.539, 0.235	1.106, 0.167	1.340, 0.144
		Median	6.75	7.13	6.88
		Q1, Q3	5.88, 7.88	6.38, 7.83	6.13, 7.88
		Min, Max	3.1, 9.1	3.8, 8.8	3.1, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.4
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Baseline			
		n	43	44	87
		Mean	6.65	6.97	6.81
		SD, SE	1.539, 0.235	1.106, 0.167	1.340, 0.144
		Median	6.75	7.13	6.88
		Q1, Q3	5.88, 7.88	6.38, 7.83	6.13, 7.88
		Min, Max	3.1, 9.1	3.8, 8.8	3.1, 9.1
		Observed			
		n	43	44	87
		Mean	6.12	6.19	6.15
		SD, SE	1.961, 0.299	1.740, 0.262	1.842, 0.198
		Median	6.38	6.50	6.38
		Q1, Q3	4.75, 7.20	5.50, 7.50	5.13, 7.50
		Min, Max	0.6, 9.9	2.1, 9.6	0.6, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.4
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Change from Baseline			
		n	43	44	87
		Mean	-0.54	-0.78	-0.66
		SD, SE	1.580, 0.241	1.491, 0.225	1.531, 0.164
		Median	-0.38	-0.25	-0.25
		Q1, Q3	-1.57, 0.50	-1.15, 0.04	-1.29, 0.25
		Min, Max	-4.0, 2.4	-5.1, 1.4	-5.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.51 (0.299)	-0.69 (0.269)	
		95% CI	(-1.10, 0.08)	(-1.21, -0.16)	
		LS Mean Difference (SE)		-0.17 (0.324)	
		95% CI		(0.46, -0.81)	
		p-value		0.5892	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.4
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Baseline			
		n	42	44	86
		Mean	6.60	6.97	6.79
		SD, SE	1.522, 0.235	1.106, 0.167	1.331, 0.144
		Median	6.63	7.13	6.88
		Q1, Q3	5.88, 7.63	6.38, 7.83	6.13, 7.67
		Min, Max	3.1, 9.1	3.8, 8.8	3.1, 9.1
		Observed			
		n	42	44	86
		Mean	6.14	6.13	6.13
		SD, SE	1.957, 0.302	1.794, 0.270	1.864, 0.201
		Median	6.25	6.19	6.25
		Q1, Q3	4.63, 7.63	4.81, 7.63	4.63, 7.63
		Min, Max	2.0, 9.9	2.3, 9.3	2.0, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.4
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Change from Baseline			
		n	42	44	86
		Mean	-0.47	-0.84	-0.66
		SD, SE	1.634, 0.252	1.571, 0.237	1.604, 0.173
		Median	-0.50	-0.69	-0.50
		Q1, Q3	-1.13, 0.25	-1.67, 0.31	-1.50, 0.25
		Min, Max	-3.8, 4.3	-5.1, 1.6	-5.1, 4.3
		GEE Estimates			
		LS Mean (SE)	-0.50 (0.312)	-0.74 (0.284)	
		95% CI	(-1.11, 0.11)	(-1.30, -0.19)	
		LS Mean Difference (SE)		-0.24 (0.332)	
		95% CI		(0.41, -0.89)	
		p-value		0.4671	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.5
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White		N_1	53	55	108
	Baseline	n	53	55	108
		Mean	6.54	6.96	6.75
		SD, SE	1.443, 0.198	1.103, 0.149	1.292, 0.124
		Median	6.50	7.13	6.79
		Q1, Q3	5.75, 7.63	6.25, 8.00	5.94, 7.79
		Min, Max	3.4, 9.1	4.1, 8.8	3.4, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.5
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Baseline			
		n	53	55	108
		Mean	6.54	6.96	6.75
		SD, SE	1.443, 0.198	1.103, 0.149	1.292, 0.124
		Median	6.50	7.13	6.79
		Q1, Q3	5.75, 7.63	6.25, 8.00	5.94, 7.79
		Min, Max	3.4, 9.1	4.1, 8.8	3.4, 9.1
		Observed			
		n	53	55	108
		Mean	6.06	6.10	6.08
		SD, SE	2.007, 0.276	1.760, 0.237	1.877, 0.181
		Median	6.50	6.38	6.40
		Q1, Q3	4.50, 7.20	5.13, 7.50	4.81, 7.38
		Min, Max	0.6, 9.9	1.9, 9.6	0.6, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.5
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Change from Baseline			
		n	53	55	108
		Mean	-0.48	-0.86	-0.67
		SD, SE	1.508, 0.207	1.486, 0.200	1.502, 0.145
		Median	-0.25	-0.50	-0.38
		Q1, Q3	-1.25, 0.50	-1.25, 0.00	-1.25, 0.19
		Min, Max	-4.0, 2.4	-6.1, 1.3	-6.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.52 (0.205)	-0.82 (0.193)	
		95% CI	(-0.92, -0.12)	(-1.20, -0.44)	
		LS Mean Difference (SE)		-0.30 (0.278)	
		95% CI		(0.25, -0.84)	
		p-value		0.2829	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.5
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Baseline			
		n	53	55	108
		Mean	6.54	6.96	6.75
		SD, SE	1.443, 0.198	1.103, 0.149	1.292, 0.124
		Median	6.50	7.13	6.79
		Q1, Q3	5.75, 7.63	6.25, 8.00	5.94, 7.79
		Min, Max	3.4, 9.1	4.1, 8.8	3.4, 9.1
		Observed			
		n	53	55	108
		Mean	6.17	5.93	6.05
		SD, SE	1.933, 0.266	1.814, 0.245	1.869, 0.180
		Median	6.25	6.13	6.19
		Q1, Q3	4.75, 7.50	4.63, 7.63	4.69, 7.56
		Min, Max	0.4, 9.9	2.1, 9.3	0.4, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.5
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Change from Baseline			
		n	53	55	108
		Mean	-0.37	-1.03	-0.71
		SD, SE	1.769, 0.243	1.588, 0.214	1.704, 0.164
		Median	-0.37	-0.88	-0.63
		Q1, Q3	-1.21, 0.50	-1.75, 0.13	-1.60, 0.25
		Min, Max	-4.9, 4.3	-5.9, 1.6	-5.9, 4.3
		GEE Estimates			
		LS Mean (SE)	-0.41 (0.229)	-0.99 (0.207)	
		95% CI	(-0.86, 0.04)	(-1.39, -0.58)	
		LS Mean Difference (SE)		-0.58 (0.304)	
		95% CI		(0.02, -1.17)	
		p-value		0.0572	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.5
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White		N_1	13	13	26
	Baseline	n	13	13	26
		Mean	6.56	6.17	6.37
		SD, SE	1.451, 0.402	1.884, 0.522	1.659, 0.325
		Median	7.00	6.38	6.69
		Q1, Q3	5.88, 7.25	4.13, 7.38	5.75, 7.38
		Min, Max	3.1, 8.8	3.0, 8.9	3.0, 8.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.5
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Baseline			
		n	13	13	26
		Mean	6.56	6.17	6.37
		SD, SE	1.451, 0.402	1.884, 0.522	1.659, 0.325
		Median	7.00	6.38	6.69
		Q1, Q3	5.88, 7.25	4.13, 7.38	5.75, 7.38
		Min, Max	3.1, 8.8	3.0, 8.9	3.0, 8.9
		Observed			
		n	13	13	26
		Mean	5.88	5.52	5.70
		SD, SE	1.792, 0.497	1.760, 0.488	1.749, 0.343
		Median	6.00	6.13	6.06
		Q1, Q3	4.75, 7.63	3.88, 7.00	4.25, 7.00
		Min, Max	2.4, 8.3	2.9, 7.6	2.4, 8.3

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.5
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Change from Baseline			
		n	13	13	26
		Mean	-0.68	-0.65	-0.66
		SD, SE	1.820, 0.505	1.396, 0.387	1.589, 0.312
		Median	-0.50	-0.25	-0.31
		Q1, Q3	-2.13, 0.50	-1.00, 0.13	-2.13, 0.38
		Min, Max	-4.0, 2.4	-3.3, 1.4	-4.0, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.48 (0.385)	-0.65 (0.318)	
		95% CI	(-1.23, 0.28)	(-1.27, -0.02)	
		LS Mean Difference (SE)		-0.17 (0.491)	
		95% CI		(0.79, -1.13)	
		p-value		0.7325	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.5
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Baseline			
		n	12	12	24
		Mean	6.38	6.07	6.22
		SD, SE	1.351, 0.390	1.931, 0.557	1.637, 0.334
		Median	6.56	6.38	6.38
		Q1, Q3	5.81, 7.25	4.00, 7.42	5.50, 7.29
		Min, Max	3.1, 8.3	3.0, 8.9	3.0, 8.9
		Observed			
		n	12	12	24
		Mean	5.72	5.33	5.53
		SD, SE	2.395, 0.691	2.356, 0.680	2.332, 0.476
		Median	5.75	5.06	5.44
		Q1, Q3	3.75, 7.88	3.19, 7.44	3.31, 7.44
		Min, Max	2.0, 9.0	2.5, 8.8	2.0, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.5
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Change from Baseline			
		n	12	12	24
		Mean	-0.66	-0.74	-0.70
		SD, SE	1.769, 0.511	1.491, 0.430	1.600, 0.327
		Median	-0.63	-0.50	-0.50
		Q1, Q3	-1.88, 0.48	-1.81, 0.38	-1.88, 0.38
		Min, Max	-3.4, 2.4	-3.1, 1.3	-3.4, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.66 (0.483)	-0.75 (0.379)	
		95% CI	(-1.60, 0.29)	(-1.49, -0.00)	
		LS Mean Difference (SE)		-0.09 (0.590)	
		95% CI		(1.07, -1.25)	
		p-value		0.8807	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.6
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years		N_1	36	31	67
	Baseline	n	36	31	67
		Mean	6.83	6.96	6.89
		SD, SE	1.280, 0.213	1.448, 0.260	1.351, 0.165
		Median	7.06	7.33	7.13
		Q1, Q3	5.94, 7.75	6.25, 8.00	6.13, 7.88
		Min, Max	3.1, 9.0	3.0, 8.9	3.0, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.6
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Baseline			
		n	36	31	67
		Mean	6.83	6.96	6.89
		SD, SE	1.280, 0.213	1.448, 0.260	1.351, 0.165
		Median	7.06	7.33	7.13
		Q1, Q3	5.94, 7.75	6.25, 8.00	6.13, 7.88
		Min, Max	3.1, 9.0	3.0, 8.9	3.0, 9.0
		Observed			
		n	36	31	67
		Mean	6.30	6.26	6.28
		SD, SE	1.524, 0.254	1.765, 0.317	1.627, 0.199
		Median	6.46	6.75	6.50
		Q1, Q3	5.44, 7.23	5.00, 7.50	5.25, 7.50
		Min, Max	2.4, 9.0	2.9, 9.6	2.4, 9.6

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.6
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Change from Baseline			
		n	36	31	67
		Mean	-0.53	-0.70	-0.61
		SD, SE	1.323, 0.221	1.131, 0.203	1.232, 0.150
		Median	-0.38	-0.50	-0.50
		Q1, Q3	-1.66, 0.44	-1.25, 0.00	-1.46, 0.00
		Min, Max	-2.6, 2.4	-3.3, 1.3	-3.3, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.44 (0.201)	-0.66 (0.208)	
		95% CI	(-0.84, -0.05)	(-1.07, -0.25)	
		LS Mean Difference (SE)		-0.22 (0.265)	
		95% CI		(0.30, -0.74)	
		p-value		0.4139	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.6
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Baseline			
		n	36	31	67
		Mean	6.83	6.96	6.89
		SD, SE	1.280, 0.213	1.448, 0.260	1.351, 0.165
		Median	7.06	7.33	7.13
		Q1, Q3	5.94, 7.75	6.25, 8.00	6.13, 7.88
		Min, Max	3.1, 9.0	3.0, 8.9	3.0, 9.0
		Observed			
		n	36	31	67
		Mean	6.10	5.85	5.98
		SD, SE	1.767, 0.294	1.942, 0.349	1.840, 0.225
		Median	6.13	6.25	6.25
		Q1, Q3	4.69, 7.25	4.25, 7.38	4.63, 7.38
		Min, Max	2.0, 9.5	2.5, 9.3	2.0, 9.5

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.6
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Change from Baseline			
		n	36	31	67
		Mean	-0.73	-1.10	-0.90
		SD, SE	1.319, 0.220	1.236, 0.222	1.286, 0.157
		Median	-0.63	-1.13	-0.88
		Q1, Q3	-1.50, 0.06	-2.00, 0.00	-1.75, 0.00
		Min, Max	-3.4, 2.4	-3.1, 1.3	-3.4, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.64 (0.223)	-1.07 (0.223)	
		95% CI	(-1.08, -0.20)	(-1.50, -0.63)	
		LS Mean Difference (SE)		-0.42 (0.296)	
		95% CI		(0.16, -1.00)	
		p-value		0.1516	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.6
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years		N_1	30	37	67
	Baseline	n	30	37	67
		Mean	6.20	6.68	6.47
		SD, SE	1.551, 0.283	1.185, 0.195	1.371, 0.168
		Median	6.13	6.75	6.50
		Q1, Q3	5.13, 7.13	6.13, 7.38	5.75, 7.38
		Min, Max	3.4, 9.1	3.8, 8.8	3.4, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.6
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Baseline			
		n	30	37	67
		Mean	6.20	6.68	6.47
		SD, SE	1.551, 0.283	1.185, 0.195	1.371, 0.168
		Median	6.13	6.75	6.50
		Q1, Q3	5.13, 7.13	6.13, 7.38	5.75, 7.38
		Min, Max	3.4, 9.1	3.8, 8.8	3.4, 9.1
		Observed			
		n	30	37	67
		Mean	5.70	5.76	5.73
		SD, SE	2.358, 0.430	1.751, 0.288	2.029, 0.248
		Median	6.38	6.00	6.13
		Q1, Q3	3.75, 7.88	5.00, 6.88	4.00, 7.13
		Min, Max	0.6, 9.9	1.9, 8.5	0.6, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.6
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Change from Baseline			
		n	30	37	67
		Mean	-0.50	-0.92	-0.73
		SD, SE	1.830, 0.334	1.699, 0.279	1.758, 0.215
		Median	-0.25	-0.38	-0.38
		Q1, Q3	-1.75, 0.88	-1.20, 0.07	-1.29, 0.38
		Min, Max	-4.0, 2.4	-6.1, 1.4	-6.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.17 (0.367)	-0.51 (0.236)	
		95% CI	(-0.89, 0.55)	(-0.97, -0.04)	
		LS Mean Difference (SE)		-0.33 (0.427)	
		95% CI		(0.50, -1.17)	
		p-value		0.4340	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.6
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Baseline			
		n	29	36	65
		Mean	6.11	6.66	6.42
		SD, SE	1.500, 0.279	1.196, 0.199	1.357, 0.168
		Median	6.13	6.73	6.50
		Q1, Q3	5.13, 6.88	6.06, 7.44	5.75, 7.38
		Min, Max	3.4, 9.1	3.8, 8.8	3.4, 9.1
		Observed			
		n	29	36	65
		Mean	6.07	5.80	5.92
		SD, SE	2.316, 0.430	1.921, 0.320	2.093, 0.260
		Median	6.63	5.94	6.13
		Q1, Q3	4.50, 7.75	4.56, 7.56	4.50, 7.63
		Min, Max	0.4, 9.9	2.1, 8.8	0.4, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.6
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Change from Baseline			
		n	29	36	65
		Mean	-0.04	-0.87	-0.50
		SD, SE	2.150, 0.399	1.810, 0.302	1.996, 0.248
		Median	0.00	-0.50	-0.38
		Q1, Q3	-0.88, 1.04	-1.44, 0.50	-1.38, 0.54
		Min, Max	-4.9, 4.3	-5.9, 1.6	-5.9, 4.3
		GEE Estimates			
		LS Mean (SE)	0.19 (0.438)	-0.44 (0.276)	
		95% CI	(-0.66, 1.05)	(-0.98, 0.10)	
		LS Mean Difference (SE)		-0.64 (0.476)	
		95% CI		(0.30, -1.57)	
		p-value		0.1822	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.7
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5		N_1	41	39	80
	Baseline	n	41	39	80
		Mean	6.28	6.37	6.32
		SD, SE	1.503, 0.235	1.440, 0.231	1.464, 0.164
		Median	6.13	6.50	6.44
		Q1, Q3	5.25, 7.38	5.20, 7.38	5.23, 7.38
		Min, Max	3.1, 8.8	3.0, 8.8	3.0, 8.8

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.7
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline			
		n	41	39	80
		Mean	6.28	6.37	6.32
		SD, SE	1.503, 0.235	1.440, 0.231	1.464, 0.164
		Median	6.13	6.50	6.44
		Q1, Q3	5.25, 7.38	5.20, 7.38	5.23, 7.38
		Min, Max	3.1, 8.8	3.0, 8.8	3.0, 8.8
		Observed			
		n	41	39	80
		Mean	5.70	5.62	5.66
		SD, SE	1.990, 0.311	1.702, 0.273	1.844, 0.206
		Median	5.88	5.88	5.88
		Q1, Q3	4.50, 7.13	4.25, 6.88	4.44, 7.06
		Min, Max	0.6, 9.9	1.9, 8.5	0.6, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.7
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline			
		n	41	39	80
		Mean	-0.58	-0.76	-0.66
		SD, SE	1.609, 0.251	1.349, 0.216	1.481, 0.166
		Median	-0.50	-0.38	-0.44
		Q1, Q3	-1.75, 0.25	-1.20, 0.00	-1.48, 0.02
		Min, Max	-4.0, 2.4	-6.1, 1.4	-6.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.62 (0.248)	-0.80 (0.235)	
		95% CI	(-1.10, -0.13)	(-1.26, -0.34)	
		LS Mean Difference (SE)		-0.18 (0.315)	
		95% CI		(0.43, -0.80)	
		p-value		0.5588	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.7
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline			
		n	41	39	80
		Mean	6.28	6.37	6.32
		SD, SE	1.503, 0.235	1.440, 0.231	1.464, 0.164
		Median	6.13	6.50	6.44
		Q1, Q3	5.25, 7.38	5.20, 7.38	5.23, 7.38
		Min, Max	3.1, 8.8	3.0, 8.8	3.0, 8.8
		Observed			
		n	41	39	80
		Mean	5.82	5.42	5.63
		SD, SE	1.796, 0.281	1.852, 0.296	1.823, 0.204
		Median	5.88	5.38	5.88
		Q1, Q3	4.63, 7.00	3.38, 7.13	4.25, 7.06
		Min, Max	2.0, 9.9	2.1, 8.1	2.0, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.7
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline			
		n	41	39	80
		Mean	-0.46	-0.95	-0.70
		SD, SE	1.750, 0.273	1.404, 0.225	1.600, 0.179
		Median	-0.63	-0.75	-0.69
		Q1, Q3	-1.13, 0.00	-1.63, 0.13	-1.54, 0.13
		Min, Max	-3.8, 4.3	-5.9, 1.3	-5.9, 4.3
		GEE Estimates			
		LS Mean (SE)	-0.50 (0.242)	-0.99 (0.234)	
		95% CI	(-0.97, -0.02)	(-1.45, -0.53)	
		LS Mean Difference (SE)		-0.49 (0.328)	
		95% CI		(0.15, -1.14)	
		p-value		0.1316	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.7
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5		N_1	25	29	54
	Baseline	n	25	29	54
		Mean	6.98	7.39	7.20
		SD, SE	1.217, 0.243	0.815, 0.151	1.031, 0.140
		Median	6.75	7.38	7.31
		Q1, Q3	6.13, 8.00	6.83, 8.00	6.38, 8.00
		Min, Max	4.3, 9.1	5.8, 8.9	4.3, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.7
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline			
		n	25	29	54
		Mean	6.98	7.39	7.20
		SD, SE	1.217, 0.243	0.815, 0.151	1.031, 0.140
		Median	6.75	7.38	7.31
		Q1, Q3	6.13, 8.00	6.83, 8.00	6.38, 8.00
		Min, Max	4.3, 9.1	5.8, 8.9	4.3, 9.1
		Observed			
		n	25	29	54
		Mean	6.56	6.49	6.52
		SD, SE	1.809, 0.362	1.744, 0.324	1.758, 0.239
		Median	7.00	6.88	6.94
		Q1, Q3	6.25, 8.13	5.43, 7.63	5.43, 7.88
		Min, Max	2.3, 9.0	2.4, 9.6	2.3, 9.6

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.7
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline			
		n	25	29	54
		Mean	-0.42	-0.90	-0.68
		SD, SE	1.506, 0.301	1.622, 0.301	1.573, 0.214
		Median	-0.04	-0.50	-0.31
		Q1, Q3	-1.00, 0.75	-1.29, 0.07	-1.25, 0.50
		Min, Max	-4.0, 1.9	-5.1, 1.3	-5.1, 1.9
		GEE Estimates			
		LS Mean (SE)	0.09 (0.297)	-0.34 (0.276)	
		95% CI	(-0.49, 0.67)	(-0.89, 0.20)	
		LS Mean Difference (SE)		-0.44 (0.415)	
		95% CI		(0.38, -1.25)	
		p-value		0.2942	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.7
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline			
		n	24	28	52
		Mean	6.91	7.39	7.17
		SD, SE	1.184, 0.242	0.830, 0.157	1.028, 0.143
		Median	6.75	7.44	7.19
		Q1, Q3	6.13, 7.81	6.79, 8.06	6.31, 8.00
		Min, Max	4.3, 9.1	5.8, 8.9	4.3, 9.1
		Observed			
		n	24	28	52
		Mean	6.55	6.38	6.45
		SD, SE	2.306, 0.471	1.897, 0.359	2.077, 0.288
		Median	7.13	6.63	6.81
		Q1, Q3	4.75, 8.56	4.81, 7.94	4.75, 8.13
		Min, Max	0.4, 9.5	2.3, 9.3	0.4, 9.5

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.7
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline			
		n	24	28	52
		Mean	-0.36	-1.02	-0.71
		SD, SE	1.809, 0.369	1.790, 0.338	1.811, 0.251
		Median	0.13	-0.85	-0.38
		Q1, Q3	-1.38, 0.79	-2.53, 0.44	-2.06, 0.63
		Min, Max	-4.9, 2.5	-5.1, 1.6	-5.1, 2.5
		GEE Estimates			
		LS Mean (SE)	0.02 (0.390)	-0.44 (0.316)	
		95% CI	(-0.74, 0.79)	(-1.06, 0.18)	
		LS Mean Difference (SE)		-0.46 (0.482)	
		95% CI		(0.48, -1.41)	
		p-value		0.3354	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.8
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	6.13	6.19	6.16
		SD, SE	1.262, 0.207	1.433, 0.262	1.331, 0.163
		Median	6.13	6.31	6.25
		Q1, Q3	5.25, 7.13	5.13, 7.33	5.20, 7.17
		Min, Max	3.1, 8.3	3.0, 8.8	3.0, 8.8

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.8
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline			
		n	37	30	67
		Mean	6.13	6.19	6.16
		SD, SE	1.262, 0.207	1.433, 0.262	1.331, 0.163
		Median	6.13	6.31	6.25
		Q1, Q3	5.25, 7.13	5.13, 7.33	5.20, 7.17
		Min, Max	3.1, 8.3	3.0, 8.8	3.0, 8.8
		Observed			
		n	37	30	67
		Mean	5.65	5.31	5.50
		SD, SE	1.803, 0.296	1.486, 0.271	1.665, 0.203
		Median	6.00	5.28	5.60
		Q1, Q3	4.38, 7.00	4.25, 6.75	4.25, 6.88
		Min, Max	2.3, 8.6	2.1, 7.6	2.1, 8.6

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Table 2.2.2.1.24.8
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-0.47	-0.88	-0.66
		SD, SE	1.604, 0.264	1.243, 0.227	1.457, 0.178
		Median	-0.25	-0.56	-0.50
		Q1, Q3	-1.75, 0.50	-1.50, 0.00	-1.75, 0.38
		Min, Max	-4.0, 2.4	-3.3, 1.4	-4.0, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.47 (0.239)	-0.89 (0.238)	
		95% CI	(-0.94, -0.00)	(-1.36, -0.43)	
		LS Mean Difference (SE)		-0.42 (0.325)	
		95% CI		(0.22, -1.06)	
		p-value		0.1957	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.1.24.8
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline			
		n	37	30	67
		Mean	6.13	6.19	6.16
		SD, SE	1.262, 0.207	1.433, 0.262	1.331, 0.163
		Median	6.13	6.31	6.25
		Q1, Q3	5.25, 7.13	5.13, 7.33	5.20, 7.17
		Min, Max	3.1, 8.3	3.0, 8.8	3.0, 8.8
		Observed			
		n	37	30	67
		Mean	5.38	5.09	5.25
		SD, SE	1.912, 0.314	1.637, 0.299	1.787, 0.218
		Median	5.88	5.31	5.38
		Q1, Q3	4.25, 6.80	3.38, 6.13	3.63, 6.75
		Min, Max	0.4, 9.0	2.5, 8.0	0.4, 9.0

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Table 2.2.2.1.24.8
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-0.75	-1.10	-0.91
		SD, SE	1.858, 0.305	1.250, 0.228	1.613, 0.197
		Median	-0.63	-0.88	-0.75
		Q1, Q3	-1.75, 0.13	-1.75, -0.26	-1.75, 0.00
		Min, Max	-4.9, 4.0	-3.5, 1.6	-4.9, 4.0
		GEE Estimates			
		LS Mean (SE)	-0.74 (0.245)	-1.11 (0.236)	
		95% CI	(-1.22, -0.26)	(-1.58, -0.65)	
		LS Mean Difference (SE)		-0.37 (0.355)	
		95% CI		(0.33, -1.07)	
		p-value		0.2988	

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Table 2.2.2.1.24.8
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	7.08	7.29	7.20
		SD, SE	1.484, 0.276	0.973, 0.158	1.215, 0.148
		Median	7.13	7.38	7.38
		Q1, Q3	6.13, 8.29	6.63, 8.00	6.38, 8.13
		Min, Max	3.4, 9.1	4.1, 8.9	3.4, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
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		n	29	38	67
		Mean	7.08	7.29	7.20
		SD, SE	1.484, 0.276	0.973, 0.158	1.215, 0.148
		Median	7.13	7.38	7.38
		Q1, Q3	6.13, 8.29	6.63, 8.00	6.38, 8.13
		Min, Max	3.4, 9.1	4.1, 8.9	3.4, 9.1
		Observed			
		n	29	38	67
		Mean	6.50	6.52	6.51
		SD, SE	2.069, 0.384	1.796, 0.291	1.903, 0.233
		Median	7.00	6.88	6.88
		Q1, Q3	4.75, 8.13	5.88, 7.75	5.63, 8.00
		Min, Max	0.6, 9.9	1.9, 9.6	0.6, 9.9

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Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-0.58	-0.77	-0.68
		SD, SE	1.531, 0.284	1.629, 0.264	1.578, 0.193
		Median	-0.38	-0.25	-0.25
		Q1, Q3	-1.25, 0.38	-0.88, 0.07	-1.25, 0.25
		Min, Max	-4.0, 2.4	-6.1, 1.3	-6.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.04 (0.372)	-0.24 (0.246)	
		95% CI	(-0.77, 0.69)	(-0.72, 0.24)	
		LS Mean Difference (SE)		-0.20 (0.390)	
		95% CI		(0.56, -0.97)	
		p-value		0.6003	

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Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.8
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline			
		n	28	37	65
		Mean	7.02	7.29	7.17
		SD, SE	1.475, 0.279	0.987, 0.162	1.218, 0.151
		Median	6.94	7.38	7.38
		Q1, Q3	6.13, 8.27	6.63, 8.00	6.38, 8.00
		Min, Max	3.4, 9.1	4.1, 8.9	3.4, 9.1
		Observed			
		n	28	37	65
		Mean	7.02	6.41	6.67
		SD, SE	1.776, 0.336	1.940, 0.319	1.881, 0.233
		Median	7.38	6.88	7.00
		Q1, Q3	5.31, 8.50	5.13, 7.63	5.13, 8.13
		Min, Max	3.6, 9.9	2.1, 9.3	2.1, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
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Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline			
		n	28	37	65
		Mean	0.00	-0.87	-0.50
		SD, SE	1.550, 0.293	1.790, 0.294	1.734, 0.215
		Median	-0.06	-0.63	-0.50
		Q1, Q3	-0.88, 0.94	-1.75, 0.50	-1.38, 0.63
		Min, Max	-3.3, 4.3	-5.9, 1.3	-5.9, 4.3
		GEE Estimates			
		LS Mean (SE)	0.44 (0.372)	-0.34 (0.280)	
		95% CI	(-0.29, 1.17)	(-0.89, 0.21)	
		LS Mean Difference (SE)		-0.78 (0.398)	
		95% CI		(0.00, -1.56)	
		p-value		0.0501	

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Table 2.2.2.1.24.9
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50		N_1	42	32	74
	Baseline	n	42	32	74
		Mean	6.20	6.12	6.17
		SD, SE	1.272, 0.196	1.361, 0.241	1.302, 0.151
		Median	6.13	6.25	6.13
		Q1, Q3	5.50, 7.13	5.16, 7.13	5.25, 7.13
		Min, Max	3.1, 8.6	3.0, 8.8	3.0, 8.8

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
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Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Baseline			
		n	42	32	74
		Mean	6.20	6.12	6.17
		SD, SE	1.272, 0.196	1.361, 0.241	1.302, 0.151
		Median	6.13	6.25	6.13
		Q1, Q3	5.50, 7.13	5.16, 7.13	5.25, 7.13
		Min, Max	3.1, 8.6	3.0, 8.8	3.0, 8.8
		Observed			
		n	42	32	74
		Mean	5.81	5.16	5.53
		SD, SE	1.833, 0.283	1.512, 0.267	1.721, 0.200
		Median	6.31	5.46	5.63
		Q1, Q3	4.50, 7.13	3.94, 6.31	4.00, 6.88
		Min, Max	2.3, 8.6	1.9, 7.5	1.9, 8.6

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Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Change from Baseline			
		n	42	32	74
		Mean	-0.39	-0.96	-0.64
		SD, SE	1.551, 0.239	1.466, 0.259	1.531, 0.178
		Median	-0.25	-0.50	-0.39
		Q1, Q3	-1.57, 0.50	-1.48, -0.06	-1.50, 0.25
		Min, Max	-4.0, 2.4	-6.1, 1.4	-6.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.28 (0.232)	-0.96 (0.252)	
		95% CI	(-0.74, 0.17)	(-1.46, -0.47)	
		LS Mean Difference (SE)		-0.68 (0.332)	
		95% CI		(-0.03, -1.33)	
		p-value		0.0411	

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(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Baseline			
		n	42	32	74
		Mean	6.20	6.12	6.17
		SD, SE	1.272, 0.196	1.361, 0.241	1.302, 0.151
		Median	6.13	6.25	6.13
		Q1, Q3	5.50, 7.13	5.16, 7.13	5.25, 7.13
		Min, Max	3.1, 8.6	3.0, 8.8	3.0, 8.8
		Observed			
		n	42	32	74
		Mean	5.70	4.94	5.37
		SD, SE	2.010, 0.310	1.677, 0.296	1.899, 0.221
		Median	5.88	5.06	5.38
		Q1, Q3	4.63, 7.13	3.38, 6.06	3.63, 6.88
		Min, Max	0.4, 9.0	2.1, 8.1	0.4, 9.0

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Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Change from Baseline			
		n	42	32	74
		Mean	-0.49	-1.18	-0.79
		SD, SE	1.844, 0.285	1.475, 0.261	1.718, 0.200
		Median	-0.25	-0.88	-0.56
		Q1, Q3	-1.38, 0.25	-1.94, -0.19	-1.63, 0.13
		Min, Max	-4.9, 4.0	-5.9, 1.0	-5.9, 4.0
		GEE Estimates			
		LS Mean (SE)	-0.39 (0.258)	-1.18 (0.252)	
		95% CI	(-0.90, 0.11)	(-1.68, -0.69)	
		LS Mean Difference (SE)		-0.79 (0.364)	
		95% CI		(-0.08, -1.50)	
		p-value		0.0296	

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Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50		N_1	24	35	59
	Baseline	n	24	35	59
		Mean	7.15	7.45	7.33
		SD, SE	1.523, 0.311	0.898, 0.152	1.190, 0.155
		Median	7.31	7.50	7.50
		Q1, Q3	6.31, 8.46	6.88, 8.00	6.71, 8.25
		Min, Max	3.4, 9.1	4.1, 8.9	3.4, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
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		n	24	35	59
		Mean	7.15	7.45	7.33
		SD, SE	1.523, 0.311	0.898, 0.152	1.190, 0.155
		Median	7.31	7.50	7.50
		Q1, Q3	6.31, 8.46	6.88, 8.00	6.71, 8.25
		Min, Max	3.4, 9.1	4.1, 8.9	3.4, 9.1
		Observed			
		n	24	35	59
		Mean	6.41	6.76	6.62
		SD, SE	2.138, 0.436	1.659, 0.280	1.860, 0.242
		Median	6.81	7.25	7.00
		Q1, Q3	4.75, 8.19	6.38, 8.00	5.75, 8.00
		Min, Max	0.6, 9.9	2.4, 9.6	0.6, 9.9

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Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.9
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Change from Baseline			
		n	24	35	59
		Mean	-0.74	-0.69	-0.71
		SD, SE	1.586, 0.324	1.488, 0.252	1.515, 0.197
		Median	-0.44	-0.25	-0.38
		Q1, Q3	-1.94, 0.31	-0.88, 0.07	-1.25, 0.25
		Min, Max	-4.0, 2.4	-5.1, 1.3	-5.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.40 (0.387)	-0.24 (0.284)	
		95% CI	(-1.16, 0.35)	(-0.79, 0.32)	
		LS Mean Difference (SE)		0.17 (0.415)	
		95% CI		(0.98, -0.65)	
		p-value		0.6899	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.9
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Baseline			
		n	23	34	57
		Mean	7.08	7.45	7.30
		SD, SE	1.518, 0.317	0.912, 0.156	1.195, 0.158
		Median	7.25	7.50	7.50
		Q1, Q3	6.25, 8.29	6.88, 8.00	6.71, 8.13
		Min, Max	3.4, 9.1	4.1, 8.9	3.4, 9.1
		Observed			
		n	23	34	57
		Mean	6.79	6.70	6.73
		SD, SE	1.862, 0.388	1.754, 0.301	1.782, 0.236
		Median	6.75	7.00	7.00
		Q1, Q3	5.13, 8.63	5.88, 8.00	5.57, 8.00
		Min, Max	3.6, 9.9	2.3, 9.3	2.3, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.9
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Change from Baseline			
		n	23	34	57
		Mean	-0.29	-0.75	-0.57
		SD, SE	1.624, 0.339	1.652, 0.283	1.642, 0.217
		Median	-0.50	-0.69	-0.63
		Q1, Q3	-0.88, 0.71	-1.50, 0.50	-1.38, 0.50
		Min, Max	-3.4, 4.3	-5.1, 1.6	-5.1, 4.3
		GEE Estimates			
		LS Mean (SE)	-0.07 (0.396)	-0.30 (0.319)	
		95% CI	(-0.84, 0.71)	(-0.92, 0.33)	
		LS Mean Difference (SE)		-0.23 (0.425)	
		95% CI		(0.60, -1.06)	
		p-value		0.5876	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.10
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	6.13	6.17	6.14
		SD, SE	1.262, 0.207	1.420, 0.259	1.324, 0.162
		Median	6.13	6.25	6.25
		Q1, Q3	5.25, 7.13	5.13, 7.13	5.20, 7.13
		Min, Max	3.1, 8.3	3.0, 8.8	3.0, 8.8

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.10
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Baseline			
		n	37	30	67
		Mean	6.13	6.17	6.14
		SD, SE	1.262, 0.207	1.420, 0.259	1.324, 0.162
		Median	6.13	6.25	6.25
		Q1, Q3	5.25, 7.13	5.13, 7.13	5.20, 7.13
		Min, Max	3.1, 8.3	3.0, 8.8	3.0, 8.8
		Observed			
		n	37	30	67
		Mean	5.65	5.32	5.51
		SD, SE	1.803, 0.296	1.449, 0.265	1.650, 0.202
		Median	6.00	5.34	5.60
		Q1, Q3	4.38, 7.00	4.25, 6.63	4.25, 6.75
		Min, Max	2.3, 8.6	2.1, 7.6	2.1, 8.6

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.10
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-0.47	-0.84	-0.64
		SD, SE	1.604, 0.264	1.135, 0.207	1.416, 0.173
		Median	-0.25	-0.56	-0.50
		Q1, Q3	-1.75, 0.50	-1.46, 0.00	-1.57, 0.25
		Min, Max	-4.0, 2.4	-3.3, 1.4	-4.0, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.46 (0.238)	-0.85 (0.230)	
		95% CI	(-0.93, 0.01)	(-1.30, -0.40)	
		LS Mean Difference (SE)		-0.39 (0.315)	
		95% CI		(0.23, -1.01)	
		p-value		0.2165	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.10
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Baseline			
		n	37	30	67
		Mean	6.13	6.17	6.14
		SD, SE	1.262, 0.207	1.420, 0.259	1.324, 0.162
		Median	6.13	6.25	6.25
		Q1, Q3	5.25, 7.13	5.13, 7.13	5.20, 7.13
		Min, Max	3.1, 8.3	3.0, 8.8	3.0, 8.8
		Observed			
		n	37	30	67
		Mean	5.38	5.04	5.23
		SD, SE	1.912, 0.314	1.597, 0.292	1.773, 0.217
		Median	5.88	5.31	5.38
		Q1, Q3	4.25, 6.80	3.38, 6.13	3.63, 6.75
		Min, Max	0.4, 9.0	2.5, 8.0	0.4, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.10
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-0.75	-1.12	-0.91
		SD, SE	1.858, 0.305	1.146, 0.209	1.580, 0.193
		Median	-0.63	-0.88	-0.75
		Q1, Q3	-1.75, 0.13	-1.75, -0.26	-1.75, 0.00
		Min, Max	-4.9, 4.0	-3.5, 0.5	-4.9, 4.0
		GEE Estimates			
		LS Mean (SE)	-0.73 (0.244)	-1.13 (0.229)	
		95% CI	(-1.21, -0.25)	(-1.58, -0.68)	
		LS Mean Difference (SE)		-0.40 (0.347)	
		95% CI		(0.28, -1.08)	
		p-value		0.2536	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.10
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	7.08	7.31	7.21
		SD, SE	1.484, 0.276	0.962, 0.156	1.211, 0.148
		Median	7.13	7.38	7.38
		Q1, Q3	6.13, 8.29	6.63, 8.00	6.38, 8.13
		Min, Max	3.4, 9.1	4.1, 8.9	3.4, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.10
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Baseline			
		n	29	38	67
		Mean	7.08	7.31	7.21
		SD, SE	1.484, 0.276	0.962, 0.156	1.211, 0.148
		Median	7.13	7.38	7.38
		Q1, Q3	6.13, 8.29	6.63, 8.00	6.38, 8.13
		Min, Max	3.4, 9.1	4.1, 8.9	3.4, 9.1
		Observed			
		n	29	38	67
		Mean	6.50	6.51	6.51
		SD, SE	2.069, 0.384	1.826, 0.296	1.919, 0.234
		Median	7.00	6.94	7.00
		Q1, Q3	4.75, 8.13	5.88, 7.75	5.63, 8.00
		Min, Max	0.6, 9.9	1.9, 9.6	0.6, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.10
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-0.58	-0.80	-0.70
		SD, SE	1.531, 0.284	1.691, 0.274	1.615, 0.197
		Median	-0.38	-0.25	-0.25
		Q1, Q3	-1.25, 0.38	-0.88, 0.07	-1.25, 0.25
		Min, Max	-4.0, 2.4	-6.1, 1.3	-6.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.04 (0.372)	-0.26 (0.245)	
		95% CI	(-0.76, 0.69)	(-0.74, 0.22)	
		LS Mean Difference (SE)		-0.23 (0.398)	
		95% CI		(0.55, -1.01)	
		p-value		0.5671	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.10
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Baseline			
		n	28	37	65
		Mean	7.02	7.31	7.18
		SD, SE	1.475, 0.279	0.975, 0.160	1.214, 0.151
		Median	6.94	7.38	7.38
		Q1, Q3	6.13, 8.27	6.63, 8.00	6.38, 8.00
		Min, Max	3.4, 9.1	4.1, 8.9	3.4, 9.1
		Observed			
		n	28	37	65
		Mean	7.02	6.45	6.70
		SD, SE	1.776, 0.336	1.940, 0.319	1.878, 0.233
		Median	7.38	6.88	7.00
		Q1, Q3	5.31, 8.50	5.13, 7.88	5.13, 8.13
		Min, Max	3.6, 9.9	2.1, 9.3	2.1, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.10
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Change from Baseline			
		n	28	37	65
		Mean	0.00	-0.86	-0.49
		SD, SE	1.550, 0.293	1.843, 0.303	1.763, 0.219
		Median	-0.06	-0.63	-0.50
		Q1, Q3	-0.88, 0.94	-1.75, 0.50	-1.38, 0.71
		Min, Max	-3.3, 4.3	-5.9, 1.6	-5.9, 4.3
		GEE Estimates			
		LS Mean (SE)	0.44 (0.370)	-0.31 (0.279)	
		95% CI	(-0.29, 1.17)	(-0.86, 0.23)	
		LS Mean Difference (SE)		-0.75 (0.404)	
		95% CI		(0.04, -1.54)	
		p-value		0.0619	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.11
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes		N_1	44	47	91
	Baseline	n	44	47	91
		Mean	6.61	7.01	6.82
		SD, SE	1.402, 0.211	1.005, 0.147	1.223, 0.128
		Median	6.50	7.13	6.83
		Q1, Q3	5.88, 7.56	6.38, 7.75	6.13, 7.67
		Min, Max	3.4, 9.1	4.9, 8.9	3.4, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.11
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	44	47	91
		Mean	6.61	7.01	6.82
		SD, SE	1.402, 0.211	1.005, 0.147	1.223, 0.128
		Median	6.50	7.13	6.83
		Q1, Q3	5.88, 7.56	6.38, 7.75	6.13, 7.67
		Min, Max	3.4, 9.1	4.9, 8.9	3.4, 9.1
		Observed			
		n	44	47	91
		Mean	5.85	6.13	5.99
		SD, SE	1.939, 0.292	1.775, 0.259	1.851, 0.194
		Median	6.25	6.63	6.38
		Q1, Q3	4.44, 7.06	5.00, 7.38	4.75, 7.25
		Min, Max	0.6, 9.0	1.9, 9.6	0.6, 9.6

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.11
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	44	47	91
		Mean	-0.76	-0.88	-0.82
		SD, SE	1.593, 0.240	1.561, 0.228	1.569, 0.164
		Median	-0.38	-0.50	-0.38
		Q1, Q3	-1.81, 0.38	-1.20, 0.00	-1.75, 0.04
		Min, Max	-4.0, 2.4	-6.1, 1.3	-6.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.64 (0.520)	-0.69 (0.457)	
		95% CI	(-1.66, 0.38)	(-1.58, 0.21)	
		LS Mean Difference (SE)		-0.05 (0.322)	
		95% CI		(0.58, -0.68)	
		p-value		0.8851	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.11
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	43	46	89
		Mean	6.56	7.00	6.79
		SD, SE	1.379, 0.210	1.015, 0.150	1.218, 0.129
		Median	6.50	7.13	6.75
		Q1, Q3	5.88, 7.50	6.38, 7.75	6.13, 7.63
		Min, Max	3.4, 9.1	4.9, 8.9	3.4, 9.1
		Observed			
		n	43	46	89
		Mean	6.11	5.92	6.01
		SD, SE	1.959, 0.299	1.848, 0.272	1.894, 0.201
		Median	6.50	6.13	6.25
		Q1, Q3	4.63, 7.63	4.50, 7.63	4.63, 7.63
		Min, Max	0.4, 9.5	2.1, 9.3	0.4, 9.5

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.11
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	43	46	89
		Mean	-0.45	-1.08	-0.78
		SD, SE	1.726, 0.263	1.694, 0.250	1.729, 0.183
		Median	-0.50	-0.85	-0.63
		Q1, Q3	-1.38, 0.54	-2.13, 0.13	-1.63, 0.25
		Min, Max	-4.9, 4.3	-5.9, 1.6	-5.9, 4.3
		GEE Estimates			
		LS Mean (SE)	-0.39 (0.530)	-0.87 (0.480)	
		95% CI	(-1.43, 0.65)	(-1.81, 0.07)	
		LS Mean Difference (SE)		-0.48 (0.344)	
		95% CI		(0.20, -1.15)	
		p-value		0.1636	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.11
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No		N_1	22	21	43
	Baseline	n	22	21	43
		Mean	6.42	6.35	6.38
		SD, SE	1.518, 0.324	1.758, 0.384	1.620, 0.247
		Median	6.69	6.38	6.50
		Q1, Q3	5.75, 7.50	5.63, 8.00	5.63, 7.63
		Min, Max	3.1, 8.8	3.0, 8.8	3.0, 8.8

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.11
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Baseline			
		n	22	21	43
		Mean	6.42	6.35	6.38
		SD, SE	1.518, 0.324	1.758, 0.384	1.620, 0.247
		Median	6.69	6.38	6.50
		Q1, Q3	5.75, 7.50	5.63, 8.00	5.63, 7.63
		Min, Max	3.1, 8.8	3.0, 8.8	3.0, 8.8
		Observed			
		n	22	21	43
		Mean	6.37	5.67	6.03
		SD, SE	1.985, 0.423	1.733, 0.378	1.878, 0.286
		Median	6.69	5.63	6.50
		Q1, Q3	5.38, 7.63	4.25, 7.25	4.63, 7.50
		Min, Max	2.4, 9.9	2.9, 8.0	2.4, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.11
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Change from Baseline			
		n	22	21	43
		Mean	-0.04	-0.67	-0.35
		SD, SE	1.411, 0.301	1.233, 0.269	1.349, 0.206
		Median	0.00	-0.40	-0.25
		Q1, Q3	-0.96, 0.75	-1.25, 0.07	-1.00, 0.50
		Min, Max	-2.6, 2.4	-3.3, 1.4	-3.3, 2.4
		GEE Estimates			
		LS Mean (SE)	0.02 (0.263)	-0.69 (0.260)	
		95% CI	(-0.50, 0.54)	(-1.20, -0.18)	
		LS Mean Difference (SE)		-0.71 (0.367)	
		95% CI		(0.01, -1.43)	
		p-value		0.0529	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.11
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Baseline			
		n	22	21	43
		Mean	6.42	6.35	6.38
		SD, SE	1.518, 0.324	1.758, 0.384	1.620, 0.247
		Median	6.69	6.38	6.50
		Q1, Q3	5.75, 7.50	5.63, 8.00	5.63, 7.63
		Min, Max	3.1, 8.8	3.0, 8.8	3.0, 8.8
		Observed			
		n	22	21	43
		Mean	6.05	5.60	5.83
		SD, SE	2.163, 0.461	2.086, 0.455	2.112, 0.322
		Median	6.13	5.57	5.88
		Q1, Q3	4.63, 7.50	3.38, 7.13	4.13, 7.38
		Min, Max	2.0, 9.9	2.5, 8.8	2.0, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.11
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Change from Baseline			
		n	22	21	43
		Mean	-0.37	-0.75	-0.56
		SD, SE	1.861, 0.397	1.243, 0.271	1.582, 0.241
		Median	-0.38	-0.50	-0.50
		Q1, Q3	-1.21, 0.25	-1.58, 0.00	-1.58, 0.25
		Min, Max	-3.4, 4.0	-3.1, 1.3	-3.4, 4.0
		GEE Estimates			
		LS Mean (SE)	-0.31 (0.336)	-0.77 (0.278)	
		95% CI	(-0.97, 0.35)	(-1.31, -0.22)	
		LS Mean Difference (SE)		-0.46 (0.444)	
		95% CI		(0.41, -1.33)	
		p-value		0.3000	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.12
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes		N_1	13	17	30
	Baseline	n	13	17	30
		Mean	6.58	7.36	7.02
		SD, SE	1.436, 0.398	1.000, 0.243	1.248, 0.228
		Median	6.13	7.38	7.25
		Q1, Q3	5.88, 7.50	6.75, 8.00	6.13, 8.00
		Min, Max	4.1, 9.1	5.1, 8.8	4.1, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.12
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	13	17	30
		Mean	6.58	7.36	7.02
		SD, SE	1.436, 0.398	1.000, 0.243	1.248, 0.228
		Median	6.13	7.38	7.25
		Q1, Q3	5.88, 7.50	6.75, 8.00	6.13, 8.00
		Min, Max	4.1, 9.1	5.1, 8.8	4.1, 9.1
		Observed			
		n	13	17	30
		Mean	6.16	6.35	6.27
		SD, SE	2.124, 0.589	1.968, 0.477	2.003, 0.366
		Median	6.38	6.88	6.63
		Q1, Q3	4.25, 8.13	5.00, 8.00	4.50, 8.13
		Min, Max	2.9, 8.9	2.9, 9.6	2.9, 9.6

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.12
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	13	17	30
		Mean	-0.42	-1.01	-0.76
		SD, SE	1.595, 0.442	1.470, 0.356	1.528, 0.279
		Median	-0.13	-0.50	-0.31
		Q1, Q3	-1.00, 0.38	-1.75, -0.25	-1.75, 0.00
		Min, Max	-4.0, 2.1	-5.1, 1.3	-5.1, 2.1
		GEE Estimates			
		LS Mean (SE)	-0.37 (0.431)	-1.06 (0.328)	
		95% CI	(-1.21, 0.48)	(-1.70, -0.41)	
		LS Mean Difference (SE)		-0.69 (0.533)	
		95% CI		(0.36, -1.73)	
		p-value		0.1964	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.12
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	13	16	29
		Mean	6.58	7.36	7.01
		SD, SE	1.436, 0.398	1.033, 0.258	1.269, 0.236
		Median	6.13	7.56	7.13
		Q1, Q3	5.88, 7.50	6.63, 8.19	6.13, 8.00
		Min, Max	4.1, 9.1	5.1, 8.8	4.1, 9.1
		Observed			
		n	13	16	29
		Mean	6.23	6.21	6.22
		SD, SE	1.863, 0.517	2.083, 0.521	1.952, 0.363
		Median	5.88	6.44	6.13
		Q1, Q3	4.75, 7.63	4.06, 8.13	4.75, 8.13
		Min, Max	3.1, 8.9	3.3, 9.3	3.1, 9.3

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.12
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	13	16	29
		Mean	-0.35	-1.15	-0.79
		SD, SE	1.367, 0.379	1.507, 0.377	1.476, 0.274
		Median	-0.13	-0.75	-0.63
		Q1, Q3	-0.88, 0.54	-2.13, 0.13	-1.38, 0.13
		Min, Max	-3.8, 1.8	-4.6, 0.9	-4.6, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.30 (0.364)	-1.15 (0.331)	
		95% CI	(-1.01, 0.41)	(-1.80, -0.50)	
		LS Mean Difference (SE)		-0.85 (0.477)	
		95% CI		(0.08, -1.79)	
		p-value		0.0743	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.12
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No		N_1	53	51	104
	Baseline	n	53	51	104
		Mean	6.54	6.62	6.58
		SD, SE	1.446, 0.199	1.355, 0.190	1.396, 0.137
		Median	6.50	6.75	6.75
		Q1, Q3	5.75, 7.50	5.83, 7.50	5.79, 7.50
		Min, Max	3.1, 9.0	3.0, 8.9	3.0, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.12
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Baseline			
		n	53	51	104
		Mean	6.54	6.62	6.58
		SD, SE	1.446, 0.199	1.355, 0.190	1.396, 0.137
		Median	6.50	6.75	6.75
		Q1, Q3	5.75, 7.50	5.83, 7.50	5.79, 7.50
		Min, Max	3.1, 9.0	3.0, 8.9	3.0, 9.0
		Observed			
		n	53	51	104
		Mean	5.99	5.87	5.93
		SD, SE	1.931, 0.265	1.691, 0.237	1.810, 0.177
		Median	6.43	6.25	6.38
		Q1, Q3	4.75, 7.13	5.13, 7.25	4.75, 7.16
		Min, Max	0.6, 9.9	1.9, 8.1	0.6, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.12
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Change from Baseline			
		n	53	51	104
		Mean	-0.54	-0.75	-0.65
		SD, SE	1.567, 0.215	1.468, 0.206	1.516, 0.149
		Median	-0.38	-0.40	-0.38
		Q1, Q3	-1.75, 0.50	-1.20, 0.13	-1.27, 0.25
		Min, Max	-4.0, 2.4	-6.1, 1.4	-6.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.40 (0.219)	-0.60 (0.208)	
		95% CI	(-0.83, 0.03)	(-1.01, -0.19)	
		LS Mean Difference (SE)		-0.20 (0.281)	
		95% CI		(0.35, -0.75)	
		p-value		0.4834	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.12
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Baseline			
		n	52	51	103
		Mean	6.49	6.62	6.56
		SD, SE	1.426, 0.198	1.355, 0.190	1.386, 0.137
		Median	6.50	6.75	6.75
		Q1, Q3	5.75, 7.44	5.83, 7.50	5.75, 7.50
		Min, Max	3.1, 9.0	3.0, 8.9	3.0, 9.0
		Observed			
		n	52	51	103
		Mean	6.05	5.70	5.88
		SD, SE	2.065, 0.286	1.866, 0.261	1.967, 0.194
		Median	6.25	5.88	6.13
		Q1, Q3	4.63, 7.50	4.38, 7.38	4.50, 7.38
		Min, Max	0.4, 9.9	2.1, 8.8	0.4, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.12
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Change from Baseline			
		n	52	51	103
		Mean	-0.44	-0.92	-0.68
		SD, SE	1.855, 0.257	1.593, 0.223	1.739, 0.171
		Median	-0.50	-0.88	-0.50
		Q1, Q3	-1.42, 0.38	-1.75, 0.25	-1.63, 0.25
		Min, Max	-4.9, 4.3	-5.9, 1.6	-5.9, 4.3
		GEE Estimates			
		LS Mean (SE)	-0.35 (0.248)	-0.77 (0.234)	
		95% CI	(-0.84, 0.14)	(-1.23, -0.31)	
		LS Mean Difference (SE)		-0.42 (0.322)	
		95% CI		(0.21, -1.05)	
		p-value		0.1909	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.14
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes		N_1	38	32	70
	Baseline	n	38	32	70
		Mean	6.85	6.61	6.74
		SD, SE	1.255, 0.204	1.309, 0.231	1.276, 0.153
		Median	7.06	6.56	6.85
		Q1, Q3	6.13, 7.83	5.92, 7.44	6.00, 7.63
		Min, Max	4.1, 9.0	3.8, 8.9	3.8, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.2.1.24.14
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Baseline			
		n	38	32	70
		Mean	6.85	6.61	6.74
		SD, SE	1.255, 0.204	1.309, 0.231	1.276, 0.153
		Median	7.06	6.56	6.85
		Q1, Q3	6.13, 7.83	5.92, 7.44	6.00, 7.63
		Min, Max	4.1, 9.0	3.8, 8.9	3.8, 9.0
		Observed			
		n	38	32	70
		Mean	6.30	5.57	5.96
		SD, SE	1.620, 0.263	1.974, 0.349	1.815, 0.217
		Median	6.56	5.88	6.40
		Q1, Q3	4.75, 7.25	3.81, 7.38	4.63, 7.25
		Min, Max	3.0, 9.0	1.9, 8.1	1.9, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.1.24.14
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Change from Baseline			
		n	38	32	70
		Mean	-0.55	-1.04	-0.78
		SD, SE	1.555, 0.252	1.645, 0.291	1.604, 0.192
		Median	-0.38	-0.45	-0.39
		Q1, Q3	-1.75, 0.50	-1.94, 0.00	-1.75, 0.38
		Min, Max	-4.0, 2.4	-6.1, 0.9	-6.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.10 (0.281)	-0.69 (0.267)	
		95% CI	(-0.65, 0.45)	(-1.22, -0.17)	
		LS Mean Difference (SE)		-0.60 (0.381)	
		95% CI		(0.15, -1.34)	
		p-value		0.1179	

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Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.14
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Baseline			
		n	37	31	68
		Mean	6.80	6.59	6.70
		SD, SE	1.232, 0.202	1.323, 0.238	1.269, 0.154
		Median	7.00	6.38	6.79
		Q1, Q3	6.13, 7.63	5.83, 7.50	5.94, 7.63
		Min, Max	4.1, 9.0	3.8, 8.9	3.8, 9.0
		Observed			
		n	37	31	68
		Mean	6.34	5.53	5.97
		SD, SE	1.725, 0.284	2.013, 0.361	1.893, 0.230
		Median	6.50	5.57	6.19
		Q1, Q3	4.75, 7.50	3.38, 7.50	4.69, 7.50
		Min, Max	2.8, 9.5	2.1, 8.8	2.1, 9.5

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.2.1.24.14
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Change from Baseline			
		n	37	31	68
		Mean	-0.46	-1.06	-0.73
		SD, SE	1.529, 0.251	1.758, 0.316	1.652, 0.200
		Median	-0.50	-0.88	-0.63
		Q1, Q3	-1.38, 0.25	-1.75, 0.13	-1.63, 0.25
		Min, Max	-3.8, 2.6	-5.9, 1.6	-5.9, 2.6
		GEE Estimates			
		LS Mean (SE)	-0.07 (0.304)	-0.70 (0.300)	
		95% CI	(-0.67, 0.52)	(-1.29, -0.11)	
		LS Mean Difference (SE)		-0.62 (0.394)	
		95% CI		(0.15, -1.40)	
		p-value		0.1137	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.14
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No		N_1	28	36	64
	Baseline	n	28	36	64
		Mean	6.13	6.98	6.61
		SD, SE	1.571, 0.297	1.302, 0.217	1.477, 0.185
		Median	6.06	7.23	6.75
		Q1, Q3	5.25, 7.06	6.50, 7.94	5.75, 7.65
		Min, Max	3.1, 9.1	3.0, 8.8	3.0, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.14
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Baseline			
		n	28	36	64
		Mean	6.13	6.98	6.61
		SD, SE	1.571, 0.297	1.302, 0.217	1.477, 0.185
		Median	6.06	7.23	6.75
		Q1, Q3	5.25, 7.06	6.50, 7.94	5.75, 7.65
		Min, Max	3.1, 9.1	3.0, 8.8	3.0, 9.1
		Observed			
		n	28	36	64
		Mean	5.66	6.36	6.05
		SD, SE	2.314, 0.437	1.478, 0.246	1.906, 0.238
		Median	6.13	6.50	6.38
		Q1, Q3	3.69, 7.38	5.38, 7.38	5.13, 7.38
		Min, Max	0.6, 9.9	2.9, 9.6	0.6, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.14
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Change from Baseline			
		n	28	36	64
		Mean	-0.47	-0.62	-0.55
		SD, SE	1.596, 0.302	1.267, 0.211	1.410, 0.176
		Median	-0.25	-0.44	-0.31
		Q1, Q3	-0.98, 0.50	-1.06, 0.06	-1.00, 0.25
		Min, Max	-4.0, 2.4	-5.1, 1.4	-5.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.58 (0.348)	-0.65 (0.285)	
		95% CI	(-1.26, 0.10)	(-1.21, -0.09)	
		LS Mean Difference (SE)		-0.07 (0.363)	
		95% CI		(0.64, -0.78)	
		p-value		0.8482	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.14
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Baseline			
		n	28	36	64
		Mean	6.13	6.98	6.61
		SD, SE	1.571, 0.297	1.302, 0.217	1.477, 0.185
		Median	6.06	7.23	6.75
		Q1, Q3	5.25, 7.06	6.50, 7.94	5.75, 7.65
		Min, Max	3.1, 9.1	3.0, 8.8	3.0, 9.1
		Observed			
		n	28	36	64
		Mean	5.75	6.07	5.93
		SD, SE	2.330, 0.440	1.819, 0.303	2.047, 0.256
		Median	5.94	6.63	6.06
		Q1, Q3	3.94, 7.50	4.50, 7.50	4.31, 7.50
		Min, Max	0.4, 9.9	2.5, 9.3	0.4, 9.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.14
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-0.38	-0.90	-0.67
		SD, SE	2.053, 0.388	1.398, 0.233	1.721, 0.215
		Median	-0.43	-0.69	-0.50
		Q1, Q3	-1.17, 0.79	-1.81, 0.25	-1.60, 0.31
		Min, Max	-4.9, 4.3	-4.6, 1.0	-4.9, 4.3
		GEE Estimates			
		LS Mean (SE)	-0.49 (0.329)	-0.94 (0.277)	
		95% CI	(-1.13, 0.16)	(-1.48, -0.39)	
		LS Mean Difference (SE)		-0.45 (0.414)	
		95% CI		(0.36, -1.26)	
		p-value		0.2800	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.15
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High		N_1	29	37	66
	Baseline	n	29	37	66
		Mean	7.25	6.87	7.04
		SD, SE	1.157, 0.215	1.361, 0.224	1.280, 0.158
		Median	7.25	7.13	7.25
		Q1, Q3	6.38, 8.25	6.38, 7.88	6.38, 8.00
		Min, Max	4.1, 9.1	3.0, 8.8	3.0, 9.1

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.15
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Baseline			
		n	29	37	66
		Mean	7.25	6.87	7.04
		SD, SE	1.157, 0.215	1.361, 0.224	1.280, 0.158
		Median	7.25	7.13	7.25
		Q1, Q3	6.38, 8.25	6.38, 7.88	6.38, 8.00
		Min, Max	4.1, 9.1	3.0, 8.8	3.0, 9.1
		Observed			
		n	29	37	66
		Mean	6.71	6.03	6.33
		SD, SE	1.496, 0.278	2.025, 0.333	1.830, 0.225
		Median	7.00	6.75	6.75
		Q1, Q3	5.50, 8.13	5.00, 7.50	5.00, 7.57
		Min, Max	4.0, 9.0	1.9, 9.6	1.9, 9.6

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.15
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Change from Baseline			
		n	29	37	66
		Mean	-0.54	-0.84	-0.71
		SD, SE	1.507, 0.280	1.676, 0.276	1.599, 0.197
		Median	-0.38	-0.25	-0.25
		Q1, Q3	-1.75, 0.38	-1.00, 0.00	-1.25, 0.25
		Min, Max	-4.0, 2.4	-6.1, 1.3	-6.1, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.02 (0.359)	-0.45 (0.263)	
		95% CI	(-0.72, 0.69)	(-0.97, 0.06)	
		LS Mean Difference (SE)		-0.44 (0.399)	
		95% CI		(0.34, -1.22)	
		p-value		0.2727	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.2.1.24.15
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Baseline			
		n	28	36	64
		Mean	7.20	6.86	7.01
		SD, SE	1.142, 0.216	1.378, 0.230	1.281, 0.160
		Median	7.25	7.13	7.19
		Q1, Q3	6.31, 8.13	6.38, 7.94	6.38, 8.00
		Min, Max	4.1, 9.1	3.0, 8.8	3.0, 9.1
		Observed			
		n	28	36	64
		Mean	6.94	5.88	6.34
		SD, SE	1.428, 0.270	2.125, 0.354	1.913, 0.239
		Median	6.81	6.00	6.75
		Q1, Q3	5.94, 8.31	3.94, 7.63	5.13, 7.63
		Min, Max	4.6, 9.5	2.1, 9.3	2.1, 9.5

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
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Table 2.2.2.1.24.15
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-0.26	-0.97	-0.66
		SD, SE	1.365, 0.258	1.734, 0.289	1.611, 0.201
		Median	0.00	-0.69	-0.50
		Q1, Q3	-0.75, 0.67	-1.63, 0.31	-1.31, 0.50
		Min, Max	-3.3, 1.8	-5.9, 1.3	-5.9, 1.8
		GEE Estimates			
		LS Mean (SE)	0.17 (0.310)	-0.58 (0.290)	
		95% CI	(-0.44, 0.78)	(-1.15, -0.01)	
		LS Mean Difference (SE)		-0.75 (0.382)	
		95% CI		(-0.00, -1.50)	
		p-value		0.0492	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.2.1.24.15
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low		N_1	36	30	66
	Baseline	n	36	30	66
		Mean	5.91	6.75	6.29
		SD, SE	1.330, 0.222	1.277, 0.233	1.362, 0.168
		Median	5.88	6.73	6.25
		Q1, Q3	5.00, 6.94	6.13, 7.63	5.50, 7.33
		Min, Max	3.1, 8.6	3.8, 8.9	3.1, 8.9

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.15
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Baseline			
		n	36	30	66
		Mean	5.91	6.75	6.29
		SD, SE	1.330, 0.222	1.277, 0.233	1.362, 0.168
		Median	5.88	6.73	6.25
		Q1, Q3	5.00, 6.94	6.13, 7.63	5.50, 7.33
		Min, Max	3.1, 8.6	3.8, 8.9	3.1, 8.9
		Observed			
		n	36	30	66
		Mean	5.37	5.96	5.64
		SD, SE	2.014, 0.336	1.435, 0.262	1.786, 0.220
		Median	5.75	6.00	5.94
		Q1, Q3	3.69, 6.88	4.88, 7.25	4.25, 7.13
		Min, Max	0.6, 8.6	3.0, 8.0	0.6, 8.6

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.15
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Change from Baseline			
		n	36	30	66
		Mean	-0.54	-0.79	-0.66
		SD, SE	1.624, 0.271	1.203, 0.220	1.443, 0.178
		Median	-0.31	-0.56	-0.50
		Q1, Q3	-1.66, 0.50	-1.46, 0.00	-1.50, 0.25
		Min, Max	-4.0, 2.4	-3.3, 1.4	-4.0, 2.4
		GEE Estimates			
		LS Mean (SE)	-0.46 (0.235)	-0.38 (0.245)	
		95% CI	(-0.92, 0.00)	(-0.86, 0.10)	
		LS Mean Difference (SE)		0.07 (0.361)	
		95% CI		(0.78, -0.63)	
		p-value		0.8356	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.15
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Baseline			
		n	36	30	66
		Mean	5.91	6.75	6.29
		SD, SE	1.330, 0.222	1.277, 0.233	1.362, 0.168
		Median	5.88	6.73	6.25
		Q1, Q3	5.00, 6.94	6.13, 7.63	5.50, 7.33
		Min, Max	3.1, 8.6	3.8, 8.9	3.1, 8.9
		Observed			
		n	36	30	66
		Mean	5.32	5.80	5.54
		SD, SE	2.061, 0.343	1.673, 0.305	1.896, 0.233
		Median	4.88	6.06	5.47
		Q1, Q3	3.69, 7.13	4.50, 7.13	4.25, 7.13
		Min, Max	0.4, 9.0	2.6, 8.5	0.4, 9.0

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.2.1.24.15
Subgroup Analysis: Change from baseline to week 24 in Brief Pain Inventory (BPI) Worst Pain score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Change from Baseline			
		n	36	30	66
		Mean	-0.59	-0.94	-0.75
		SD, SE	2.027, 0.338	1.380, 0.252	1.759, 0.216
		Median	-0.75	-1.00	-0.88
		Q1, Q3	-1.50, 0.06	-1.75, 0.00	-1.63, 0.00
		Min, Max	-4.9, 4.3	-3.1, 1.6	-4.9, 4.3
		GEE Estimates			
		LS Mean (SE)	-0.51 (0.233)	-0.54 (0.254)	
		95% CI	(-0.96, -0.05)	(-1.03, -0.04)	
		LS Mean Difference (SE)		-0.03 (0.396)	
		95% CI		(0.75, -0.81)	
		p-value		0.9396	

The GEE Estimates are from the GEE model which includes the change from baseline for BPI worst pain as the dependent variable, region, visit, treatment and visit by treatment as fixed factors, and baseline of BPI Worst Pain as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: t_bpi_SUB.sas

Table 2.2.10.1.1.24.2
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
BPI Average Pain at BL <= 6	N1	48	49
	Responder - n(%)	21 (43.8%)	20 (40.8%)
	Difference in responder (KRN23 vs Placebo) - %	2.9%	
	Logistic Regression[1]		
	Responder - %	46.3%	43.8%
	95% C.I.	31.3%, 62.0%	28.8%, 60.0%
	Odds ratio (KRN23 vs Placebo)	1.109	
	95% C.I. of odds ratio	0.488, 2.518	
	P-value	0.8036	
	RR[3] (95% CI), P-value	1.072 (0.673, 1.707), 0.8384	
	ARR[3] (95% CI), P-value	1.109 (0.493, 2.491), 0.8030	
	ARD[4]		
	Difference (95% C.I.)	0.029 (-0.167, 0.226)	
	P-value	0.8384	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.2
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
BPI Average Pain at BL > 6	N1	20	17
	Responder - n(%)	8 (40.0%)	3 (17.6%)
	Difference in responder (KRN23 vs Placebo) - %	22.4%	
	Logistic Regression[1]		
	Responder - %	44.5%	22.9%
	95% C.I.	22.0%, 69.4%	6.1%, 57.7%
	Odds ratio (KRN23 vs Placebo)	2.697	
	95% C.I. of odds ratio	0.523, 13.899	
	P-value	0.2273	
	RR[3] (95% CI), P-value	2.267 (0.711, 7.221), 0.1691	
	ARR[3] (95% CI), P-value	2.697 (0.555, 13.112), 0.2188	
	ARD[4]		
	Difference (95% C.I.)	0.224 (-0.057, 0.504)	
	P-value	0.1691	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.1
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
BPI Worst Pain at BL <= 6	N1	17	27
	Responder - n(%)	9 (52.9%)	13 (48.1%)
	Difference in responder (KRN23 vs Placebo) - %	4.8%	
	Logistic Regression[1]		
	Responder - %	54.1%	49.7%
	95% C.I.	29.7%, 76.7%	29.2%, 70.3%
	Odds ratio (KRN23 vs Placebo)	1.192	
	95% C.I. of odds ratio	0.339, 4.193	
	P-value	0.7788	
	RR[3] (95% CI), P-value	1.100 (0.606, 1.994), 1.0000	
	ARR[3] (95% CI), P-value	1.192 (0.352, 4.041), 0.7774	
	ARD[4]		
	Difference (95% C.I.)	0.048 (-0.255, 0.351)	
	P-value	1.0000	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.1
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
BPI Worst Pain at BL > 6	N1	51	39
	Responder - n(%)	20 (39.2%)	10 (25.6%)
	Difference in responder (KRN23 vs Placebo) - %	13.6%	
	Logistic Regression[1]		
	Responder - %	43.1%	30.1%
	95% C.I.	28.2%, 59.3%	15.6%, 50.3%
	Odds ratio (KRN23 vs Placebo)	1.756	
	95% C.I. of odds ratio	0.687, 4.485	
	P-value	0.2360	
	RR[3] (95% CI), P-value	1.529 (0.811, 2.884), 0.2591	
	ARR[3] (95% CI), P-value	1.755 (0.696, 4.425), 0.2329	
	ARD[4]		
	Difference (95% C.I.)	0.136 (-0.056, 0.327)	
	P-value	0.2591	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.3
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Region

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
North America/EU	N1	58	58
	Responder - n(%)	25 (43.1%)	19 (32.8%)
	Difference in responder (KRN23 vs Placebo) - %	10.3%	
	Logistic Regression[1]		
	Responder - %	45.2%	35.4%
	95% C.I.	31.8%, 59.3%	22.5%, 50.9%
	Odds ratio (KRN23 vs Placebo)	1.501	
	95% C.I. of odds ratio	0.695, 3.244	
	P-value	0.2987	
	RR[3] (95% CI), P-value	1.316 (0.820, 2.111), 0.3387	
	ARR[3] (95% CI), P-value	1.501 (0.700, 3.218), 0.2965	
	ARD[4]		
	Difference (95% C.I.)	0.103 (-0.072, 0.279)	
	P-value	0.3387	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.3
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Region

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Asia	N1	10	8
	Responder - n(%)	4 (40.0%)	4 (50.0%)
	Difference in responder (KRN23 vs Placebo) - %	-10.0%	
	Logistic Regression[1]		
	Responder - %	99.7%	99.8%
	95% C.I.	0.0%, 100.0%	0.0%, 100.0%
	Odds ratio (KRN23 vs Placebo)	0.667	
	95% C.I. of odds ratio	0.073, 6.129	
	P-value	0.7023	
	RR[3] (95% CI), P-value	0.800 (0.286, 2.236), 1.0000	
	ARR[3] (95% CI), P-value	0.667 (0.087, 5.127), 0.6969	
	ARD[4]		
	Difference (95% C.I.)	-0.100 (-0.561, 0.361)	
	P-value	1.0000	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.4
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Gender

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Sex = Male	N1	24	23
	Responder - n(%)	12 (50.0%)	9 (39.1%)
	Difference in responder (KRN23 vs Placebo) - %	10.9%	
	Logistic Regression[1]		
	Responder - %	46.9%	35.4%
	95% C.I.	25.3%, 69.7%	15.9%, 61.4%
	Odds ratio (KRN23 vs Placebo)	1.612	
	95% C.I. of odds ratio	0.484, 5.366	
	P-value	0.4283	
	RR[3] (95% CI), P-value	1.278 (0.668, 2.443), 0.5612	
	ARR[3] (95% CI), P-value	1.612 (0.500, 5.191), 0.4240	
	ARD[4]		
	Difference (95% C.I.)	0.109 (-0.174, 0.391)	
	P-value	0.5612	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.4
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Gender

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Sex = Female	N1	44	43
	Responder - n(%)	17 (38.6%)	14 (32.6%)
	Difference in responder (KRN23 vs Placebo) - %	6.1%	
	Logistic Regression[1]		
	Responder - %	44.5%	40.1%
	95% C.I.	28.9%, 61.2%	24.2%, 58.4%
	Odds ratio (KRN23 vs Placebo)	1.197	
	95% C.I. of odds ratio	0.478, 2.994	
	P-value	0.6977	
	RR[3] (95% CI), P-value	1.187 (0.672, 2.096), 0.6557	
	ARR[3] (95% CI), P-value	1.197 (0.485, 2.954), 0.6968	
	ARD[4]		
	Difference (95% C.I.)	0.061 (-0.140, 0.262)	
	P-value	0.6557	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.5
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Race

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Race = White	N1	55	53
	Responder - n(%)	23 (41.8%)	18 (34.0%)
	Difference in responder (KRN23 vs Placebo) - %	7.9%	
	Logistic Regression[1]		
	Responder - %	43.9%	36.8%
	95% C.I.	30.4%, 58.3%	23.3%, 52.6%
	Odds ratio (KRN23 vs Placebo)	1.345	
	95% C.I. of odds ratio	0.606, 2.988	
	P-value	0.4625	
	RR[3] (95% CI), P-value	1.231 (0.756, 2.006), 0.4331	
	ARR[3] (95% CI), P-value	1.345 (0.611, 2.961), 0.4609	
	ARD[4]		
	Difference (95% C.I.)	0.079 (-0.104, 0.261)	
	P-value	0.4331	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.5
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Race

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Race = Non-White	N1	13	13
	Responder - n(%)	6 (46.2%)	5 (38.5%)
	Difference in responder (KRN23 vs Placebo) - %	7.7%	
	Logistic Regression[1]		
	Responder - %	99.8%	99.7%
	95% C.I.	0.0%, 100.0%	0.0%, 100.0%
	Odds ratio (KRN23 vs Placebo)	1.429	
	95% C.I. of odds ratio	0.248, 8.243	
	P-value	0.6777	
	RR[3] (95% CI), P-value	1.200 (0.486, 2.964), 1.0000	
	ARR[3] (95% CI), P-value	1.429 (0.271, 7.518), 0.6738	
	ARD[4]		
	Difference (95% C.I.)	0.077 (-0.302, 0.456)	
	P-value	1.0000	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.6
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Age

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Age <= 41 Years	N1	31	36
	Responder - n(%)	17 (54.8%)	14 (38.9%)
	Difference in responder (KRN23 vs Placebo) - %	15.9%	
	Logistic Regression[1]		
	Responder - %	54.8%	38.9%
	95% C.I.	37.1%, 71.4%	24.3%, 55.7%
	Odds ratio (KRN23 vs Placebo)	1.908	
	95% C.I. of odds ratio	0.707, 5.150	
	P-value	0.1983	
	RR[3] (95% CI), P-value	1.410 (0.839, 2.370), 0.2255	
	ARR[3] (95% CI), P-value	1.908 (0.720, 5.056), 0.1937	
	ARD[4]		
	Difference (95% C.I.)	0.159 (-0.077, 0.396)	
	P-value	0.2255	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.6
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Age

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Age > 41 Years	N1	37	30
	Responder - n(%)	12 (32.4%)	9 (30.0%)
	Difference in responder (KRN23 vs Placebo) - %	2.4%	
	Logistic Regression[1]		
	Responder - %	32.7%	33.4%
	95% C.I.	18.8%, 50.5%	17.8%, 53.8%
	Odds ratio (KRN23 vs Placebo)	0.969	
	95% C.I. of odds ratio	0.314, 2.989	
	P-value	0.9563	
	RR[3] (95% CI), P-value	1.081 (0.527, 2.216), 1.0000	
	ARR[3] (95% CI), P-value	0.969 (0.321, 2.926), 0.9561	
	ARD[4]		
	Difference (95% C.I.)	0.024 (-0.198, 0.247)	
	P-value	1.0000	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.7
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Stiffness at BL cat <= 62.5	N1	39	41
	Responder - n(%)	19 (48.7%)	16 (39.0%)
	Difference in responder (KRN23 vs Placebo) - %	9.7%	
	Logistic Regression[1]		
	Responder - %	48.9%	39.2%
	95% C.I.	31.8%, 66.2%	22.3%, 59.2%
	Odds ratio (KRN23 vs Placebo)	1.480	
	95% C.I. of odds ratio	0.592, 3.702	
	P-value	0.3969	
	RR[3] (95% CI), P-value	1.248 (0.757, 2.058), 0.4993	
	ARR[3] (95% CI), P-value	1.480 (0.600, 3.649), 0.3943	
	ARD[4]		
	Difference (95% C.I.)	0.097 (-0.120, 0.314)	
	P-value	0.4993	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.7
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Stiffness at BL cat > 62.5	N1	29	25
	Responder - n(%)	10 (34.5%)	7 (28.0%)
	Difference in responder (KRN23 vs Placebo) - %	6.5%	
	Logistic Regression[1]		
	Responder - %	41.5%	33.9%
	95% C.I.	23.0%, 62.8%	16.5%, 57.3%
	Odds ratio (KRN23 vs Placebo)	1.384	
	95% C.I. of odds ratio	0.402, 4.767	
	P-value	0.6004	
	RR[3] (95% CI), P-value	1.232 (0.551, 2.752), 0.7703	
	ARR[3] (95% CI), P-value	1.384 (0.414, 4.629), 0.5981	
	ARD[4]		
	Difference (95% C.I.)	0.065 (-0.182, 0.312)	
	P-value	0.7703	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.8
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Physical Function at BL cat <= 47.8	N1	30	37
	Responder - n(%)	15 (50.0%)	15 (40.5%)
	Difference in responder (KRN23 vs Placebo) - %	9.5%	
	Logistic Regression[1]		
	Responder - %	55.1%	46.9%
	95% C.I.	34.2%, 74.3%	27.1%, 67.8%
	Odds ratio (KRN23 vs Placebo)	1.386	
	95% C.I. of odds ratio	0.508, 3.777	
	P-value	0.5183	
	RR[3] (95% CI), P-value	1.233 (0.726, 2.094), 0.4689	
	ARR[3] (95% CI), P-value	1.386 (0.518, 3.706), 0.5160	
	ARD[4]		
	Difference (95% C.I.)	0.095 (-0.144, 0.333)	
	P-value	0.4689	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.8
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Physical Function at BL cat > 47.8	N1	38	29
	Responder - n(%)	14 (36.8%)	8 (27.6%)
	Difference in responder (KRN23 vs Placebo) - %	9.3%	
	Logistic Regression[1]		
	Responder - %	40.0%	31.0%
	95% C.I.	24.5%, 57.9%	15.6%, 52.2%
	Odds ratio (KRN23 vs Placebo)	1.487	
	95% C.I. of odds ratio	0.507, 4.366	
	P-value	0.4642	
	RR[3] (95% CI), P-value	1.336 (0.649, 2.749), 0.4467	
	ARR[3] (95% CI), P-value	1.487 (0.517, 4.277), 0.4616	
	ARD[4]		
	Difference (95% C.I.)	0.093 (-0.131, 0.316)	
	P-value	0.4467	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.9
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Pain Score at BL cat <= 50	N1	32	42
	Responder - n(%)	18 (56.3%)	16 (38.1%)
	Difference in responder (KRN23 vs Placebo) - %	18.2%	
	Logistic Regression[1]		
	Responder - %	59.1%	41.9%
	95% C.I.	39.7%, 76.0%	25.1%, 60.8%
	Odds ratio (KRN23 vs Placebo)	2.002	
	95% C.I. of odds ratio	0.766, 5.233	
	P-value	0.1543	
	RR[3] (95% CI), P-value	1.477 (0.903, 2.415), 0.1592	
	ARR[3] (95% CI), P-value	2.002 (0.778, 5.148), 0.1500	
	ARD[4]		
	Difference (95% C.I.)	0.182 (-0.045, 0.408)	
	P-value	0.1592	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.9
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Pain Score at BL cat > 50	N1	35	24
	Responder - n(%)	10 (28.6%)	7 (29.2%)
	Difference in responder (KRN23 vs Placebo) - %	-0.6%	
	Logistic Regression[1]		
	Responder - %	32.4%	34.2%
	95% C.I.	17.5%, 52.1%	16.1%, 58.4%
	Odds ratio (KRN23 vs Placebo)	0.923	
	95% C.I. of odds ratio	0.282, 3.027	
	P-value	0.8932	
	RR[3] (95% CI), P-value	0.980 (0.434, 2.212), 1.0000	
	ARR[3] (95% CI), P-value	0.923 (0.289, 2.950), 0.8928	
	ARD[4]		
	Difference (95% C.I.)	-0.006 (-0.241, 0.230)	
	P-value	1.0000	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.10
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Total Score at BL cat <= 49.5	N1	30	37
	Responder - n(%)	16 (53.3%)	15 (40.5%)
	Difference in responder (KRN23 vs Placebo) - %	12.8%	
	Logistic Regression[1]		
	Responder - %	55.3%	43.3%
	95% C.I.	35.3%, 73.7%	24.6%, 64.1%
	Odds ratio (KRN23 vs Placebo)	1.618	
	95% C.I. of odds ratio	0.592, 4.419	
	P-value	0.3423	
	RR[3] (95% CI), P-value	1.316 (0.787, 2.200), 0.3328	
	ARR[3] (95% CI), P-value	1.618 (0.604, 4.335), 0.3387	
	ARD[4]		
	Difference (95% C.I.)	0.128 (-0.111, 0.366)	
	P-value	0.3328	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.10
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Total Score at BL cat > 49.5	N1	38	29
	Responder - n(%)	13 (34.2%)	8 (27.6%)
	Difference in responder (KRN23 vs Placebo) - %	6.6%	
	Logistic Regression[1]		
	Responder - %	39.0%	32.3%
	95% C.I.	23.3%, 57.5%	16.4%, 53.8%
	Odds ratio (KRN23 vs Placebo)	1.340	
	95% C.I. of odds ratio	0.450, 3.992	
	P-value	0.5939	
	RR[3] (95% CI), P-value	1.240 (0.594, 2.590), 0.6052	
	ARR[3] (95% CI), P-value	1.340 (0.459, 3.910), 0.5922	
	ARD[4]		
	Difference (95% C.I.)	0.066 (-0.156, 0.288)	
	P-value	0.6052	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.11
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Pain Medication Use at BL = Yes	N1	47	44
	Responder - n(%)	18 (38.3%)	14 (31.8%)
	Difference in responder (KRN23 vs Placebo) - %	6.5%	
	Logistic Regression[1]		
	Responder - %	41.6%	36.3%
	95% C.I.	27.4%, 57.4%	21.8%, 53.7%
	Odds ratio (KRN23 vs Placebo)	1.252	
	95% C.I. of odds ratio	0.514, 3.048	
	P-value	0.6169	
	RR[3] (95% CI), P-value	1.204 (0.684, 2.117), 0.6608	
	ARR[3] (95% CI), P-value	1.252 (0.521, 3.011), 0.6157	
	ARD[4]		
	Difference (95% C.I.)	0.065 (-0.131, 0.260)	
	P-value	0.6608	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.11
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Pain Medication Use at BL cat=No	N1	21	22
	Responder - n(%)	11 (52.4%)	9 (40.9%)
	Difference in responder (KRN23 vs Placebo) - %	11.5%	
	Logistic Regression[1]		
	Responder - %	57.5%	46.6%
	95% C.I.	30.0%, 80.9%	21.0%, 74.1%
	Odds ratio (KRN23 vs Placebo)	1.548	
	95% C.I. of odds ratio	0.443, 5.412	
	P-value	0.4843	
	RR[3] (95% CI), P-value	1.280 (0.670, 2.445), 0.5467	
	ARR[3] (95% CI), P-value	1.548 (0.460, 5.211), 0.4802	
	ARD[4]		
	Difference (95% C.I.)	0.115 (-0.182, 0.411)	
	P-value	0.5467	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.12
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Opioid Pain Medication Use at BL = Yes	N1	17	13
	Responder - n(%)	6 (35.3%)	4 (30.8%)
	Difference in responder (KRN23 vs Placebo) - %	4.5%	
	Logistic Regression[1]		
	Responder - %	48.1%	42.0%
	95% C.I.	20.7%, 76.7%	14.6%, 75.4%
	Odds ratio (KRN23 vs Placebo)	1.275	
	95% C.I. of odds ratio	0.210, 7.762	
	P-value	0.7844	
	RR[3] (95% CI), P-value	1.147 (0.406, 3.241), 1.0000	
	ARR[3] (95% CI), P-value	1.275 (0.227, 7.159), 0.7823	
	ARD[4]		
	Difference (95% C.I.)	0.045 (-0.293, 0.384)	
	P-value	1.0000	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.12
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Opioid Pain Medication Use at BL cat = No	N1	51	53
	Responder - n(%)	23 (45.1%)	19 (35.8%)
	Difference in responder (KRN23 vs Placebo) - %	9.2%	
	Logistic Regression[1]		
	Responder - %	45.2%	36.0%
	95% C.I.	30.7%, 60.6%	22.1%, 52.7%
	Odds ratio (KRN23 vs Placebo)	1.467	
	95% C.I. of odds ratio	0.657, 3.276	
	P-value	0.3467	
	RR[3] (95% CI), P-value	1.258 (0.786, 2.014), 0.4245	
	ARR[3] (95% CI), P-value	1.467 (0.663, 3.245), 0.3444	
	ARD[4]		
	Difference (95% C.I.)	0.092 (-0.095, 0.280)	
	P-value	0.4245	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.14
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Active fractures and pseudo-fractures at BL = Yes	N1	32	38
	Responder - n(%)	13 (40.6%)	11 (28.9%)
	Difference in responder (KRN23 vs Placebo) - %	11.7%	
	Logistic Regression[1]		
	Responder - %	50.2%	36.9%
	95% C.I.	28.8%, 71.5%	19.6%, 58.4%
	Odds ratio (KRN23 vs Placebo)	1.720	
	95% C.I. of odds ratio	0.614, 4.821	
	P-value	0.2971	
	RR[3] (95% CI), P-value	1.403 (0.732, 2.691), 0.3252	
	ARR[3] (95% CI), P-value	1.720 (0.625, 4.731), 0.2934	
	ARD[4]		
	Difference (95% C.I.)	0.117 (-0.106, 0.340)	
	P-value	0.3252	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.14
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Active fractures and pseudo-fractures at BL = No	N1	36	28
	Responder - n(%)	16 (44.4%)	12 (42.9%)
	Difference in responder (KRN23 vs Placebo) - %	1.6%	
	Logistic Regression[1]		
	Responder - %	45.2%	44.2%
	95% C.I.	29.1%, 62.3%	25.4%, 64.9%
	Odds ratio (KRN23 vs Placebo)	1.038	
	95% C.I. of odds ratio	0.370, 2.916	
	P-value	0.9425	
	RR[3] (95% CI), P-value	1.037 (0.591, 1.820), 1.0000	
	ARR[3] (95% CI), P-value	1.038 (0.377, 2.857), 0.9423	
	ARD[4]		
	Difference (95% C.I.)	0.016 (-0.229, 0.261)	
	P-value	1.0000	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.15
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: 6MWT at baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
6MWT score at BL = High	N1	37	29
	Responder - n(%)	14 (37.8%)	6 (20.7%)
	Difference in responder (KRN23 vs Placebo) - %	17.1%	
	Logistic Regression[1]		
	Responder - %	40.5%	23.7%
	95% C.I.	24.3%, 59.2%	9.8%, 47.0%
	Odds ratio (KRN23 vs Placebo)	2.192	
	95% C.I. of odds ratio	0.690, 6.967	
	P-value	0.1799	
	RR[3] (95% CI), P-value	1.829 (0.803, 4.167), 0.1797	
	ARR[3] (95% CI), P-value	2.192 (0.705, 6.814), 0.1751	
	ARD[4]		
	Difference (95% C.I.)	0.171 (-0.043, 0.386)	
	P-value	0.1797	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.1.24.15
Subgroup Analysis: BPI Worst Pain responder analyses (at least 15% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: 6MWT at baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
6MWT score at BL = Low	N1	30	36
	Responder - n(%)	14 (46.7%)	17 (47.2%)
	Difference in responder (KRN23 vs Placebo) - %	-0.6%	
	Logistic Regression[1]		
	Responder - %	51.6%	53.4%
	95% C.I.	32.0%, 70.7%	34.0%, 71.9%
	Odds ratio (KRN23 vs Placebo)	0.930	
	95% C.I. of odds ratio	0.340, 2.539	
	P-value	0.8851	
	RR[3] (95% CI), P-value	0.988 (0.590, 1.655), 1.0000	
	ARR[3] (95% CI), P-value	0.930 (0.347, 2.490), 0.8846	
	ARD[4]		
	Difference (95% C.I.)	-0.006 (-0.247, 0.236)	
	P-value	1.0000	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.1
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
BPI Worst Pain at BL <= 6	N1	17	27
	Responder - n(%)	5 (29.4%)	5 (18.5%)
	Difference in responder (KRN23 vs Placebo) - %	10.9%	
	Logistic Regression[1]		
	Responder - %	30.6%	19.7%
	95% C.I.	12.6%, 57.4%	7.7%, 41.9%
	Odds ratio (KRN23 vs Placebo)	1.798	
	95% C.I. of odds ratio	0.412, 7.857	
	P-value	0.4261	
	RR[3] (95% CI), P-value	1.588 (0.539, 4.681), 0.4727	
	ARR[3] (95% CI), P-value	1.798 (0.430, 7.523), 0.4215	
	ARD[4]		
	Difference (95% C.I.)	0.109 (-0.153, 0.370)	
	P-value	0.4727	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.1
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
BPI Worst Pain at BL > 6	N1	51	39
	Responder - n(%)	12 (23.5%)	7 (17.9%)
	Difference in responder (KRN23 vs Placebo) - %	5.6%	
	Logistic Regression[1]		
	Responder - %	27.0%	22.4%
	95% C.I.	15.3%, 43.2%	10.1%, 42.5%
	Odds ratio (KRN23 vs Placebo)	1.286	
	95% C.I. of odds ratio	0.438, 3.777	
	P-value	0.6441	
	RR[3] (95% CI), P-value	1.311 (0.570, 3.018), 0.6074	
	ARR[3] (95% CI), P-value	1.286 (0.444, 3.720), 0.6430	
	ARD[4]		
	Difference (95% C.I.)	0.056 (-0.112, 0.223)	
	P-value	0.6074	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.2
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
BPI Average Pain at BL <= 6	N1	48	49
	Responder - n(%)	13 (27.1%)	10 (20.4%)
	Difference in responder (KRN23 vs Placebo) - %	6.7%	
	Logistic Regression[1]		
	Responder - %	27.4%	20.7%
	95% C.I.	15.6%, 43.6%	10.6%, 36.6%
	Odds ratio (KRN23 vs Placebo)	1.444	
	95% C.I. of odds ratio	0.555, 3.758	
	P-value	0.4470	
	RR[3] (95% CI), P-value	1.327 (0.645, 2.732), 0.4815	
	ARR[3] (95% CI), P-value	1.444 (0.562, 3.711), 0.4451	
	ARD[4]		
	Difference (95% C.I.)	0.067 (-0.102, 0.236)	
	P-value	0.4815	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.2
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
BPI Average Pain at BL > 6	N1	20	17
	Responder - n(%)	4 (20.0%)	2 (11.8%)
	Difference in responder (KRN23 vs Placebo) - %	8.2%	
	Logistic Regression[1]		
	Responder - %	25.0%	24.0%
	95% C.I.	8.6%, 54.1%	5.1%, 64.9%
	Odds ratio (KRN23 vs Placebo)	1.056	
	95% C.I. of odds ratio	0.122, 9.154	
	P-value	0.9593	
	RR[3] (95% CI), P-value	1.700 (0.354, 8.166), 0.6665	
	ARR[3] (95% CI), P-value	1.056 (0.132, 8.477), 0.9590	
	ARD[4]		
	Difference (95% C.I.)	0.082 (-0.150, 0.315)	
	P-value	0.6665	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.3
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Region

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
North America/EU	N1	58	58
	Responder - n(%)	16 (27.6%)	9 (15.5%)
	Difference in responder (KRN23 vs Placebo) - %	12.1%	
	Logistic Regression[1]		
	Responder - %	29.5%	17.4%
	95% C.I.	18.4%, 43.9%	8.8%, 31.7%
	Odds ratio (KRN23 vs Placebo)	1.986	
	95% C.I. of odds ratio	0.781, 5.047	
	P-value	0.1480	
	RR[3] (95% CI), P-value	1.778 (0.856, 3.693), 0.1748	
	ARR[3] (95% CI), P-value	1.986 (0.789, 4.997), 0.1452	
	ARD[4]		
	Difference (95% C.I.)	0.121 (-0.027, 0.269)	
	P-value	0.1748	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.3
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Region

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Asia	N1	10	8
	Responder - n(%)	1 (10.0%)	3 (37.5%)
	Difference in responder (KRN23 vs Placebo) - %	-27.5%	
	Logistic Regression[1]		
	Responder - %	15.9%	51.9%
	95% C.I.	1.5%, 69.4%	11.4%, 90.1%
	Odds ratio (KRN23 vs Placebo)	0.174	
	95% C.I. of odds ratio	0.010, 3.000	
	P-value	0.2104	
	RR[3] (95% CI), P-value	0.267 (0.034, 2.099), 0.2745	
	ARR[3] (95% CI), P-value	0.174 (0.013, 2.386), 0.1908	
	ARD[4]		
	Difference (95% C.I.)	-0.275 (-0.659, 0.109)	
	P-value	0.2745	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.4
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Gender

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Sex = Male	N1	24	23
	Responder - n(%)	7 (29.2%)	4 (17.4%)
	Difference in responder (KRN23 vs Placebo) - %	11.8%	
	Logistic Regression[1]		
	Responder - %	29.3%	17.5%
	95% C.I.	12.6%, 54.2%	5.5%, 43.7%
	Odds ratio (KRN23 vs Placebo)	1.953	
	95% C.I. of odds ratio	0.464, 8.231	
	P-value	0.3533	
	RR[3] (95% CI), P-value	1.677 (0.565, 4.974), 0.4936	
	ARR[3] (95% CI), P-value	1.953 (0.482, 7.912), 0.3482	
	ARD[4]		
	Difference (95% C.I.)	0.118 (-0.121, 0.357)	
	P-value	0.4936	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.4
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Gender

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Sex = Female	N1	44	43
	Responder - n(%)	10 (22.7%)	8 (18.6%)
	Difference in responder (KRN23 vs Placebo) - %	4.1%	
	Logistic Regression[1]		
	Responder - %	26.0%	22.8%
	95% C.I.	14.2%, 42.7%	11.2%, 40.7%
	Odds ratio (KRN23 vs Placebo)	1.190	
	95% C.I. of odds ratio	0.405, 3.492	
	P-value	0.7491	
	RR[3] (95% CI), P-value	1.222 (0.533, 2.799), 0.7922	
	ARR[3] (95% CI), P-value	1.190 (0.412, 3.438), 0.7483	
	ARD[4]		
	Difference (95% C.I.)	0.041 (-0.129, 0.211)	
	P-value	0.7922	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.5
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Race

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Race = White	N1	55	53
	Responder - n(%)	15 (27.3%)	8 (15.1%)
	Difference in responder (KRN23 vs Placebo) - %	12.2%	
	Logistic Regression[1]		
	Responder - %	29.2%	17.0%
	95% C.I.	18.0%, 43.8%	8.3%, 31.8%
	Odds ratio (KRN23 vs Placebo)	2.013	
	95% C.I. of odds ratio	0.757, 5.351	
	P-value	0.1588	
	RR[3] (95% CI), P-value	1.807 (0.836, 3.905), 0.1597	
	ARR[3] (95% CI), P-value	2.013 (0.766, 5.291), 0.1558	
	ARD[4]		
	Difference (95% C.I.)	0.122 (-0.030, 0.274)	
	P-value	0.1597	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.5
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Race

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Race = Non-White	N1	13	13
	Responder - n(%)	2 (15.4%)	4 (30.8%)
	Difference in responder (KRN23 vs Placebo) - %	-15.4%	
	Logistic Regression[1]		
	Responder - %	23.8%	44.2%
	95% C.I.	4.2%, 69.3%	11.3%, 83.1%
	Odds ratio (KRN23 vs Placebo)	0.395	
	95% C.I. of odds ratio	0.050, 3.111	
	P-value	0.3617	
	RR[3] (95% CI), P-value	0.500 (0.110, 2.271), 0.6447	
	ARR[3] (95% CI), P-value	0.395 (0.056, 2.791), 0.3520	
	ARD[4]		
	Difference (95% C.I.)	-0.154 (-0.472, 0.165)	
	P-value	0.6447	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.6
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Age

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Age <= 41 Years	N1	31	36
	Responder - n(%)	9 (29.0%)	7 (19.4%)
	Difference in responder (KRN23 vs Placebo) - %	9.6%	
	Logistic Regression[1]		
	Responder - %	29.0%	19.4%
	95% C.I.	15.7%, 47.4%	9.4%, 35.9%
	Odds ratio (KRN23 vs Placebo)	1.695	
	95% C.I. of odds ratio	0.534, 5.374	
	P-value	0.3646	
	RR[3] (95% CI), P-value	1.493 (0.630, 3.539), 0.4008	
	ARR[3] (95% CI), P-value	1.695 (0.546, 5.260), 0.3613	
	ARD[4]		
	Difference (95% C.I.)	0.096 (-0.110, 0.301)	
	P-value	0.4008	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.6
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Age

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Age > 41 Years	N1	37	30
	Responder - n(%)	8 (21.6%)	5 (16.7%)
	Difference in responder (KRN23 vs Placebo) - %	5.0%	
	Logistic Regression[1]		
	Responder - %	21.4%	18.0%
	95% C.I.	10.6%, 38.4%	7.4%, 37.4%
	Odds ratio (KRN23 vs Placebo)	1.241	
	95% C.I. of odds ratio	0.338, 4.551	
	P-value	0.7409	
	RR[3] (95% CI), P-value	1.297 (0.473, 3.556), 0.7591	
	ARR[3] (95% CI), P-value	1.241 (0.347, 4.440), 0.7398	
	ARD[4]		
	Difference (95% C.I.)	0.050 (-0.139, 0.238)	
	P-value	0.7591	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.7
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Stiffness at BL cat <= 62.5	N1	39	41
	Responder - n(%)	9 (23.1%)	8 (19.5%)
	Difference in responder (KRN23 vs Placebo) - %	3.6%	
	Logistic Regression[1]		
	Responder - %	23.4%	20.0%
	95% C.I.	11.6%, 41.7%	8.6%, 39.9%
	Odds ratio (KRN23 vs Placebo)	1.224	
	95% C.I. of odds ratio	0.404, 3.710	
	P-value	0.7170	
	RR[3] (95% CI), P-value	1.183 (0.508, 2.755), 0.7876	
	ARR[3] (95% CI), P-value	1.224 (0.411, 3.646), 0.7160	
	ARD[4]		
	Difference (95% C.I.)	0.036 (-0.144, 0.215)	
	P-value	0.7876	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.7
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Stiffness at BL cat > 62.5	N1	29	25
	Responder - n(%)	8 (27.6%)	4 (16.0%)
	Difference in responder (KRN23 vs Placebo) - %	11.6%	
	Logistic Regression[1]		
	Responder - %	32.8%	19.1%
	95% C.I.	16.6%, 54.5%	7.1%, 42.2%
	Odds ratio (KRN23 vs Placebo)	2.069	
	95% C.I. of odds ratio	0.503, 8.508	
	P-value	0.3066	
	RR[3] (95% CI), P-value	1.724 (0.589, 5.049), 0.3466	
	ARR[3] (95% CI), P-value	2.069 (0.521, 8.227), 0.3017	
	ARD[4]		
	Difference (95% C.I.)	0.116 (-0.101, 0.333)	
	P-value	0.3466	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.8
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Physical Function at BL cat <= 47.8	N1	30	37
	Responder - n(%)	8 (26.7%)	10 (27.0%)
	Difference in responder (KRN23 vs Placebo) - %	-0.4%	
	Logistic Regression[1]		
	Responder - %	30.8%	32.8%
	95% C.I.	15.2%, 52.5%	16.4%, 54.9%
	Odds ratio (KRN23 vs Placebo)	0.910	
	95% C.I. of odds ratio	0.294, 2.816	
	P-value	0.8687	
	RR[3] (95% CI), P-value	0.987 (0.445, 2.186), 1.0000	
	ARR[3] (95% CI), P-value	0.910 (0.301, 2.756), 0.8681	
	ARD[4]		
	Difference (95% C.I.)	-0.004 (-0.217, 0.210)	
	P-value	1.0000	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.8
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Physical Function at BL cat > 47.8	N1	38	29
	Responder - n(%)	9 (23.7%)	2 (6.9%)
	Difference in responder (KRN23 vs Placebo) - %	16.8%	
	Logistic Regression[1]		
	Responder - %	26.3%	8.0%
	95% C.I.	13.7%, 44.4%	1.9%, 28.0%
	Odds ratio (KRN23 vs Placebo)	4.083	
	95% C.I. of odds ratio	0.778, 21.440	
	P-value	0.0950	
	RR[3] (95% CI), P-value	3.434 (0.802, 14.699), 0.0974	
	ARR[3] (95% CI), P-value	4.083 (0.802, 20.779), 0.0901	
	ARD[4]		
	Difference (95% C.I.)	0.168 (0.004, 0.332)	
	P-value	0.0974	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.9
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Pain Score at BL cat <= 50	N1	32	42
	Responder - n(%)	9 (28.1%)	10 (23.8%)
	Difference in responder (KRN23 vs Placebo) - %	4.3%	
	Logistic Regression[1]		
	Responder - %	28.9%	24.8%
	95% C.I.	14.8%, 48.6%	12.2%, 43.7%
	Odds ratio (KRN23 vs Placebo)	1.232	
	95% C.I. of odds ratio	0.420, 3.616	
	P-value	0.6998	
	RR[3] (95% CI), P-value	1.181 (0.545, 2.562), 0.7898	
	ARR[3] (95% CI), P-value	1.232 (0.428, 3.550), 0.6987	
	ARD[4]		
	Difference (95% C.I.)	0.043 (-0.159, 0.245)	
	P-value	0.7898	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.9
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Pain Score at BL cat > 50	N1	35	24
	Responder - n(%)	7 (20.0%)	2 (8.3%)
	Difference in responder (KRN23 vs Placebo) - %	11.7%	
	Logistic Regression[1]		
	Responder - %	24.8%	11.3%
	95% C.I.	11.8%, 44.9%	2.7%, 36.8%
	Odds ratio (KRN23 vs Placebo)	2.602	
	95% C.I. of odds ratio	0.454, 14.910	
	P-value	0.2771	
	RR[3] (95% CI), P-value	2.400 (0.545, 10.576), 0.2869	
	ARR[3] (95% CI), P-value	2.602 (0.472, 14.358), 0.2724	
	ARD[4]		
	Difference (95% C.I.)	0.117 (-0.056, 0.289)	
	P-value	0.2869	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.10
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Total Score at BL cat <= 49.5	N1	30	37
	Responder - n(%)	8 (26.7%)	10 (27.0%)
	Difference in responder (KRN23 vs Placebo) - %	-0.4%	
	Logistic Regression[1]		
	Responder - %	29.4%	31.4%
	95% C.I.	14.6%, 50.3%	15.6%, 53.2%
	Odds ratio (KRN23 vs Placebo)	0.910	
	95% C.I. of odds ratio	0.293, 2.824	
	P-value	0.8679	
	RR[3] (95% CI), P-value	0.987 (0.445, 2.186), 1.0000	
	ARR[3] (95% CI), P-value	0.910 (0.299, 2.764), 0.8674	
	ARD[4]		
	Difference (95% C.I.)	-0.004 (-0.217, 0.210)	
	P-value	1.0000	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.10
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
WOMAC Total Score at BL cat > 49.5	N1	38	29
	Responder - n(%)	9 (23.7%)	2 (6.9%)
	Difference in responder (KRN23 vs Placebo) - %	16.8%	
	Logistic Regression[1]		
	Responder - %	27.3%	8.2%
	95% C.I.	14.2%, 46.0%	2.0%, 28.5%
	Odds ratio (KRN23 vs Placebo)	4.181	
	95% C.I. of odds ratio	0.792, 22.064	
	P-value	0.0906	
	RR[3] (95% CI), P-value	3.434 (0.802, 14.699), 0.0974	
	ARR[3] (95% CI), P-value	4.181 (0.818, 21.381), 0.0858	
	ARD[4]		
	Difference (95% C.I.)	0.168 (0.004, 0.332)	
	P-value	0.0974	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.11
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Pain Medication Use at BL = Yes	N1	47	44
	Responder - n(%)	13 (27.7%)	7 (15.9%)
	Difference in responder (KRN23 vs Placebo) - %	11.8%	
	Logistic Regression[1]		
	Responder - %	29.3%	17.5%
	95% C.I.	17.3%, 45.1%	8.1%, 33.9%
	Odds ratio (KRN23 vs Placebo)	1.950	
	95% C.I. of odds ratio	0.681, 5.582	
	P-value	0.2103	
	RR[3] (95% CI), P-value	1.739 (0.764, 3.954), 0.2112	
	ARR[3] (95% CI), P-value	1.950 (0.691, 5.502), 0.2070	
	ARD[4]		
	Difference (95% C.I.)	0.118 (-0.050, 0.285)	
	P-value	0.2112	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.11
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Pain Medication Use at BL cat=No	N1	21	22
	Responder - n(%)	4 (19.0%)	5 (22.7%)
	Difference in responder (KRN23 vs Placebo) - %	-3.7%	
	Logistic Regression[1]		
	Responder - %	25.1%	31.2%
	95% C.I.	8.6%, 54.6%	11.1%, 62.2%
	Odds ratio (KRN23 vs Placebo)	0.738	
	95% C.I. of odds ratio	0.155, 3.509	
	P-value	0.6961	
	RR[3] (95% CI), P-value	0.838 (0.260, 2.703), 1.0000	
	ARR[3] (95% CI), P-value	0.738 (0.163, 3.347), 0.6940	
	ARD[4]		
	Difference (95% C.I.)	-0.037 (-0.279, 0.206)	
	P-value	1.0000	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.12
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Opioid Pain Medication Use at BL = Yes	N1	17	13
	Responder - n(%)	5 (29.4%)	1 (7.7%)
	Difference in responder (KRN23 vs Placebo) - %	21.7%	
	Logistic Regression[1]		
	Responder - %	33.0%	8.8%
	95% C.I.	12.9%, 62.1%	1.1%, 45.8%
	Odds ratio (KRN23 vs Placebo)	5.097	
	95% C.I. of odds ratio	0.455, 57.059	
	P-value	0.1778	
	RR[3] (95% CI), P-value	3.824 (0.506, 28.879), 0.1961	
	ARR[3] (95% CI), P-value	5.097 (0.507, 51.210), 0.1665	
	ARD[4]		
	Difference (95% C.I.)	0.217 (-0.043, 0.478)	
	P-value	0.1961	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.12
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Opioid Pain Medication Use at BL cat = No	N1	51	53
	Responder - n(%)	12 (23.5%)	11 (20.8%)
	Difference in responder (KRN23 vs Placebo) - %	2.8%	
	Logistic Regression[1]		
	Responder - %	26.2%	24.4%
	95% C.I.	15.0%, 41.7%	13.0%, 41.1%
	Odds ratio (KRN23 vs Placebo)	1.099	
	95% C.I. of odds ratio	0.424, 2.851	
	P-value	0.8441	
	RR[3] (95% CI), P-value	1.134 (0.551, 2.334), 0.8151	
	ARR[3] (95% CI), P-value	1.099 (0.429, 2.818), 0.8437	
	ARD[4]		
	Difference (95% C.I.)	0.028 (-0.132, 0.187)	
	P-value	0.8151	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.14
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Active fractures and pseudo-fractures at BL = Yes	N1	32	38
	Responder - n(%)	8 (25.0%)	6 (15.8%)
	Difference in responder (KRN23 vs Placebo) - %	9.2%	
	Logistic Regression[1]		
	Responder - %	31.0%	19.9%
	95% C.I.	14.4%, 54.4%	8.3%, 40.6%
	Odds ratio (KRN23 vs Placebo)	1.808	
	95% C.I. of odds ratio	0.535, 6.104	
	P-value	0.3350	
	RR[3] (95% CI), P-value	1.583 (0.613, 4.087), 0.3810	
	ARR[3] (95% CI), P-value	1.808 (0.547, 5.972), 0.3315	
	ARD[4]		
	Difference (95% C.I.)	0.092 (-0.097, 0.282)	
	P-value	0.3810	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.14
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
Active fractures and pseudo-fractures at BL = No	N1	36	28
	Responder - n(%)	9 (25.0%)	6 (21.4%)
	Difference in responder (KRN23 vs Placebo) - %	3.6%	
	Logistic Regression[1]		
	Responder - %	26.1%	23.6%
	95% C.I.	13.8%, 43.8%	10.2%, 45.5%
	Odds ratio (KRN23 vs Placebo)	1.145	
	95% C.I. of odds ratio	0.337, 3.890	
	P-value	0.8254	
	RR[3] (95% CI), P-value	1.167 (0.471, 2.891), 0.7754	
	ARR[3] (95% CI), P-value	1.145 (0.345, 3.796), 0.8247	
	ARD[4]		
	Difference (95% C.I.)	0.036 (-0.172, 0.243)	
	P-value	0.7754	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.15
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: 6MWT at baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
6MWT score at BL = High	N1	37	29
	Responder - n(%)	10 (27.0%)	3 (10.3%)
	Difference in responder (KRN23 vs Placebo) - %	16.7%	
	Logistic Regression[1]		
	Responder - %	30.4%	13.1%
	95% C.I.	16.3%, 49.4%	3.9%, 36.0%
	Odds ratio (KRN23 vs Placebo)	2.902	
	95% C.I. of odds ratio	0.683, 12.333	
	P-value	0.1460	
	RR[3] (95% CI), P-value	2.613 (0.791, 8.632), 0.1232	
	ARR[3] (95% CI), P-value	2.902 (0.702, 11.994), 0.1411	
	ARD[4]		
	Difference (95% C.I.)	0.167 (-0.014, 0.348)	
	P-value	0.1232	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.10.1.2.24.15
Subgroup Analysis: BPI Worst Pain responder analyses (at least 30% decrease from baseline in the endpoint of worst pain)
Primary Analysis Set_24 Weeks analysis
Subgroup: 6MWT at baseline

Subgroup	Statistics	KRN23 (N=68)	Placebo (N=66)
6MWT score at BL = Low	N1	30	36
	Responder - n(%)	6 (20.0%)	9 (25.0%)
	Difference in responder (KRN23 vs Placebo) - %	-5.0%	
	Logistic Regression[1]		
	Responder - %	22.2%	28.5%
	95% C.I.	9.9%, 42.8%	14.2%, 48.9%
	Odds ratio (KRN23 vs Placebo)	0.717	
	95% C.I. of odds ratio	0.215, 2.396	
	P-value	0.5842	
	RR[3] (95% CI), P-value	0.800 (0.321, 1.992), 0.7704	
	ARR[3] (95% CI), P-value	0.717 (0.220, 2.342), 0.5822	
	ARD[4]		
	Difference (95% C.I.)	-0.050 (-0.251, 0.151)	
	P-value	0.7704	

N1 = number of subjects in the analysis population of each subgroup. The percentage is based on the N1.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
Logistic regression estimates are from a logistic regression model which includes treatment group, region and actual randomization stratification by treatment as independent variables.
The estimated responder rate, 95% CI, odds ratio and 2-sided p-value are from the logistic regression model.
Data source: ADBPI.sas7bdat, ADSL.sas7bdat Program source: s-logistic_bpi.sas

Table 2.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Worst Pain at BL <= 6		N1	27	17	44	27	17	44
	Baseline	n	27	16	43	27	16	43
		Mean	417.26	383.63	404.74	59.75	55.30	58.09
		SD, SE	100.269, 19.297	112.350, 28.087	104.893, 15.996	13.242, 2.548	17.584, 4.396	14.957, 2.281
		Median	412.00	356.00	396.00	59.75	54.72	58.23
		Q1, Q3	366.00, 486.00	314.00, 455.50	334.00, 473.00	52.53, 69.56	42.13, 65.85	46.99, 68.63
		Min, Max	237.0, 615.0	203.0, 643.0	203.0, 643.0	33.5, 85.7	25.9, 92.4	25.9, 92.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Worst Pain at BL <= 6	Week 12	Baseline						
		n	27	16	43	27	16	43
		Mean	417.26	383.63	404.74	59.75	55.30	58.09
		SD, SE	100.269, 19.297	112.350, 28.087	104.893, 15.996	13.242, 2.548	17.584, 4.396	14.957, 2.281
		Median	412.00	356.00	396.00	59.75	54.72	58.23
		Q1, Q3	366.00, 486.00	314.00, 455.50	334.00, 473.00	52.53, 69.56	42.13, 65.85	46.99, 68.63
		Min, Max	237.0, 615.0	203.0, 643.0	203.0, 643.0	33.5, 85.7	25.9, 92.4	25.9, 92.4
		Observed						
		n	27	16	43	27	16	43
		Mean	406.41	416.44	410.14	58.38	59.97	58.97
		SD, SE	90.967, 17.507	101.140, 25.285	93.808, 14.306	12.463, 2.398	15.861, 3.965	13.660, 2.083
		Median	412.00	395.00	403.00	57.88	58.03	57.88
		Q1, Q3	348.00, 457.00	369.50, 481.00	360.00, 462.00	48.53, 68.96	52.94, 67.92	50.88, 68.07
		Min, Max	227.0, 573.0	240.0, 660.0	227.0, 660.0	32.1, 79.1	30.6, 94.9	30.6, 94.9

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Worst Pain at BL <= 6	Week 12	Change from Baseline						
		n	27	16	43	27	16	43
		Mean	-10.85	32.81	5.40	-1.37	4.67	0.88
		SD, SE	26.900, 5.177	33.044, 8.261	35.972, 5.486	3.948, 0.760	4.754, 1.188	5.144, 0.784
		Median	-6.00	25.00	0.00	-0.87	3.80	0.05
		Q1, Q3	-29.00, 4.00	12.50, 56.00	-16.00, 26.00	-4.32, 0.63	1.73, 8.45	-2.35, 3.99
		Min, Max	-64.0, 37.0	-16.0, 93.0	-64.0, 93.0	-8.7, 6.3	-2.4, 12.8	-8.7, 12.8
		GEE Estimates						
		LS Mean (SE)	-25.58 (6.204)	12.53 (7.993)		-3.79 (0.897)	1.55 (1.095)	
		95% CI	(-37.74, -13.42)	(-3.14, 28.20)		(-5.55, -2.03)	(-0.60, 3.69)	
		LS Mean Difference (SE)		38.11 (7.668)			5.34 (1.128)	
		95% CI		(23.08, 53.14)			(3.13, 7.55)	
		p-value		<.0001			<.0001	
		HedgesG (95% CI)		1.429 (0.740, 2.117)			1.360 (0.678, 2.042)	

6MWT = Six Minute Walk Test.
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Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Worst Pain at BL <= 6	Week 24	Baseline						
		n	27	16	43	27	16	43
		Mean	417.26	383.63	404.74	59.75	55.30	58.09
		SD, SE	100.269, 19.297	112.350, 28.087	104.893, 15.996	13.242, 2.548	17.584, 4.396	14.957, 2.281
		Median	412.00	356.00	396.00	59.75	54.72	58.23
		Q1, Q3	366.00, 486.00	314.00, 455.50	334.00, 473.00	52.53, 69.56	42.13, 65.85	46.99, 68.63
		Min, Max	237.0, 615.0	203.0, 643.0	203.0, 643.0	33.5, 85.7	25.9, 92.4	25.9, 92.4
		Observed						
		n	27	16	43	27	16	43
		Mean	400.44	415.31	405.98	57.43	59.96	58.37
		SD, SE	97.746, 18.811	100.213, 25.053	97.745, 14.906	12.734, 2.451	16.167, 4.042	13.974, 2.131
		Median	400.00	394.00	400.00	58.70	59.41	59.36
		Q1, Q3	335.00, 465.00	375.50, 450.00	365.00, 452.00	49.70, 63.96	53.11, 65.61	49.70, 63.96
		Min, Max	221.0, 617.0	231.0, 619.0	221.0, 619.0	31.3, 85.2	29.5, 89.1	29.5, 89.1

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Table 2.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Worst Pain at BL <= 6	Week 24	Change from Baseline						
		n	27	16	43	27	16	43
		Mean	-16.81	31.69	1.23	-2.32	4.66	0.27
		SD, SE	36.422, 7.009	49.976, 12.494	47.706, 7.275	5.122, 0.986	7.183, 1.796	6.806, 1.038
		Median	-18.00	28.00	-3.00	-2.59	4.01	-0.28
		Q1, Q3	-39.00, 9.00	-4.50, 74.00	-28.00, 28.00	-5.66, 1.33	-0.57, 10.39	-3.85, 3.83
		Min, Max	-109.0, 48.0	-38.0, 140.0	-109.0, 140.0	-15.1, 6.8	-5.2, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-31.54 (7.638)	11.40 (11.095)		-4.74 (1.091)	1.53 (1.588)	
		95% CI	(-46.51, -16.57)	(-10.34, 33.15)		(-6.88, -2.60)	(-1.58, 4.64)	
		LS Mean Difference (SE)		42.95 (12.539)			6.27 (1.817)	
		95% CI		(18.37, 67.52)			(2.71, 9.83)	
		p-value		0.0006			0.0006	
		HedgesG (95% CI)		1.110 (0.448, 1.771)			1.123 (0.460, 1.785)	

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Table 2.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Worst Pain at BL > 6		N1	39	51	90	39	51	90
	Baseline	n	38	51	89	38	51	89
		Mean	332.00	348.35	341.37	46.92	50.22	48.81
		SD, SE	91.271, 14.806	108.291, 15.164	101.153, 10.722	13.806, 2.240	15.221, 2.131	14.645, 1.552
		Median	330.50	347.00	336.00	46.56	50.60	48.13
		Q1, Q3	279.00, 376.00	283.00, 437.00	283.00, 416.00	38.96, 56.21	42.80, 62.54	40.01, 60.25
		Min, Max	160.0, 534.0	55.0, 538.0	55.0, 538.0	23.1, 88.4	7.6, 80.4	7.6, 88.4

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Table 2.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Worst Pain at BL > Week 12 6	Baseline							
		n	37	48	85	37	48	85
		Mean	333.43	346.63	340.88	47.10	49.98	48.73
		SD, SE	92.096, 15.141	110.984, 16.019	102.812, 11.152	13.947, 2.293	15.580, 2.249	14.874, 1.613
		Median	335.00	344.50	336.00	46.56	50.29	48.13
		Q1, Q3	289.00, 376.00	280.50, 443.50	283.00, 419.00	38.96, 56.21	42.65, 63.15	39.95, 60.25
		Min, Max	160.0, 534.0	55.0, 538.0	55.0, 538.0	23.1, 88.4	7.6, 80.4	7.6, 88.4
	Observed							
		n	37	48	85	37	48	85
		Mean	345.03	359.81	353.38	48.57	52.04	50.53
		SD, SE	98.685, 16.224	104.920, 15.144	101.919, 11.055	13.850, 2.277	15.034, 2.170	14.549, 1.578
		Median	328.00	358.00	350.00	48.13	51.92	50.35
		Q1, Q3	291.00, 403.00	308.50, 431.50	304.00, 423.00	41.29, 54.01	45.03, 63.78	43.35, 59.24
		Min, Max	170.0, 600.0	80.0, 542.0	80.0, 600.0	25.3, 84.6	11.1, 80.0	11.1, 84.6

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Table 2.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Worst Pain at BL > 6	Week 12	Change from Baseline						
		n	37	48	85	37	48	85
		Mean	11.59	13.19	12.49	1.47	2.06	1.81
		SD, SE	45.698, 7.513	43.416, 6.267	44.162, 4.790	6.366, 1.047	6.322, 0.913	6.310, 0.684
		Median	11.00	9.00	10.00	1.69	1.34	1.51
		Q1, Q3	-10.00, 40.00	-3.50, 32.50	-7.00, 37.00	-1.39, 5.89	-0.43, 4.68	-0.94, 5.75
		Min, Max	-95.0, 132.0	-136.0, 155.0	-136.0, 155.0	-14.5, 16.4	-16.8, 24.6	-16.8, 24.6
		GEE Estimates						
		LS Mean (SE)	4.04 (14.351)	7.87 (11.527)		0.10 (1.876)	1.17 (1.504)	
		95% CI	(-24.09, 32.16)	(-14.72, 30.46)		(-3.58, 3.78)	(-1.77, 4.12)	
		LS Mean Difference (SE)		3.83 (9.789)			1.07 (1.387)	
		95% CI		(-15.35, 23.02)			(-1.64, 3.79)	
		p-value		0.6955			0.4386	
		HedgesG (95% CI)		0.035 (-0.394, 0.464)			0.092 (-0.337, 0.521)	

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Table 2.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Worst Pain at BL > Week 24 6	Baseline							
		n	37	49	86	37	49	86
		Mean	330.81	351.63	342.67	46.63	50.75	48.97
		SD, SE	92.232, 15.163	108.734, 15.533	101.916, 10.990	13.878, 2.282	15.208, 2.173	14.710, 1.586
		Median	326.00	347.00	338.50	46.55	51.30	48.38
		Q1, Q3	279.00, 374.00	300.00, 437.00	283.00, 419.00	38.96, 53.01	43.16, 62.54	40.01, 60.37
		Min, Max	160.0, 534.0	55.0, 538.0	55.0, 538.0	23.1, 88.4	7.6, 80.4	7.6, 88.4
	Observed							
		n	37	49	86	37	49	86
		Mean	346.81	370.39	360.24	48.77	53.63	51.54
		SD, SE	102.749, 16.892	109.729, 15.676	106.811, 11.518	14.482, 2.381	15.605, 2.229	15.239, 1.643
		Median	340.00	360.00	357.00	48.84	53.56	50.36
		Q1, Q3	300.00, 411.00	317.00, 461.00	302.00, 437.00	42.46, 54.86	45.49, 65.60	44.29, 61.67
		Min, Max	156.0, 575.0	100.0, 587.0	100.0, 587.0	23.9, 82.9	13.8, 86.8	13.8, 86.8

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Table 2.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Worst Pain at BL > Week 24	6	Change from Baseline						
		n	37	49	86	37	49	86
		Mean	16.00	18.76	17.57	2.15	2.89	2.57
		SD, SE	42.145, 6.929	48.757, 6.965	45.789, 4.938	5.761, 0.947	7.187, 1.027	6.585, 0.710
		Median	14.00	19.00	16.50	2.08	2.69	2.58
		Q1, Q3	-6.00, 40.00	-4.00, 47.00	-6.00, 45.00	-0.86, 5.73	-0.42, 6.64	-0.81, 6.32
		Min, Max	-64.0, 125.0	-147.0, 138.0	-147.0, 138.0	-10.1, 15.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	7.16 (13.643)	13.44 (11.608)		0.58 (1.778)	2.00 (1.552)	
		95% CI	(-19.58, 33.90)	(-9.31, 36.19)		(-2.91, 4.06)	(-1.04, 5.05)	
		LS Mean Difference (SE)		6.28 (10.168)			1.43 (1.444)	
		95% CI		(-13.65, 26.21)			(-1.40, 4.26)	
		p-value		0.5371			0.3235	
		HedgesG (95% CI)		0.059 (-0.368, 0.486)			0.110 (-0.318, 0.537)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Average Pain at BL <= 6		N1	49	48	97	49	48	97
	Baseline	n	49	47	96	49	47	96
		Mean	385.86	368.43	377.32	54.78	53.31	54.06
		SD, SE	106.379, 15.197	100.163, 14.610	103.210, 10.534	15.403, 2.200	14.872, 2.169	15.084, 1.539
		Median	382.00	352.00	374.00	56.50	51.30	54.69
		Q1, Q3	291.00, 455.00	300.00, 437.00	296.50, 450.50	41.53, 65.35	42.80, 63.81	42.34, 64.58
		Min, Max	164.0, 615.0	146.0, 643.0	146.0, 643.0	24.7, 88.4	22.3, 92.4	22.3, 92.4

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Table 2.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Average Pain at BL <= 6	Week 12	Baseline						
		n	48	45	93	48	45	93
		Mean	388.08	366.84	377.81	55.09	53.08	54.12
		SD, SE	106.345, 15.350	102.088, 15.218	104.287, 10.814	15.413, 2.225	15.153, 2.259	15.238, 1.580
		Median	388.00	347.00	374.00	56.65	50.60	54.48
		Q1, Q3	293.50, 459.00	300.00, 437.00	297.00, 455.00	41.53, 66.10	42.80, 63.81	42.49, 65.35
		Min, Max	164.0, 615.0	146.0, 643.0	146.0, 643.0	24.7, 88.4	22.3, 92.4	22.3, 92.4
		Observed						
		n	48	45	93	48	45	93
		Mean	390.85	384.00	387.54	55.46	55.66	55.55
		SD, SE	102.972, 14.863	98.032, 14.614	100.125, 10.382	14.632, 2.112	14.799, 2.206	14.633, 1.517
		Median	403.00	377.00	386.00	55.99	54.87	54.99
		Q1, Q3	316.50, 465.00	323.00, 425.00	320.00, 457.00	44.51, 65.58	45.37, 67.69	45.37, 66.26
		Min, Max	175.0, 600.0	160.0, 660.0	160.0, 660.0	25.3, 84.6	24.5, 94.9	24.5, 94.9

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Table 2.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Average Pain at BL <= 6	Week 12	Change from Baseline						
		n	48	45	93	48	45	93
		Mean	2.77	17.16	9.73	0.37	2.58	1.44
		SD, SE	40.266, 5.812	36.085, 5.379	38.772, 4.020	5.556, 0.802	4.941, 0.737	5.355, 0.555
		Median	-1.50	14.00	6.00	-0.15	2.03	1.05
		Q1, Q3	-25.00, 29.00	3.00, 37.00	-8.00, 33.00	-3.50, 4.02	0.46, 4.85	-0.96, 4.74
		Min, Max	-64.0, 132.0	-136.0, 93.0	-136.0, 132.0	-9.5, 16.4	-16.8, 12.8	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-3.13 (7.930)	9.66 (7.400)		-0.59 (1.028)	1.48 (0.972)	
		95% CI	(-18.67, 12.41)	(-4.85, 24.16)		(-2.61, 1.42)	(-0.43, 3.38)	
		LS Mean Difference (SE)		12.79 (7.524)			2.07 (1.019)	
		95% CI		(-1.96, 27.54)			(0.07, 4.07)	
		p-value		0.0892			0.0422	
		HedgesG (95% CI)		0.368 (-0.042, 0.779)			0.411 (-0.000, 0.822)	

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Average Pain at BL <= 6	Week 24	Baseline						
		n	49	47	96	49	47	96
		Mean	385.86	368.43	377.32	54.78	53.31	54.06
		SD, SE	106.379, 15.197	100.163, 14.610	103.210, 10.534	15.403, 2.200	14.872, 2.169	15.084, 1.539
		Median	382.00	352.00	374.00	56.50	51.30	54.69
		Q1, Q3	291.00, 455.00	300.00, 437.00	296.50, 450.50	41.53, 65.35	42.80, 63.81	42.34, 64.58
		Min, Max	164.0, 615.0	146.0, 643.0	146.0, 643.0	24.7, 88.4	22.3, 92.4	22.3, 92.4
		Observed						
		n	49	47	96	49	47	96
		Mean	384.29	386.04	385.15	54.49	56.00	55.23
		SD, SE	108.251, 15.464	99.427, 14.503	103.482, 10.562	15.012, 2.145	15.074, 2.199	14.982, 1.529
		Median	400.00	379.00	392.00	54.74	56.07	56.03
		Q1, Q3	300.00, 465.00	321.00, 452.00	318.00, 452.00	43.12, 63.82	46.85, 65.60	45.58, 64.32
		Min, Max	158.0, 617.0	109.0, 619.0	109.0, 619.0	23.9, 85.2	16.7, 89.1	16.7, 89.1

6MWT = Six Minute Walk Test.
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Table 2.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Average Pain at BL <= 6	Week 24	Change from Baseline						
		n	49	47	96	49	47	96
		Mean	-1.57	17.62	7.82	-0.29	2.69	1.17
		SD, SE	45.143, 6.449	44.408, 6.478	45.580, 4.652	6.206, 0.887	6.381, 0.931	6.436, 0.657
		Median	-1.00	15.00	7.50	-0.08	2.27	1.09
		Q1, Q3	-32.00, 24.00	-14.00, 40.00	-22.00, 30.50	-4.47, 3.83	-2.05, 6.64	-3.00, 4.42
		Min, Max	-109.0, 125.0	-82.0, 140.0	-109.0, 140.0	-15.1, 15.7	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-7.35 (8.255)	10.27 (7.856)		-1.24 (1.081)	1.61 (1.093)	
		95% CI	(-23.52, 8.83)	(-5.13, 25.66)		(-3.36, 0.88)	(-0.53, 3.75)	
		LS Mean Difference (SE)		17.61 (8.831)			2.85 (1.234)	
		95% CI		(0.30, 34.92)			(0.43, 5.27)	
		p-value		0.0461			0.0208	
		HedgesG (95% CI)		0.421 (0.016, 0.825)			0.465 (0.060, 0.871)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Average Pain at BL > 6		N1	17	20	37	17	20	37
	Baseline	n	16	20	36	16	20	36
		Mean	310.94	329.40	321.19	44.49	47.03	45.90
		SD, SE	69.991, 17.498	127.316, 28.469	104.811, 17.469	10.159, 2.540	17.485, 3.910	14.555, 2.426
		Median	320.50	344.50	335.50	46.58	48.83	46.58
		Q1, Q3	288.50, 358.50	244.00, 453.50	276.50, 366.50	40.35, 51.09	37.34, 61.86	38.92, 54.19
		Min, Max	160.0, 419.0	55.0, 487.0	55.0, 487.0	23.1, 57.8	7.6, 70.0	7.6, 70.0

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Average Pain at BL > 6	Week 12	Baseline						
		n	16	19	35	16	19	35
		Mean	310.94	329.89	321.23	44.49	47.11	45.91
		SD, SE	69.991, 17.498	130.785, 30.004	106.341, 17.975	10.159, 2.540	17.961, 4.121	14.767, 2.496
		Median	320.50	347.00	336.00	46.58	52.05	46.61
		Q1, Q3	288.50, 358.50	241.00, 457.00	276.00, 369.00	40.35, 51.09	36.79, 62.54	37.88, 54.72
		Min, Max	160.0, 419.0	55.0, 487.0	55.0, 487.0	23.1, 57.8	7.6, 70.0	7.6, 70.0
		Observed						
		n	16	19	35	16	19	35
		Mean	311.13	350.21	332.34	44.47	50.16	47.56
		SD, SE	57.690, 14.422	122.747, 28.160	99.172, 16.763	7.890, 1.973	16.851, 3.866	13.640, 2.306
		Median	322.50	371.00	328.00	44.87	55.22	48.13
		Q1, Q3	292.50, 350.00	304.00, 442.00	294.00, 395.00	42.20, 49.73	45.15, 64.13	43.10, 55.70
		Min, Max	170.0, 381.0	80.0, 499.0	80.0, 499.0	26.0, 55.3	11.1, 69.1	11.1, 69.1

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Table 2.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Average Pain at BL > 6	Week 12	Change from Baseline						
		n	16	19	35	16	19	35
		Mean	0.19	20.32	11.11	-0.02	3.05	1.65
		SD, SE	41.291, 10.323	53.834, 12.350	48.887, 8.263	5.987, 1.497	8.239, 1.890	7.360, 1.244
		Median	-3.50	22.00	7.00	-0.44	3.11	0.91
		Q1, Q3	-14.50, 33.50	-12.00, 57.00	-14.00, 44.00	-2.08, 4.88	-1.59, 8.54	-1.86, 6.58
		Min, Max	-95.0, 60.0	-92.0, 155.0	-95.0, 155.0	-14.5, 8.7	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	-5.30 (13.669)	18.77 (5.617)		-1.40 (2.141)	2.36 (0.871)	
		95% CI	(-32.09, 21.49)	(7.76, 29.78)		(-5.60, 2.79)	(0.66, 4.07)	
		LS Mean Difference (SE)		24.07 (15.787)			3.77 (2.373)	
		95% CI		(-6.87, 55.01)			(-0.88, 8.42)	
		p-value		0.1273			0.1124	
		HedgesG (95% CI)		0.393 (-0.278, 1.065)			0.399 (-0.272, 1.071)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Average Pain at BL > 6	Week 24	Baseline						
		n	15	18	33	15	18	33
		Mean	306.60	336.22	322.76	43.62	48.11	46.07
		SD, SE	70.186, 18.122	131.550, 31.007	107.578, 18.727	9.869, 2.548	17.927, 4.225	14.782, 2.573
		Median	315.00	349.00	336.00	46.56	52.07	46.61
		Q1, Q3	277.00, 353.00	247.00, 457.00	277.00, 364.00	39.95, 50.22	37.88, 62.54	39.95, 53.65
		Min, Max	160.0, 419.0	55.0, 487.0	55.0, 487.0	23.1, 57.8	7.6, 70.0	7.6, 70.0
		Observed						
		n	15	18	33	15	18	33
		Mean	320.93	369.44	347.39	45.68	53.07	49.71
		SD, SE	68.034, 17.566	131.639, 31.028	108.778, 18.936	9.362, 2.417	18.035, 4.251	15.003, 2.612
		Median	340.00	360.00	347.00	48.03	54.92	49.31
		Q1, Q3	305.00, 361.00	300.00, 478.00	305.00, 400.00	43.97, 50.32	44.78, 69.45	44.78, 56.42
		Min, Max	156.0, 400.0	100.0, 524.0	100.0, 524.0	23.9, 56.4	13.8, 76.2	13.8, 76.2

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
BPI Average Pain at BL > 6	Week 24	Change from Baseline						
		n	15	18	33	15	18	33
		Mean	14.33	33.22	24.64	2.06	4.97	3.65
		SD, SE	32.202, 8.314	59.263, 13.968	49.099, 8.547	4.443, 1.147	8.914, 2.101	7.280, 1.267
		Median	17.00	36.50	26.00	2.52	5.00	3.71
		Q1, Q3	-6.00, 40.00	9.00, 55.00	0.00, 47.00	-0.81, 5.83	1.45, 8.75	0.10, 6.73
		Min, Max	-62.0, 61.0	-147.0, 138.0	-147.0, 138.0	-8.5, 7.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	4.81 (13.329)	31.11 (7.724)		0.05 (2.084)	4.22 (1.198)	
		95% CI	(-21.32, 30.93)	(15.97, 46.25)		(-4.04, 4.13)	(1.87, 6.57)	
		LS Mean Difference (SE)		26.30 (17.228)			4.17 (2.564)	
		95% CI		(-7.47, 60.06)			(-0.85, 9.20)	
		p-value		0.1269			0.1038	
		HedgesG (95% CI)		0.365 (-0.326, 1.056)			0.379 (-0.313, 1.070)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
North America/EU		N1	58	58	116	58	58	116
	Baseline	n	57	57	114	57	57	114
		Mean	366.11	359.14	362.62	52.35	51.92	52.14
		SD, SE	101.055, 13.385	102.400, 13.563	101.339, 9.491	14.636, 1.939	14.762, 1.955	14.636, 1.371
		Median	367.00	351.00	356.00	51.95	52.01	51.98
		Q1, Q3	291.00, 434.00	307.00, 437.00	297.00, 437.00	41.09, 60.25	43.16, 62.54	42.19, 62.10
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
North America/EU	Week 12	Baseline						
		n	56	54	110	56	54	110
		Mean	367.66	358.20	363.02	52.57	51.80	52.19
		SD, SE	101.278, 13.534	104.729, 14.252	102.622, 9.785	14.673, 1.961	15.085, 2.053	14.813, 1.412
		Median	368.00	349.00	356.00	52.30	51.30	51.98
		Q1, Q3	293.50, 437.00	300.00, 438.00	297.00, 438.00	41.31, 61.17	42.80, 63.76	42.19, 62.20
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	56	54	110	56	54	110
		Mean	369.00	380.15	374.47	52.75	55.05	53.88
		SD, SE	95.782, 12.799	102.194, 13.907	98.684, 9.409	13.678, 1.828	14.710, 2.002	14.176, 1.352
		Median	361.00	378.50	369.50	50.61	55.46	52.03
		Q1, Q3	302.00, 441.00	318.00, 440.00	311.00, 440.00	43.41, 61.99	45.37, 65.99	44.49, 64.13
		Min, Max	170.0, 600.0	80.0, 660.0	80.0, 660.0	25.3, 84.6	11.1, 94.9	11.1, 94.9

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
North America/EU	Week 12	Change from Baseline						
		n	56	54	110	56	54	110
		Mean	1.34	21.94	11.45	0.18	3.25	1.68
		SD, SE	38.606, 5.159	39.375, 5.358	40.162, 3.829	5.521, 0.738	5.899, 0.803	5.889, 0.561
		Median	-0.50	14.00	7.50	-0.03	2.10	1.14
		Q1, Q3	-19.50, 33.50	-2.00, 45.00	-10.00, 37.00	-2.65, 4.40	-0.27, 6.69	-1.38, 5.82
		Min, Max	-95.0, 93.0	-92.0, 155.0	-95.0, 155.0	-14.5, 11.9	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	1.22 (5.109)	21.03 (5.767)		0.12 (0.729)	3.13 (0.869)	
		95% CI	(-8.80, 11.23)	(9.73, 32.33)		(-1.31, 1.55)	(1.43, 4.83)	
		LS Mean Difference (SE)		19.81 (6.908)			3.01 (1.010)	
		95% CI		(6.27, 33.35)			(1.03, 4.99)	
		p-value		0.0041			0.0029	
		HedgesG (95% CI)		0.520 (0.140, 0.900)			0.529 (0.149, 0.909)	

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The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
North America/EU	Week 24	Baseline						
		n	56	55	111	56	55	111
		Mean	365.93	362.45	364.21	52.26	52.45	52.35
		SD, SE	101.960, 13.625	102.250, 13.787	101.654, 9.649	14.751, 1.971	14.673, 1.978	14.646, 1.390
		Median	366.50	352.00	358.00	51.93	52.05	52.01
		Q1, Q3	290.00, 437.00	307.00, 438.00	297.00, 438.00	40.93, 61.17	43.16, 63.76	42.19, 62.20
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	56	55	111	56	55	111
		Mean	368.50	387.22	377.77	52.58	56.16	54.36
		SD, SE	100.806, 13.471	104.702, 14.118	102.718, 9.750	14.031, 1.875	15.137, 2.041	14.634, 1.389
		Median	362.50	379.00	373.00	50.61	56.72	54.67
		Q1, Q3	303.50, 431.00	324.00, 461.00	314.00, 452.00	43.54, 62.03	46.63, 66.46	45.66, 63.96
		Min, Max	156.0, 617.0	100.0, 619.0	100.0, 619.0	23.9, 85.2	13.8, 89.1	13.8, 89.1

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
North America/EU	Week 24	Change from Baseline						
		n	56	55	111	56	55	111
		Mean	2.57	24.76	13.57	0.33	3.71	2.00
		SD, SE	42.103, 5.626	49.961, 6.737	47.286, 4.488	5.845, 0.781	7.374, 0.994	6.832, 0.648
		Median	5.50	21.00	14.00	0.85	3.00	2.08
		Q1, Q3	-26.00, 32.50	-4.00, 55.00	-18.00, 41.00	-3.77, 4.45	-0.42, 8.75	-2.59, 5.83
		Min, Max	-109.0, 125.0	-147.0, 140.0	-147.0, 140.0	-15.1, 15.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	1.64 (5.635)	23.94 (7.127)		0.14 (0.775)	3.61 (1.060)	
		95% CI	(-9.41, 12.68)	(9.97, 37.91)		(-1.38, 1.66)	(1.54, 5.69)	
		LS Mean Difference (SE)		22.30 (8.458)			3.48 (1.214)	
		95% CI		(5.73, 38.88)			(1.10, 5.86)	
		p-value		0.0084			0.0042	
		HedgesG (95% CI)		0.473 (0.096, 0.850)			0.502 (0.124, 0.880)	

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Table 2.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Asia		N1	8	10	18	8	10	18
	Baseline	n	8	10	18	8	10	18
		Mean	376.75	343.30	358.17	51.50	48.66	49.92
		SD, SE	126.322, 44.662	149.631, 47.317	136.808, 32.246	17.766, 6.281	21.714, 6.866	19.537, 4.605
		Median	401.00	333.50	358.50	54.67	48.36	51.92
		Q1, Q3	287.50, 465.00	240.00, 470.00	240.00, 470.00	36.30, 65.45	30.83, 66.03	31.07, 66.03
		Min, Max	164.0, 543.0	78.0, 541.0	78.0, 543.0	24.7, 74.4	12.1, 82.4	12.1, 82.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 2.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Asia	Week 12	Baseline						
		n	8	10	18	8	10	18
		Mean	376.75	343.30	358.17	51.50	48.66	49.92
		SD, SE	126.322, 44.662	149.631, 47.317	136.808, 32.246	17.766, 6.281	21.714, 6.866	19.537, 4.605
		Median	401.00	333.50	358.50	54.67	48.36	51.92
		Q1, Q3	287.50, 465.00	240.00, 470.00	240.00, 470.00	36.30, 65.45	30.83, 66.03	31.07, 66.03
		Min, Max	164.0, 543.0	78.0, 541.0	78.0, 543.0	24.7, 74.4	12.1, 82.4	12.1, 82.4
		Observed						
		n	8	10	18	8	10	18
		Mean	384.38	340.60	360.06	52.43	48.51	50.25
		SD, SE	130.013, 45.967	125.876, 39.805	125.895, 29.674	17.539, 6.201	19.216, 6.077	18.060, 4.257
		Median	426.00	339.50	390.50	57.15	47.47	52.69
		Q1, Q3	291.50, 462.00	251.00, 409.00	251.00, 457.00	39.00, 63.52	32.27, 64.75	32.27, 64.75
		Min, Max	175.0, 541.0	103.0, 525.0	103.0, 541.0	25.9, 74.2	15.9, 80.1	15.9, 80.1

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Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Asia	Week 12	Change from Baseline						
		n	8	10	18	8	10	18
		Mean	7.63	-2.70	1.89	0.93	-0.15	0.33
		SD, SE	52.923, 18.711	49.777, 15.741	49.929, 11.768	6.653, 2.352	6.303, 1.993	6.290, 1.483
		Median	-3.00	13.50	-0.50	-0.33	1.98	0.01
		Q1, Q3	-18.50, 6.00	-8.00, 25.00	-8.00, 21.00	-2.52, 0.96	-1.25, 3.57	-1.25, 3.20
		Min, Max	-40.0, 132.0	-136.0, 37.0	-136.0, 132.0	-5.2, 16.4	-16.8, 4.7	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	19.73 (16.389)	-1.34 (15.095)		2.34 (1.725)	0.26 (1.722)	
		95% CI	(-12.40, 51.85)	(-30.92, 28.25)		(-1.04, 5.73)	(-3.12, 3.63)	
		LS Mean Difference (SE)		-21.06 (22.701)			-2.09 (2.744)	
		95% CI		(-65.56, 23.43)			(-7.47, 3.29)	
		p-value		0.3534			0.4470	
		HedgesG (95% CI)		-0.181 (-1.113, 0.750)			-0.151 (-1.082, 0.780)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Asia	Week 24	Baseline						
		n	8	10	18	8	10	18
		Mean	376.75	343.30	358.17	51.50	48.66	49.92
		SD, SE	126.322, 44.662	149.631, 47.317	136.808, 32.246	17.766, 6.281	21.714, 6.866	19.537, 4.605
		Median	401.00	333.50	358.50	54.67	48.36	51.92
		Q1, Q3	287.50, 465.00	240.00, 470.00	240.00, 470.00	36.30, 65.45	30.83, 66.03	31.07, 66.03
		Min, Max	164.0, 543.0	78.0, 541.0	78.0, 543.0	24.7, 74.4	12.1, 82.4	12.1, 82.4
		Observed						
		n	8	10	18	8	10	18
		Mean	376.00	349.70	361.39	51.32	49.84	50.49
		SD, SE	127.659, 45.134	128.686, 40.694	125.133, 29.494	17.304, 6.118	19.382, 6.129	17.965, 4.234
		Median	417.00	338.00	399.50	55.15	51.41	53.83
		Q1, Q3	301.00, 437.00	247.00, 452.00	247.00, 440.00	40.36, 60.75	31.79, 64.94	31.79, 63.41
		Min, Max	158.0, 540.0	125.0, 538.0	125.0, 540.0	23.9, 74.1	19.4, 82.1	19.4, 82.1

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Table 2.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Asia	Week 24	Change from Baseline						
		n	8	10	18	8	10	18
		Mean	-0.75	6.40	3.22	-0.18	1.17	0.57
		SD, SE	50.239, 17.762	42.093, 13.311	44.617, 10.516	6.633, 2.345	5.776, 1.827	6.022, 1.419
		Median	-3.50	2.00	-3.00	-0.34	0.34	-0.28
		Q1, Q3	-19.00, 10.50	-14.00, 28.00	-14.00, 28.00	-2.48, 1.64	-2.05, 3.76	-2.05, 3.62
		Min, Max	-81.0, 99.0	-82.0, 73.0	-82.0, 99.0	-11.5, 12.4	-10.0, 11.1	-11.5, 12.4
		GEE Estimates						
		LS Mean (SE)	11.35 (17.018)	7.76 (13.263)		1.23 (2.008)	1.58 (1.702)	
		95% CI	(-22.00, 44.70)	(-18.23, 33.76)		(-2.71, 5.16)	(-1.75, 4.92)	
		LS Mean Difference (SE)		-3.59 (21.467)			0.36 (2.758)	
		95% CI		(-45.66, 38.48)			(-5.05, 5.76)	
		p-value		0.8672			0.8974	
		HedgesG (95% CI)		0.140 (-0.791, 1.071)			0.198 (-0.734, 1.129)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Sex = Male		N1	23	24	47	23	24	47
	Baseline	n	23	23	46	23	23	46
		Mean	386.48	370.83	378.65	51.40	49.53	50.46
		SD, SE	101.084, 21.077	108.604, 22.645	104.040, 15.340	14.490, 3.021	15.586, 3.250	14.910, 2.198
		Median	394.00	352.00	361.00	52.53	45.61	46.73
		Q1, Q3	289.00, 455.00	297.00, 470.00	296.00, 455.00	38.96, 59.12	38.71, 62.10	38.96, 61.14
		Min, Max	237.0, 615.0	203.0, 643.0	203.0, 643.0	31.1, 85.7	25.9, 92.4	25.9, 92.4

6MWT = Six Minute Walk Test.
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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 2.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Sex = Male	Week 12	Baseline						
		n	23	22	45	23	22	45
		Mean	386.48	373.14	379.96	51.40	49.71	50.57
		SD, SE	101.084, 21.077	110.580, 23.576	104.836, 15.628	14.490, 3.021	15.929, 3.396	15.060, 2.245
		Median	394.00	353.00	364.00	52.53	45.96	46.90
		Q1, Q3	289.00, 455.00	297.00, 470.00	296.00, 455.00	38.96, 59.12	38.71, 62.10	38.96, 61.14
		Min, Max	237.0, 615.0	203.0, 643.0	203.0, 643.0	31.1, 85.7	25.9, 92.4	25.9, 92.4
		Observed						
		n	23	22	45	23	22	45
		Mean	394.39	392.64	393.53	52.34	52.37	52.35
		SD, SE	95.367, 19.885	110.615, 23.583	101.921, 15.194	13.180, 2.748	16.185, 3.451	14.556, 2.170
		Median	405.00	385.00	398.00	50.62	50.07	50.62
		Q1, Q3	325.00, 467.00	329.00, 462.00	328.00, 462.00	43.00, 60.96	43.35, 64.75	43.35, 60.96
		Min, Max	200.0, 573.0	204.0, 660.0	200.0, 660.0	25.9, 79.1	27.5, 94.9	25.9, 94.9

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Table 2.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Sex = Male	Week 12	Change from Baseline						
		n	23	22	45	23	22	45
		Mean	7.91	19.50	13.58	0.94	2.66	1.78
		SD, SE	45.928, 9.577	45.675, 9.738	45.658, 6.806	5.904, 1.231	5.822, 1.241	5.862, 0.874
		Median	-1.00	17.00	11.00	-0.10	2.47	1.44
		Q1, Q3	-21.00, 36.00	6.00, 37.00	-8.00, 36.00	-2.92, 4.75	0.83, 4.74	-0.96, 4.74
		Min, Max	-55.0, 132.0	-136.0, 93.0	-136.0, 132.0	-7.6, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-3.08 (14.997)	7.35 (14.681)		-0.86 (1.892)	0.80 (1.869)	
		95% CI	(-32.47, 26.32)	(-21.42, 36.13)		(-4.56, 2.85)	(-2.86, 4.47)	
		LS Mean Difference (SE)		10.43 (12.818)			1.66 (1.623)	
		95% CI		(-14.69, 35.55)			(-1.52, 4.84)	
		p-value		0.4158			0.3066	
		HedgesG (95% CI)		0.243 (-0.344, 0.830)			0.283 (-0.305, 0.870)	

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Table 2.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Sex = Male	Week 24	Baseline						
		n	23	21	44	23	21	44
		Mean	386.48	380.62	383.68	51.40	50.69	51.06
		SD, SE	101.084, 21.077	107.452, 23.448	102.989, 15.526	14.490, 3.021	15.624, 3.409	14.869, 2.242
		Median	394.00	354.00	367.50	52.53	46.49	46.95
		Q1, Q3	289.00, 455.00	331.00, 470.00	296.50, 455.00	38.96, 59.12	42.07, 62.10	40.03, 61.16
		Min, Max	237.0, 615.0	203.0, 643.0	203.0, 643.0	31.1, 85.7	25.9, 92.4	25.9, 92.4
		Observed						
		n	23	21	44	23	21	44
		Mean	392.26	403.57	397.66	52.07	53.88	52.93
		SD, SE	101.480, 21.160	103.071, 22.492	101.206, 15.257	13.847, 2.887	15.484, 3.379	14.507, 2.187
		Median	405.00	425.00	415.00	51.88	55.92	52.81
		Q1, Q3	310.00, 443.00	345.00, 461.00	321.50, 456.50	42.46, 61.67	44.29, 62.70	43.22, 62.19
		Min, Max	208.0, 617.0	231.0, 619.0	208.0, 619.0	27.0, 85.2	29.5, 89.1	27.0, 89.1

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Sex = Male	Week 24	Change from Baseline						
		n	23	21	44	23	21	44
		Mean	5.78	22.95	13.98	0.67	3.19	1.87
		SD, SE	56.780, 11.839	51.044, 11.139	54.190, 8.169	7.500, 1.564	6.883, 1.502	7.241, 1.092
		Median	7.00	19.00	10.00	0.97	2.69	1.35
		Q1, Q3	-32.00, 42.00	-4.00, 34.00	-19.50, 41.50	-4.09, 5.57	-0.42, 4.47	-2.62, 5.52
		Min, Max	-109.0, 125.0	-82.0, 140.0	-109.0, 140.0	-15.1, 15.7	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-5.21 (15.841)	9.89 (14.406)		-1.12 (2.039)	1.21 (1.887)	
		95% CI	(-36.25, 25.84)	(-18.35, 38.13)		(-5.12, 2.87)	(-2.49, 4.91)	
		LS Mean Difference (SE)		15.10 (14.957)			2.33 (1.996)	
		95% CI		(-14.22, 44.41)			(-1.58, 6.25)	
		p-value		0.3128			0.2424	
		HedgesG (95% CI)		0.304 (-0.291, 0.899)			0.335 (-0.261, 0.931)	

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Table 2.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Sex = Female		N1	43	44	87	43	44	87
	Baseline	n	42	44	86	42	44	86
		Mean	356.98	349.43	353.12	52.71	52.43	52.57
		SD, SE	104.373, 16.105	110.437, 16.649	106.953, 11.533	15.275, 2.357	16.041, 2.418	15.580, 1.680
		Median	365.00	344.50	352.00	52.30	52.87	52.37
		Q1, Q3	291.00, 412.00	291.50, 420.00	291.00, 417.00	41.53, 62.20	43.51, 65.76	42.49, 63.20
		Min, Max	160.0, 543.0	55.0, 541.0	55.0, 543.0	23.1, 88.4	7.6, 82.4	7.6, 88.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Sex = Female	Week 12	Baseline						
		n	41	42	83	41	42	83
		Mean	358.88	346.83	352.78	53.02	52.15	52.58
		SD, SE	104.930, 16.387	112.393, 17.343	108.276, 11.885	15.331, 2.394	16.359, 2.524	15.769, 1.731
		Median	366.00	341.50	351.00	52.64	52.07	52.10
		Q1, Q3	300.00, 412.00	283.00, 423.00	291.00, 423.00	42.30, 62.20	43.16, 66.00	42.49, 65.52
		Min, Max	160.0, 543.0	55.0, 541.0	55.0, 543.0	23.1, 88.4	7.6, 82.4	7.6, 88.4
		Observed						
		n	41	42	83	41	42	83
		Mean	357.76	364.19	361.01	52.92	54.89	53.92
		SD, SE	100.585, 15.709	103.674, 15.997	101.587, 11.151	14.677, 2.292	15.269, 2.356	14.921, 1.638
		Median	340.00	366.50	362.00	51.01	56.01	54.82
		Q1, Q3	294.00, 437.00	311.00, 426.00	304.00, 437.00	43.48, 62.25	45.69, 65.99	45.15, 65.48
		Min, Max	170.0, 600.0	80.0, 535.0	80.0, 600.0	25.3, 84.6	11.1, 80.1	11.1, 84.6

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Sex = Female	Week 12	Change from Baseline						
		n	41	42	83	41	42	83
		Mean	-1.12	17.36	8.23	-0.10	2.74	1.34
		SD, SE	36.827, 5.751	40.036, 6.178	39.362, 4.321	5.495, 0.858	6.222, 0.960	6.011, 0.660
		Median	-2.00	11.00	4.00	-0.20	1.75	0.64
		Q1, Q3	-18.00, 26.00	-4.00, 43.00	-10.00, 35.00	-2.38, 3.94	-0.51, 6.59	-1.39, 5.71
		Min, Max	-95.0, 84.0	-92.0, 155.0	-95.0, 155.0	-14.5, 11.9	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	-3.38 (6.823)	14.16 (6.318)		-0.52 (1.026)	2.27 (0.973)	
		95% CI	(-16.75, 10.00)	(1.77, 26.54)		(-2.53, 1.49)	(0.36, 4.17)	
		LS Mean Difference (SE)		17.53 (7.789)			2.79 (1.202)	
		95% CI		(2.27, 32.80)			(0.43, 5.15)	
		p-value		0.0244			0.0203	
		HedgesG (95% CI)		0.470 (0.034, 0.906)			0.474 (0.038, 0.911)	

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Sex = Female	Week 24	Baseline						
		n	41	44	85	41	44	85
		Mean	356.51	349.43	352.85	52.59	52.43	52.51
		SD, SE	105.625, 16.496	110.437, 16.649	107.558, 11.666	15.445, 2.412	16.041, 2.418	15.663, 1.699
		Median	364.00	344.50	351.00	51.95	52.87	52.10
		Q1, Q3	291.00, 412.00	291.50, 420.00	291.00, 417.00	41.53, 62.20	43.51, 65.76	42.49, 63.20
		Min, Max	160.0, 543.0	55.0, 541.0	55.0, 543.0	23.1, 88.4	7.6, 82.4	7.6, 88.4
		Observed						
		n	41	44	85	41	44	85
		Mean	356.63	370.89	364.01	52.62	55.82	54.28
		SD, SE	103.455, 16.157	110.524, 16.662	106.776, 11.581	14.759, 2.305	16.171, 2.438	15.497, 1.681
		Median	361.00	374.00	364.00	52.75	56.51	54.86
		Q1, Q3	302.00, 405.00	320.00, 448.50	310.00, 420.00	45.66, 62.39	47.73, 69.15	46.63, 64.68
		Min, Max	156.0, 575.0	100.0, 587.0	100.0, 587.0	23.9, 82.9	13.8, 86.8	13.8, 86.8

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Sex = Female	Week 24	Change from Baseline						
		n	41	44	85	41	44	85
		Mean	0.12	21.45	11.16	0.03	3.39	1.77
		SD, SE	33.106, 5.170	48.572, 7.323	42.949, 4.658	4.862, 0.759	7.382, 1.113	6.480, 0.703
		Median	0.00	20.00	13.00	0.10	2.89	2.07
		Q1, Q3	-23.00, 26.00	-4.50, 50.00	-13.00, 38.00	-3.50, 3.83	-0.55, 7.65	-1.71, 5.73
		Min, Max	-81.0, 59.0	-147.0, 138.0	-147.0, 138.0	-11.5, 8.5	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-3.06 (6.873)	18.58 (7.613)		-0.54 (1.022)	2.95 (1.151)	
		95% CI	(-16.54, 10.41)	(3.66, 33.50)		(-2.55, 1.46)	(0.69, 5.21)	
		LS Mean Difference (SE)		21.64 (8.576)			3.50 (1.294)	
		95% CI		(4.84, 38.45)			(0.96, 6.03)	
		p-value		0.0116			0.0069	
		HedgesG (95% CI)		0.499 (0.067, 0.931)			0.522 (0.089, 0.954)	

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Race = White		N1	53	55	108	53	55	108
	Baseline	n	52	54	106	52	54	106
		Mean	369.37	361.13	365.17	52.82	52.33	52.57
		SD, SE	103.623, 14.370	100.969, 13.740	101.875, 9.895	14.931, 2.071	14.396, 1.959	14.593, 1.417
		Median	370.00	351.50	359.00	52.30	52.03	52.03
		Q1, Q3	293.50, 443.00	308.00, 437.00	300.00, 438.00	41.31, 61.17	43.86, 62.54	42.80, 62.10
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Race = White	Week 12	Baseline						
		n	52	51	103	52	51	103
		Mean	369.37	360.25	364.85	52.82	52.23	52.53
		SD, SE	103.623, 14.370	103.405, 14.480	103.108, 10.160	14.931, 2.071	14.729, 2.062	14.762, 1.455
		Median	370.00	351.00	358.00	52.30	52.01	52.01
		Q1, Q3	293.50, 443.00	307.00, 438.00	300.00, 440.00	41.31, 61.17	43.16, 63.76	42.30, 62.20
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	52	51	103	52	51	103
		Mean	370.15	383.57	376.80	52.93	55.68	54.29
		SD, SE	97.395, 13.506	99.941, 13.995	98.410, 9.697	13.849, 1.921	14.181, 1.986	14.014, 1.381
		Median	363.50	380.00	375.00	50.75	55.70	53.75
		Q1, Q3	302.00, 441.00	323.00, 440.00	313.00, 440.00	43.41, 61.99	46.10, 65.99	45.15, 64.13
		Min, Max	170.0, 600.0	80.0, 660.0	80.0, 660.0	25.3, 84.6	11.1, 94.9	11.1, 94.9

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 2.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Race = White	Week 12	Change from Baseline						
		n	52	51	103	52	51	103
		Mean	0.79	23.31	11.94	0.11	3.45	1.76
		SD, SE	38.503, 5.339	40.045, 5.607	40.686, 4.009	5.522, 0.766	6.004, 0.841	5.977, 0.589
		Median	-0.50	17.00	8.00	-0.03	2.40	1.24
		Q1, Q3	-19.50, 29.50	0.00, 45.00	-10.00, 37.00	-2.65, 4.02	0.05, 7.10	-1.35, 5.82
		Min, Max	-95.0, 93.0	-92.0, 155.0	-95.0, 155.0	-14.5, 11.9	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	1.14 (5.371)	22.53 (6.018)		0.11 (0.775)	3.37 (0.906)	
		95% CI	(-9.39, 11.67)	(10.74, 34.33)		(-1.41, 1.63)	(1.59, 5.14)	
		LS Mean Difference (SE)		21.39 (7.098)			3.25 (1.039)	
		95% CI		(7.48, 35.31)			(1.21, 5.29)	
		p-value		0.0026			0.0018	
		HedgesG (95% CI)		0.564 (0.170, 0.958)			0.569 (0.175, 0.963)	

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Table 2.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Race = White	Week 24	Baseline						
		n	51	53	104	51	53	104
		Mean	369.24	361.91	365.50	52.73	52.46	52.59
		SD, SE	104.650, 14.654	101.773, 13.980	102.757, 10.076	15.064, 2.109	14.504, 1.992	14.710, 1.442
		Median	369.00	352.00	359.00	51.95	52.05	52.03
		Q1, Q3	291.00, 446.00	308.00, 437.00	300.00, 439.00	41.09, 62.10	43.86, 62.54	42.55, 62.15
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	51	53	104	51	53	104
		Mean	370.88	387.58	379.39	52.93	56.31	54.65
		SD, SE	102.790, 14.394	104.495, 14.353	103.499, 10.149	14.232, 1.993	14.992, 2.059	14.652, 1.437
		Median	367.00	379.00	376.50	51.88	56.72	54.80
		Q1, Q3	305.00, 437.00	335.00, 461.00	319.50, 450.00	43.97, 62.39	46.85, 65.60	46.35, 63.89
		Min, Max	156.0, 617.0	100.0, 619.0	100.0, 619.0	23.9, 85.2	13.8, 89.1	13.8, 89.1

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Race = White	Week 24	Change from Baseline						
		n	51	53	104	51	53	104
		Mean	1.65	25.68	13.89	0.20	3.85	2.06
		SD, SE	42.664, 5.974	50.677, 6.961	48.227, 4.729	5.931, 0.831	7.480, 1.027	6.977, 0.684
		Median	7.00	21.00	14.50	0.97	3.17	2.23
		Q1, Q3	-30.00, 31.00	-4.00, 55.00	-17.50, 40.50	-4.47, 4.43	-0.42, 8.75	-2.53, 5.78
		Min, Max	-109.0, 125.0	-147.0, 140.0	-147.0, 140.0	-15.1, 15.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	1.02 (6.000)	25.24 (7.364)		0.05 (0.832)	3.81 (1.095)	
		95% CI	(-10.74, 12.78)	(10.81, 39.68)		(-1.58, 1.68)	(1.67, 5.96)	
		LS Mean Difference (SE)		24.22 (8.742)			3.76 (1.253)	
		95% CI		(7.09, 41.36)			(1.30, 6.22)	
		p-value		0.0056			0.0027	
		HedgesG (95% CI)		0.504 (0.113, 0.894)			0.530 (0.139, 0.921)	

6MWT = Six Minute Walk Test.
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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Race = Non-White		N1	13	13	26	13	13	26
	Baseline	n	13	13	26	13	13	26
		Mean	359.62	338.69	349.15	49.94	47.70	48.82
		SD, SE	106.363, 29.500	142.958, 39.649	123.911, 24.301	15.151, 4.202	21.071, 5.844	18.017, 3.533
		Median	364.00	333.00	334.50	52.53	45.42	48.93
		Q1, Q3	279.00, 434.00	240.00, 470.00	264.00, 444.00	40.01, 61.34	30.83, 66.03	33.70, 63.20
		Min, Max	164.0, 543.0	78.0, 541.0	78.0, 543.0	24.7, 74.4	12.1, 82.4	12.1, 82.4

6MWT = Six Minute Walk Test.
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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 2.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Race = Non-White	Week 12	Baseline						
		n	12	13	25	12	13	25
		Mean	366.33	338.69	351.96	50.77	47.70	49.18
		SD, SE	108.174, 31.227	142.958, 39.649	125.620, 25.124	15.515, 4.479	21.071, 5.844	18.297, 3.659
		Median	373.00	333.00	335.00	52.66	45.42	51.30
		Q1, Q3	292.00, 439.00	240.00, 470.00	264.00, 444.00	38.13, 62.27	30.83, 66.03	33.70, 63.20
		Min, Max	164.0, 543.0	78.0, 541.0	78.0, 543.0	24.7, 74.4	12.1, 82.4	12.1, 82.4
		Observed						
		n	12	13	25	12	13	25
		Mean	374.25	336.31	354.52	51.73	47.55	49.56
		SD, SE	113.063, 32.639	124.753, 34.600	118.385, 23.677	15.516, 4.479	19.174, 5.318	17.283, 3.457
		Median	397.50	329.00	350.00	53.96	45.69	49.25
		Q1, Q3	307.00, 462.00	251.00, 409.00	275.00, 457.00	42.89, 63.52	32.27, 64.75	35.13, 64.75
		Min, Max	175.0, 541.0	103.0, 525.0	103.0, 541.0	25.9, 74.2	15.9, 80.1	15.9, 80.1

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Table 2.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Race = Non-White	Week 12	Change from Baseline						
		n	12	13	25	12	13	25
		Mean	7.92	-2.38	2.56	0.96	-0.16	0.38
		SD, SE	48.388, 13.968	43.372, 12.029	45.180, 9.036	6.239, 1.801	5.493, 1.524	5.767, 1.153
		Median	-3.00	11.00	-2.00	-0.33	1.43	-0.20
		Q1, Q3	-21.50, 25.50	-8.00, 21.00	-12.00, 21.00	-3.08, 3.79	-1.25, 3.20	-1.59, 3.20
		Min, Max	-44.0, 132.0	-136.0, 37.0	-136.0, 132.0	-6.3, 16.4	-16.8, 4.7	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	6.58 (11.523)	-5.24 (13.301)		0.78 (1.417)	-0.40 (1.578)	
		95% CI	(-16.01, 29.16)	(-31.31, 20.83)		(-2.00, 3.55)	(-3.49, 2.70)	
		LS Mean Difference (SE)		-11.82 (17.348)			-1.17 (2.142)	
		95% CI		(-45.82, 22.18)			(-5.37, 3.03)	
		p-value		0.4956			0.5840	
		HedgesG (95% CI)		-0.208 (-0.995, 0.578)			-0.177 (-0.963, 0.609)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Race = Non-White	Week 24	Baseline						
		n	13	12	25	13	12	25
		Mean	359.62	348.92	354.48	49.94	49.26	49.61
		SD, SE	106.363, 29.500	144.265, 41.646	123.391, 24.678	15.151, 4.202	21.216, 6.125	17.922, 3.584
		Median	364.00	333.50	335.00	52.53	48.36	51.30
		Q1, Q3	279.00, 434.00	252.00, 480.00	276.00, 444.00	40.01, 61.34	32.26, 67.52	34.72, 63.20
		Min, Max	164.0, 543.0	78.0, 541.0	78.0, 543.0	24.7, 74.4	12.1, 82.4	12.1, 82.4
		Observed						
		n	13	12	25	13	12	25
		Mean	363.77	354.33	359.24	50.45	50.26	50.36
		SD, SE	109.757, 30.441	125.882, 36.339	115.366, 23.073	15.120, 4.194	19.181, 5.537	16.821, 3.364
		Median	394.00	338.00	356.00	53.75	51.41	53.56
		Q1, Q3	302.00, 434.00	257.50, 469.50	268.00, 440.00	42.46, 58.08	33.03, 66.73	37.36, 63.41
		Min, Max	158.0, 540.0	125.0, 538.0	125.0, 540.0	23.9, 74.1	19.4, 82.1	19.4, 82.1

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Race = Non-White	Week 24	Change from Baseline						
		n	13	12	25	13	12	25
		Mean	4.15	5.42	4.76	0.51	1.00	0.74
		SD, SE	44.875, 12.446	38.173, 11.020	40.929, 8.186	5.978, 1.658	5.244, 1.514	5.526, 1.105
		Median	-4.00	0.50	-3.00	-0.41	0.14	-0.28
		Q1, Q3	-19.00, 12.00	-9.00, 28.00	-14.00, 28.00	-2.65, 2.07	-1.28, 3.69	-2.05, 3.62
		Min, Max	-81.0, 99.0	-82.0, 73.0	-82.0, 99.0	-11.5, 12.4	-10.0, 11.1	-11.5, 12.4
		GEE Estimates						
		LS Mean (SE)	4.74 (11.249)	1.76 (12.038)		0.58 (1.437)	0.64 (1.578)	
		95% CI	(-17.30, 26.79)	(-21.84, 25.35)		(-2.23, 3.40)	(-2.45, 3.74)	
		LS Mean Difference (SE)		-2.99 (15.749)			0.06 (2.053)	
		95% CI		(-33.86, 27.88)			(-3.96, 4.08)	
		p-value		0.8495			0.9771	
		HedgesG (95% CI)		0.028 (-0.757, 0.813)			0.082 (-0.703, 0.866)	

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Age <= 41 Years		N1	36	31	67	36	31	67
	Baseline	n	36	30	66	36	30	66
		Mean	374.11	368.33	371.48	51.11	50.45	50.81
		SD, SE	97.877, 16.313	105.575, 19.275	100.696, 12.395	14.097, 2.349	15.090, 2.755	14.447, 1.778
		Median	370.00	359.00	364.00	51.06	48.48	50.10
		Q1, Q3	300.50, 449.50	307.00, 470.00	301.00, 455.00	40.39, 60.61	42.80, 62.54	41.54, 62.10
		Min, Max	160.0, 543.0	55.0, 534.0	55.0, 543.0	23.1, 76.5	7.6, 71.2	7.6, 76.5

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The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Age <= 41 Years	Week 12	Baseline						
		n	35	28	63	35	28	63
		Mean	376.83	365.79	371.92	51.43	49.88	50.74
		SD, SE	97.918, 16.551	108.904, 20.581	102.242, 12.881	14.171, 2.395	15.457, 2.921	14.655, 1.846
		Median	371.00	356.00	364.00	51.90	46.74	49.98
		Q1, Q3	301.00, 455.00	303.50, 471.50	301.00, 457.00	40.76, 62.10	42.44, 64.03	41.54, 62.54
		Min, Max	160.0, 543.0	55.0, 534.0	55.0, 543.0	23.1, 76.5	7.6, 71.2	7.6, 76.5
		Observed						
		n	35	28	63	35	28	63
		Mean	386.57	380.79	384.00	52.72	51.99	52.39
		SD, SE	95.103, 16.075	100.530, 18.998	96.796, 12.195	13.515, 2.284	14.514, 2.743	13.858, 1.746
		Median	392.00	392.50	392.00	51.57	50.18	51.01
		Q1, Q3	325.00, 457.00	310.50, 442.50	320.00, 453.00	43.89, 61.74	45.03, 63.78	44.90, 62.25
		Min, Max	179.0, 600.0	80.0, 535.0	80.0, 600.0	25.3, 84.6	11.1, 79.1	11.1, 84.6

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Age <= 41 Years	Week 12	Change from Baseline						
		n	35	28	63	35	28	63
		Mean	9.74	15.00	12.08	1.29	2.10	1.65
		SD, SE	42.847, 7.243	42.996, 8.126	42.647, 5.373	5.712, 0.965	5.616, 1.061	5.638, 0.710
		Median	-2.00	10.50	6.00	-0.20	1.44	0.89
		Q1, Q3	-15.00, 40.00	-1.50, 40.50	-10.00, 40.00	-2.09, 5.82	-0.16, 5.36	-1.35, 5.82
		Min, Max	-64.0, 132.0	-136.0, 93.0	-136.0, 132.0	-8.7, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-0.57 (10.225)	3.72 (11.877)		-0.22 (1.299)	0.44 (1.506)	
		95% CI	(-20.61, 19.47)	(-19.56, 27.00)		(-2.77, 2.32)	(-2.51, 3.40)	
		LS Mean Difference (SE)		4.29 (10.062)			0.67 (1.334)	
		95% CI		(-15.43, 24.01)			(-1.95, 3.28)	
		p-value		0.6701			0.6163	
		HedgesG (95% CI)		0.119 (-0.378, 0.616)			0.140 (-0.358, 0.637)	

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Table 2.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Age <= 41 Years	Week 24	Baseline						
		n	36	30	66	36	30	66
		Mean	374.11	368.33	371.48	51.11	50.45	50.81
		SD, SE	97.877, 16.313	105.575, 19.275	100.696, 12.395	14.097, 2.349	15.090, 2.755	14.447, 1.778
		Median	370.00	359.00	364.00	51.06	48.48	50.10
		Q1, Q3	300.50, 449.50	307.00, 470.00	301.00, 455.00	40.39, 60.61	42.80, 62.54	41.54, 62.10
		Min, Max	160.0, 543.0	55.0, 534.0	55.0, 543.0	23.1, 76.5	7.6, 71.2	7.6, 76.5
		Observed						
		n	36	30	66	36	30	66
		Mean	387.53	394.27	390.59	52.94	54.14	53.49
		SD, SE	95.709, 15.951	105.221, 19.211	99.415, 12.237	13.410, 2.235	15.464, 2.823	14.279, 1.758
		Median	402.50	390.00	400.50	53.25	54.73	53.64
		Q1, Q3	336.50, 452.50	324.00, 478.00	336.00, 470.00	46.87, 62.03	45.49, 65.54	46.23, 63.96
		Min, Max	174.0, 575.0	100.0, 587.0	100.0, 587.0	25.2, 81.2	13.8, 86.8	13.8, 86.8

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The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 2.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Age <= 41 Years	Week 24	Change from Baseline						
		n	36	30	66	36	30	66
		Mean	13.42	25.93	19.11	1.82	3.69	2.67
		SD, SE	41.781, 6.964	41.299, 7.540	41.718, 5.135	5.585, 0.931	5.585, 1.020	5.620, 0.692
		Median	13.00	20.00	16.50	1.81	2.89	2.43
		Q1, Q3	-11.00, 40.50	4.00, 53.00	-4.00, 45.00	-1.41, 5.52	0.57, 7.99	-0.41, 6.24
		Min, Max	-81.0, 125.0	-82.0, 105.0	-82.0, 125.0	-11.5, 15.7	-10.0, 15.7	-11.5, 15.7
		GEE Estimates						
		LS Mean (SE)	3.65 (9.882)	15.35 (10.942)		0.38 (1.252)	2.12 (1.410)	
		95% CI	(-15.72, 23.01)	(-6.10, 36.79)		(-2.07, 2.84)	(-0.64, 4.89)	
		LS Mean Difference (SE)		11.70 (9.649)			1.74 (1.302)	
		95% CI		(-7.21, 30.61)			(-0.81, 4.29)	
		p-value		0.2253			0.1812	
		HedgesG (95% CI)		0.293 (-0.194, 0.780)			0.326 (-0.162, 0.814)	

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Age > 41 Years		N1	30	37	67	30	37	67
	Baseline	n	29	37	66	29	37	66
		Mean	359.10	347.41	352.55	53.65	52.23	52.86
		SD, SE	111.075, 20.626	113.082, 18.591	111.495, 13.724	15.983, 2.968	16.567, 2.724	16.203, 1.994
		Median	367.00	335.00	344.50	56.50	52.01	53.33
		Q1, Q3	289.00, 412.00	278.00, 417.00	278.00, 417.00	41.53, 61.34	42.49, 63.76	42.19, 62.20
		Min, Max	160.0, 615.0	78.0, 643.0	78.0, 643.0	24.4, 88.4	12.1, 92.4	12.1, 92.4

6MWT = Six Minute Walk Test.
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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Age > 41 Years	Week 12	Baseline						
		n	29	36	65	29	36	65
		Mean	359.10	348.17	353.05	53.65	52.42	52.97
		SD, SE	111.075, 20.626	114.590, 19.098	112.288, 13.928	15.983, 2.968	16.763, 2.794	16.304, 2.022
		Median	367.00	338.00	347.00	56.50	52.03	53.65
		Q1, Q3	289.00, 412.00	278.00, 420.00	278.00, 417.00	41.53, 61.34	42.34, 63.79	42.19, 62.20
		Min, Max	160.0, 615.0	78.0, 643.0	78.0, 643.0	24.4, 88.4	12.1, 92.4	12.1, 92.4
		Observed						
		n	29	36	65	29	36	65
		Mean	352.03	368.67	361.25	52.70	55.61	54.31
		SD, SE	103.186, 19.161	111.371, 18.562	107.288, 13.307	14.921, 2.771	16.263, 2.711	15.626, 1.938
		Median	333.00	366.50	360.00	50.37	55.35	54.82
		Q1, Q3	286.00, 403.00	314.50, 420.00	294.00, 417.00	43.33, 63.93	47.32, 67.53	43.49, 65.69
		Min, Max	170.0, 573.0	103.0, 660.0	103.0, 660.0	26.0, 81.8	15.9, 94.9	15.9, 94.9

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Table 2.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Age > 41 Years	Week 12	Change from Baseline						
		n	29	36	65	29	36	65
		Mean	-7.07	20.50	8.20	-0.96	3.19	1.34
		SD, SE	35.332, 6.561	41.128, 6.855	40.767, 5.057	5.349, 0.993	6.390, 1.065	6.258, 0.776
		Median	0.00	16.50	8.00	0.04	2.46	1.24
		Q1, Q3	-29.00, 17.00	-3.50, 40.00	-10.00, 32.00	-4.32, 2.40	-0.43, 6.20	-1.38, 4.51
		Min, Max	-95.0, 44.0	-92.0, 155.0	-95.0, 155.0	-14.5, 6.5	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	-15.42 (8.947)	12.29 (8.937)		-2.12 (1.386)	2.07 (1.415)	
		95% CI	(-32.95, 2.12)	(-5.22, 29.81)		(-4.84, 0.60)	(-0.70, 4.85)	
		LS Mean Difference (SE)		27.71 (8.623)			4.19 (1.335)	
		95% CI		(10.81, 44.61)			(1.58, 6.81)	
		p-value		0.0013			0.0017	
		HedgesG (95% CI)		0.694 (0.190, 1.197)			0.678 (0.176, 1.181)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Age > 41 Years	Week 24	Baseline						
		n	28	35	63	28	35	63
		Mean	358.50	351.94	354.86	53.51	53.08	53.27
		SD, SE	113.065, 21.367	113.967, 19.264	112.697, 14.198	16.257, 3.072	16.516, 2.792	16.271, 2.050
		Median	366.50	341.00	347.00	55.70	52.05	53.65
		Q1, Q3	281.50, 415.50	278.00, 423.00	278.00, 419.00	41.31, 61.77	42.49, 63.81	42.19, 63.76
		Min, Max	160.0, 615.0	78.0, 643.0	78.0, 643.0	24.4, 88.4	12.1, 92.4	12.1, 92.4
		Observed						
		n	28	35	63	28	35	63
		Mean	346.18	370.46	359.67	51.76	56.09	54.17
		SD, SE	109.855, 20.761	111.499, 18.847	110.549, 13.928	15.658, 2.959	16.357, 2.765	16.068, 2.024
		Median	330.50	373.00	360.00	49.36	57.60	55.30
		Q1, Q3	269.50, 397.00	317.00, 436.00	300.00, 424.00	40.94, 61.87	46.85, 66.46	43.32, 63.82
		Min, Max	156.0, 617.0	109.0, 619.0	109.0, 619.0	23.9, 85.2	16.7, 89.1	16.7, 89.1

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Age > 41 Years	Week 24	Change from Baseline						
		n	28	35	63	28	35	63
		Mean	-12.32	18.51	4.81	-1.75	3.00	0.89
		SD, SE	40.235, 7.604	55.104, 9.314	51.075, 6.435	5.762, 1.089	8.365, 1.414	7.648, 0.964
		Median	-11.00	19.00	-1.00	-1.53	2.69	-0.05
		Q1, Q3	-33.00, 12.50	-16.00, 47.00	-24.00, 30.00	-5.26, 2.02	-2.10, 7.31	-3.69, 4.47
		Min, Max	-109.0, 87.0	-147.0, 140.0	-147.0, 140.0	-15.1, 11.9	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-22.48 (10.501)	9.93 (10.824)		-3.19 (1.550)	1.84 (1.680)	
		95% CI	(-43.06, -1.89)	(-11.28, 31.15)		(-6.23, -0.15)	(-1.45, 5.13)	
		LS Mean Difference (SE)		32.41 (11.518)			5.03 (1.720)	
		95% CI		(9.84, 54.99)			(1.66, 8.40)	
		p-value		0.0049			0.0035	
		HedgesG (95% CI)		0.611 (0.102, 1.119)			0.630 (0.121, 1.139)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat <= 62.5		N1	41	39	80	41	39	80
	Baseline	n	40	38	78	40	38	78
		Mean	386.85	372.00	379.62	54.73	53.48	54.12
		SD, SE	99.419, 15.720	102.092, 16.562	100.352, 11.363	14.748, 2.332	14.956, 2.426	14.766, 1.672
		Median	379.50	351.50	365.00	53.95	52.05	52.90
		Q1, Q3	300.50, 449.50	307.00, 457.00	301.00, 455.00	41.31, 65.03	44.79, 66.00	42.30, 66.00
		Min, Max	164.0, 615.0	146.0, 643.0	146.0, 643.0	24.7, 88.4	22.3, 92.4	22.3, 92.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline						
		n	39	38	77	39	38	77
		Mean	389.62	372.00	380.92	55.10	53.48	54.30
		SD, SE	99.148, 15.876	102.092, 16.562	100.340, 11.435	14.744, 2.361	14.956, 2.426	14.774, 1.684
		Median	380.00	351.50	366.00	54.90	52.05	53.01
		Q1, Q3	301.00, 455.00	307.00, 457.00	307.00, 455.00	41.53, 66.85	44.79, 66.00	42.49, 66.00
		Min, Max	164.0, 615.0	146.0, 643.0	146.0, 643.0	24.7, 88.4	22.3, 92.4	22.3, 92.4
		Observed						
		n	39	38	77	39	38	77
		Mean	389.36	384.66	387.04	54.96	55.37	55.16
		SD, SE	93.211, 14.926	97.393, 15.799	94.697, 10.792	13.391, 2.144	14.543, 2.359	13.880, 1.582
		Median	383.00	380.50	381.00	51.95	55.59	54.87
		Q1, Q3	313.00, 457.00	318.00, 425.00	318.00, 450.00	43.49, 63.93	45.69, 66.79	45.37, 65.13
		Min, Max	175.0, 600.0	160.0, 660.0	160.0, 660.0	26.4, 84.6	24.5, 94.9	24.5, 94.9

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Table 2.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline						
		n	39	38	77	39	38	77
		Mean	-0.26	12.66	6.12	-0.14	1.89	0.86
		SD, SE	45.572, 7.297	40.768, 6.614	43.472, 4.954	6.308, 1.010	5.691, 0.923	6.059, 0.690
		Median	-2.00	14.00	7.00	-0.24	2.10	1.05
		Q1, Q3	-29.00, 26.00	-3.00, 37.00	-14.00, 33.00	-4.32, 3.94	-0.36, 5.71	-1.86, 4.51
		Min, Max	-95.0, 132.0	-136.0, 93.0	-136.0, 132.0	-14.5, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-9.00 (10.294)	1.92 (10.503)		-1.64 (1.348)	0.22 (1.417)	
		95% CI	(-29.17, 11.18)	(-18.67, 22.50)		(-4.28, 1.00)	(-2.56, 3.00)	
		LS Mean Difference (SE)		10.91 (8.976)			1.86 (1.229)	
		95% CI		(-6.68, 28.51)			(-0.55, 4.27)	
		p-value		0.2241			0.1303	
		HedgesG (95% CI)		0.292 (-0.158, 0.741)			0.329 (-0.120, 0.779)	

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Table 2.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline						
		n	39	38	77	39	38	77
		Mean	387.13	372.00	379.66	54.65	53.48	54.07
		SD, SE	100.703, 16.125	102.092, 16.562	101.009, 11.511	14.933, 2.391	14.956, 2.426	14.858, 1.693
		Median	380.00	351.50	364.00	53.01	52.05	52.79
		Q1, Q3	300.00, 455.00	307.00, 457.00	301.00, 455.00	41.09, 66.85	44.79, 66.00	42.30, 66.00
		Min, Max	164.0, 615.0	146.0, 643.0	146.0, 643.0	24.7, 88.4	22.3, 92.4	22.3, 92.4
		Observed						
		n	39	38	77	39	38	77
		Mean	387.87	392.32	390.06	54.69	56.56	55.61
		SD, SE	94.089, 15.066	100.034, 16.228	96.452, 10.992	13.354, 2.138	15.072, 2.445	14.164, 1.614
		Median	390.00	380.00	388.00	54.66	56.95	55.98
		Q1, Q3	323.00, 465.00	346.00, 452.00	326.00, 452.00	45.66, 63.82	47.03, 65.60	46.85, 63.96
		Min, Max	158.0, 575.0	109.0, 619.0	109.0, 619.0	23.9, 82.9	16.7, 89.1	16.7, 89.1

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Table 2.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline						
		n	39	38	77	39	38	77
		Mean	0.74	20.32	10.40	0.04	3.08	1.54
		SD, SE	46.320, 7.417	37.150, 6.027	42.915, 4.891	6.324, 1.013	5.204, 0.844	5.960, 0.679
		Median	4.00	20.00	9.00	0.73	2.89	1.34
		Q1, Q3	-28.00, 31.00	-3.00, 40.00	-12.00, 34.00	-3.85, 4.48	-0.28, 6.64	-1.46, 4.70
		Min, Max	-109.0, 125.0	-82.0, 105.0	-109.0, 125.0	-15.1, 15.7	-10.0, 15.7	-15.1, 15.7
		GEE Estimates						
		LS Mean (SE)	-9.51 (10.301)	9.57 (9.621)		-1.69 (1.350)	1.41 (1.310)	
		95% CI	(-29.70, 10.68)	(-9.28, 28.43)		(-4.34, 0.95)	(-1.16, 3.98)	
		LS Mean Difference (SE)		19.09 (9.082)			3.10 (1.249)	
		95% CI		(1.29, 36.89)			(0.66, 5.55)	
		p-value		0.0356			0.0130	
		HedgesG (95% CI)		0.455 (0.002, 0.907)			0.512 (0.058, 0.966)	

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Table 2.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat > 62.5		N1	25	29	54	25	29	54
	Baseline	n	25	29	54	25	29	54
		Mean	336.32	336.83	336.59	48.28	48.76	48.54
		SD, SE	104.004, 20.801	117.238, 21.770	110.271, 15.006	14.563, 2.913	16.790, 3.118	15.653, 2.130
		Median	335.00	342.00	338.50	46.61	49.98	47.82
		Q1, Q3	276.00, 382.00	249.00, 423.00	249.00, 423.00	35.23, 59.75	37.88, 61.39	37.23, 61.18
		Min, Max	160.0, 569.0	55.0, 538.0	55.0, 569.0	23.1, 78.4	7.6, 80.4	7.6, 80.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline						
		n	25	26	51	25	26	51
		Mean	336.32	332.31	334.27	48.28	48.14	48.21
		SD, SE	104.004, 20.801	122.429, 24.010	112.653, 15.775	14.563, 2.913	17.516, 3.435	15.975, 2.237
		Median	335.00	338.00	335.00	46.61	47.70	46.61
		Q1, Q3	276.00, 382.00	247.00, 438.00	247.00, 438.00	35.23, 59.75	37.23, 63.76	36.79, 61.18
		Min, Max	160.0, 569.0	55.0, 538.0	55.0, 569.0	23.1, 78.4	7.6, 80.4	7.6, 80.4
		Observed						
		n	25	26	51	25	26	51
		Mean	342.16	358.35	350.41	49.19	52.06	50.66
		SD, SE	104.176, 20.835	117.926, 23.127	110.586, 15.485	14.610, 2.922	16.921, 3.318	15.739, 2.204
		Median	333.00	354.00	340.00	49.09	54.41	50.61
		Q1, Q3	289.00, 403.00	311.00, 440.00	294.00, 437.00	41.29, 61.57	43.62, 64.75	43.00, 64.13
		Min, Max	170.0, 573.0	80.0, 542.0	80.0, 573.0	25.3, 79.1	11.1, 80.0	11.1, 80.0

6MWT = Six Minute Walk Test.
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Table 2.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline						
		n	25	26	51	25	26	51
		Mean	5.84	26.04	16.14	0.91	3.93	2.45
		SD, SE	30.532, 6.106	42.583, 8.351	38.185, 5.347	4.385, 0.877	6.439, 1.263	5.681, 0.796
		Median	0.00	14.00	6.00	0.05	2.25	0.89
		Q1, Q3	-10.00, 35.00	-3.00, 57.00	-10.00, 36.00	-1.39, 5.75	-0.37, 8.54	-1.35, 5.82
		Min, Max	-54.0, 60.0	-46.0, 155.0	-54.0, 155.0	-8.5, 8.7	-6.6, 24.6	-8.5, 24.6
		GEE Estimates						
		LS Mean (SE)	-2.97 (7.458)	15.40 (6.798)		-0.44 (1.116)	2.37 (0.987)	
		95% CI	(-17.59, 11.65)	(2.08, 28.73)		(-2.63, 1.75)	(0.43, 4.30)	
		LS Mean Difference (SE)		18.37 (9.304)			2.81 (1.387)	
		95% CI		(0.13, 36.60)			(0.09, 5.53)	
		p-value		0.0484			0.0429	
		HedgesG (95% CI)		0.524 (-0.034, 1.083)			0.526 (-0.032, 1.085)	

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Table 2.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline						
		n	25	27	52	25	27	52
		Mean	336.32	341.93	339.23	48.28	49.60	48.97
		SD, SE	104.004, 20.801	119.174, 22.935	111.080, 15.404	14.563, 2.913	16.957, 3.263	15.711, 2.179
		Median	335.00	347.00	344.50	46.61	51.30	49.51
		Q1, Q3	276.00, 382.00	249.00, 438.00	262.50, 430.50	35.23, 59.75	37.88, 63.76	37.56, 61.26
		Min, Max	160.0, 569.0	55.0, 538.0	55.0, 569.0	23.1, 78.4	7.6, 80.4	7.6, 80.4
		Observed						
		n	25	27	52	25	27	52
		Mean	340.68	366.15	353.90	48.90	53.27	51.17
		SD, SE	112.369, 22.474	119.593, 23.016	115.752, 16.052	15.341, 3.068	17.004, 3.272	16.218, 2.249
		Median	337.00	373.00	358.50	50.32	53.07	51.39
		Q1, Q3	271.00, 405.00	300.00, 478.00	298.00, 422.50	40.36, 57.96	44.29, 66.46	42.89, 62.90
		Min, Max	156.0, 617.0	100.0, 578.0	100.0, 617.0	23.9, 85.2	13.8, 84.4	13.8, 85.2

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline						
		n	25	27	52	25	27	52
		Mean	4.36	24.22	14.67	0.61	3.67	2.20
		SD, SE	37.367, 7.473	62.722, 12.071	52.565, 7.289	5.260, 1.052	9.372, 1.804	7.757, 1.076
		Median	0.00	19.00	14.50	0.05	2.69	2.13
		Q1, Q3	-18.00, 30.00	-16.00, 62.00	-16.50, 46.00	-2.59, 4.36	-2.10, 9.29	-2.34, 6.51
		Min, Max	-64.0, 87.0	-147.0, 140.0	-147.0, 140.0	-10.1, 11.9	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-4.45 (8.633)	13.90 (10.452)		-0.74 (1.262)	2.16 (1.564)	
		95% CI	(-21.37, 12.47)	(-6.58, 34.38)		(-3.21, 1.74)	(-0.91, 5.22)	
		LS Mean Difference (SE)		18.35 (13.312)			2.90 (1.948)	
		95% CI		(-7.74, 44.44)			(-0.92, 6.71)	
		p-value		0.1681			0.1372	
		HedgesG (95% CI)		0.368 (-0.180, 0.917)			0.384 (-0.165, 0.933)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat <= 47.8		N1	37	30	67	37	30	67
	Baseline	n	37	30	67	37	30	67
		Mean	404.22	398.07	401.46	56.34	56.70	56.50
		SD, SE	106.034, 17.432	97.394, 17.782	101.538, 12.405	15.516, 2.551	14.588, 2.663	14.996, 1.832
		Median	394.00	401.50	394.00	56.21	56.58	56.21
		Q1, Q3	349.00, 472.00	331.00, 473.00	334.00, 473.00	46.55, 66.85	46.49, 66.64	46.49, 66.85
		Min, Max	164.0, 615.0	203.0, 643.0	164.0, 643.0	24.7, 88.4	25.9, 92.4	24.7, 92.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline						
		n	36	28	64	36	28	64
		Mean	407.69	397.64	403.30	56.79	56.58	56.70
		SD, SE	105.375, 17.563	100.870, 19.063	102.736, 12.842	15.486, 2.581	15.089, 2.852	15.193, 1.899
		Median	407.00	387.50	402.50	56.51	56.37	56.51
		Q1, Q3	351.00, 479.00	331.00, 475.00	334.50, 475.00	47.60, 68.21	45.84, 67.17	46.52, 67.27
		Min, Max	164.0, 615.0	203.0, 643.0	164.0, 643.0	24.7, 88.4	25.9, 92.4	24.7, 92.4
		Observed						
		n	36	28	64	36	28	64
		Mean	410.58	415.29	412.64	57.10	59.22	58.03
		SD, SE	99.839, 16.640	92.847, 17.546	96.113, 12.014	14.237, 2.373	14.451, 2.731	14.256, 1.782
		Median	416.00	399.00	407.00	56.78	58.83	57.59
		Q1, Q3	344.00, 468.00	358.00, 489.50	355.50, 477.00	48.33, 65.97	48.29, 68.59	48.33, 67.92
		Min, Max	175.0, 600.0	240.0, 660.0	175.0, 660.0	25.3, 84.6	30.6, 94.9	25.3, 94.9

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Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline						
		n	36	28	64	36	28	64
		Mean	2.89	17.64	9.34	0.31	2.65	1.33
		SD, SE	43.410, 7.235	39.208, 7.410	41.954, 5.244	5.870, 0.978	5.214, 0.985	5.671, 0.709
		Median	-2.50	19.00	6.50	-0.28	2.68	0.98
		Q1, Q3	-25.00, 29.00	6.00, 37.00	-9.00, 34.00	-3.50, 4.02	0.86, 5.28	-1.32, 4.75
		Min, Max	-64.0, 132.0	-136.0, 93.0	-136.0, 132.0	-9.5, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-1.42 (8.619)	12.23 (10.398)		-0.47 (1.103)	1.89 (1.382)	
		95% CI	(-18.31, 15.48)	(-8.15, 32.61)		(-2.63, 1.69)	(-0.82, 4.60)	
		LS Mean Difference (SE)		13.65 (9.472)			2.36 (1.281)	
		95% CI		(-4.91, 32.21)			(-0.15, 4.87)	

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Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
		p-value		0.1495			0.0651	
		HedgesG (95% CI)		0.345 (-0.153, 0.842)			0.406 (-0.093, 0.905)	

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Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline						
		n	37	30	67	37	30	67
		Mean	404.22	398.07	401.46	56.34	56.70	56.50
		SD, SE	106.034, 17.432	97.394, 17.782	101.538, 12.405	15.516, 2.551	14.588, 2.663	14.996, 1.832
		Median	394.00	401.50	394.00	56.21	56.58	56.21
		Q1, Q3	349.00, 472.00	331.00, 473.00	334.00, 473.00	46.55, 66.85	46.49, 66.64	46.49, 66.85
		Min, Max	164.0, 615.0	203.0, 643.0	164.0, 643.0	24.7, 88.4	25.9, 92.4	24.7, 92.4
		Observed						
		n	37	30	67	37	30	67
		Mean	407.54	415.27	411.00	56.71	59.32	57.88
		SD, SE	105.350, 17.319	87.797, 16.029	97.240, 11.880	14.747, 2.424	13.760, 2.512	14.266, 1.743
		Median	411.00	400.50	405.00	56.39	59.14	56.42
		Q1, Q3	347.00, 475.00	361.00, 478.00	360.00, 478.00	47.18, 64.69	50.39, 68.91	49.49, 68.91
		Min, Max	158.0, 617.0	231.0, 619.0	158.0, 619.0	23.9, 85.2	29.5, 89.1	23.9, 89.1

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Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline						
		n	37	30	67	37	30	67
		Mean	3.32	17.20	9.54	0.38	2.62	1.38
		SD, SE	49.904, 8.204	45.764, 8.355	48.239, 5.893	6.788, 1.116	6.460, 1.179	6.689, 0.817
		Median	8.00	17.00	12.00	1.22	2.48	1.54
		Q1, Q3	-32.00, 37.00	-4.00, 43.00	-24.00, 41.00	-5.09, 5.32	-0.51, 6.64	-3.28, 5.46
		Min, Max	-109.0, 125.0	-82.0, 140.0	-109.0, 140.0	-15.1, 15.7	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-0.79 (9.031)	11.96 (10.377)		-0.38 (1.191)	1.89 (1.447)	
		95% CI	(-18.49, 16.91)	(-8.37, 32.30)		(-2.72, 1.95)	(-0.94, 4.73)	
		LS Mean Difference (SE)		12.75 (10.795)			2.27 (1.504)	
		95% CI		(-8.41, 33.91)			(-0.67, 5.22)	

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Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
		p-value		0.2375			0.1307	
		HedgesG (95% CI)		0.281 (-0.203, 0.765)			0.330 (-0.155, 0.814)	

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat > 47.8		N1	29	38	67	29	38	67
	Baseline	n	28	37	65	28	37	65
		Mean	318.79	323.30	321.35	46.84	47.17	47.03
		SD, SE	77.768, 14.697	108.416, 17.823	95.750, 11.876	12.333, 2.331	15.688, 2.579	14.235, 1.766
		Median	311.50	334.00	326.00	45.94	45.61	45.61
		Q1, Q3	276.50, 375.00	249.00, 386.00	276.00, 376.00	38.60, 57.71	37.88, 58.23	37.88, 57.76
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline						
		n	28	36	64	28	36	64
		Mean	318.79	323.39	321.38	46.84	47.21	47.05
		SD, SE	77.768, 14.697	109.952, 18.325	96.507, 12.063	12.333, 2.331	15.909, 2.651	14.346, 1.793
		Median	311.50	334.00	329.50	45.94	46.16	45.99
		Q1, Q3	276.50, 375.00	248.00, 394.00	268.00, 381.00	38.60, 57.71	37.56, 59.30	37.56, 58.00
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4
		Observed						
		n	28	36	64	28	36	64
		Mean	319.93	341.83	332.25	47.06	49.98	48.71
		SD, SE	73.596, 13.908	105.773, 17.629	93.042, 11.630	11.806, 2.231	15.277, 2.546	13.839, 1.730
		Median	320.00	344.00	327.00	44.87	51.92	49.17
		Q1, Q3	284.50, 370.00	305.50, 424.00	288.50, 388.50	41.18, 54.66	43.49, 58.96	42.15, 56.86
		Min, Max	170.0, 481.0	80.0, 535.0	80.0, 535.0	25.9, 73.8	11.1, 80.0	11.1, 80.0

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline						
		n	28	36	64	28	36	64
		Mean	1.14	18.44	10.88	0.22	2.77	1.66
		SD, SE	36.440, 6.887	44.103, 7.350	41.527, 5.191	5.390, 1.019	6.687, 1.114	6.238, 0.780
		Median	-0.50	10.50	6.00	-0.03	1.47	0.89
		Q1, Q3	-12.00, 31.00	-6.50, 44.50	-10.00, 36.00	-1.73, 4.85	-0.90, 6.95	-1.36, 5.78
		Min, Max	-95.0, 60.0	-92.0, 155.0	-95.0, 155.0	-14.5, 8.7	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	-11.32 (8.945)	8.13 (6.449)		-1.87 (1.335)	1.01 (0.938)	
		95% CI	(-28.86, 6.21)	(-4.51, 20.77)		(-4.49, 0.75)	(-0.83, 2.84)	
		LS Mean Difference (SE)		19.45 (9.796)			2.88 (1.470)	
		95% CI		(0.25, 38.65)			(-0.01, 5.76)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
		p-value		0.0470			0.0505	
		HedgesG (95% CI)		0.411 (-0.088, 0.910)			0.403 (-0.096, 0.901)	

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Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline						
		n	27	35	62	27	35	62
		Mean	316.67	326.46	322.19	46.44	47.73	47.17
		SD, SE	78.421, 15.092	109.982, 18.590	96.888, 12.305	12.381, 2.383	15.829, 2.676	14.332, 1.820
		Median	308.00	334.00	329.50	45.32	46.90	45.99
		Q1, Q3	276.00, 374.00	249.00, 402.00	276.00, 386.00	37.24, 57.76	37.88, 60.37	37.88, 58.23
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4
		Observed						
		n	27	35	62	27	35	62
		Mean	317.22	352.46	337.11	46.55	51.65	49.43
		SD, SE	75.063, 14.446	117.029, 19.781	101.713, 12.918	11.591, 2.231	16.848, 2.848	14.899, 1.892
		Median	323.00	346.00	336.50	48.03	53.07	49.05
		Q1, Q3	271.00, 364.00	300.00, 461.00	296.00, 390.00	40.36, 54.86	44.29, 64.94	42.46, 58.70
		Min, Max	156.0, 470.0	100.0, 587.0	100.0, 587.0	23.9, 66.5	13.8, 86.8	13.8, 86.8

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Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline						
		n	27	35	62	27	35	62
		Mean	0.56	26.00	14.92	0.11	3.92	2.26
		SD, SE	31.296, 6.023	51.905, 8.774	45.617, 5.793	4.509, 0.868	7.772, 1.314	6.780, 0.861
		Median	0.00	21.00	12.50	0.10	3.17	1.76
		Q1, Q3	-22.00, 26.00	-5.00, 55.00	-14.00, 40.00	-3.09, 3.83	-0.59, 8.75	-2.05, 5.83
		Min, Max	-64.0, 61.0	-147.0, 138.0	-147.0, 138.0	-10.1, 7.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-13.94 (8.435)	15.42 (7.702)		-2.30 (1.229)	2.13 (1.125)	
		95% CI	(-30.47, 2.60)	(0.33, 30.52)		(-4.71, 0.11)	(-0.08, 4.33)	
		LS Mean Difference (SE)		29.36 (10.768)			4.43 (1.592)	
		95% CI		(8.25, 50.46)			(1.31, 7.55)	

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Table 2.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
		p-value		0.0064			0.0054	
		HedgesG (95% CI)		0.560 (0.048, 1.071)			0.565 (0.053, 1.077)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat <= 62.5		N1	42	32	74	42	32	74
	Baseline	n	42	32	74	42	32	74
		Mean	395.48	381.31	389.35	55.58	54.83	55.26
		SD, SE	99.636, 15.374	99.643, 17.615	99.206, 11.532	14.437, 2.228	14.997, 2.651	14.584, 1.695
		Median	379.50	360.00	375.00	53.95	53.29	53.74
		Q1, Q3	312.00, 471.00	310.00, 461.00	312.00, 471.00	42.95, 65.35	43.18, 66.01	42.95, 66.00
		Min, Max	189.0, 615.0	203.0, 643.0	189.0, 643.0	26.7, 88.4	25.9, 92.4	25.9, 92.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 2.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline						
		n	41	32	73	41	32	73
		Mean	398.32	381.31	390.86	55.96	54.83	55.47
		SD, SE	99.136, 15.483	99.643, 17.615	99.031, 11.591	14.402, 2.249	14.997, 2.651	14.574, 1.706
		Median	380.00	360.00	376.00	54.90	53.29	54.48
		Q1, Q3	335.00, 471.00	310.00, 461.00	320.00, 471.00	44.94, 65.35	43.18, 66.01	43.86, 66.00
		Min, Max	189.0, 615.0	203.0, 643.0	189.0, 643.0	26.7, 88.4	25.9, 92.4	25.9, 92.4
		Observed						
		n	41	32	73	41	32	73
		Mean	393.90	399.38	396.30	55.27	57.52	56.26
		SD, SE	96.675, 15.098	91.949, 16.255	94.021, 11.004	13.570, 2.119	14.236, 2.517	13.814, 1.617
		Median	394.00	388.00	392.00	51.57	57.00	54.99
		Q1, Q3	320.00, 457.00	354.50, 451.00	333.00, 457.00	46.46, 65.00	47.68, 67.86	46.46, 66.26
		Min, Max	179.0, 600.0	240.0, 660.0	179.0, 660.0	25.3, 84.6	30.6, 94.9	25.3, 94.9

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline						
		n	41	32	73	41	32	73
		Mean	-4.41	18.06	5.44	-0.70	2.69	0.79
		SD, SE	43.553, 6.802	39.055, 6.904	42.856, 5.016	6.012, 0.939	5.277, 0.933	5.911, 0.692
		Median	-4.00	17.00	3.00	-0.46	2.47	0.55
		Q1, Q3	-34.00, 13.00	0.50, 37.00	-10.00, 26.00	-4.43, 1.71	0.14, 5.23	-1.39, 3.99
		Min, Max	-95.0, 132.0	-136.0, 93.0	-136.0, 132.0	-14.5, 16.4	-16.8, 12.8	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-12.48 (10.271)	8.34 (10.486)		-2.15 (1.382)	1.22 (1.422)	
		95% CI	(-32.61, 7.65)	(-12.21, 28.89)		(-4.86, 0.56)	(-1.57, 4.00)	
		LS Mean Difference (SE)		20.82 (8.983)			3.36 (1.220)	
		95% CI		(3.21, 38.43)			(0.97, 5.75)	
		p-value		0.0205			0.0059	
		HedgesG (95% CI)		0.527 (0.056, 0.997)			0.580 (0.108, 1.051)	

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Table 2.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline						
		n	41	32	73	41	32	73
		Mean	395.95	381.31	389.53	55.53	54.83	55.22
		SD, SE	100.825, 15.746	99.643, 17.615	99.880, 11.690	14.612, 2.282	14.997, 2.651	14.683, 1.718
		Median	380.00	360.00	374.00	53.01	53.29	53.01
		Q1, Q3	312.00, 471.00	310.00, 461.00	312.00, 471.00	42.95, 65.35	43.18, 66.01	42.95, 66.00
		Min, Max	189.0, 615.0	203.0, 643.0	189.0, 643.0	26.7, 88.4	25.9, 92.4	25.9, 92.4
		Observed						
		n	41	32	73	41	32	73
		Mean	395.10	402.91	398.52	55.36	58.15	56.58
		SD, SE	99.611, 15.557	90.822, 16.055	95.285, 11.152	13.810, 2.157	14.385, 2.543	14.036, 1.643
		Median	400.00	380.00	400.00	54.66	58.12	55.98
		Q1, Q3	326.00, 443.00	360.00, 452.00	346.00, 452.00	47.07, 63.41	48.26, 67.48	47.07, 64.68
		Min, Max	189.0, 617.0	231.0, 619.0	189.0, 619.0	26.7, 85.2	29.5, 89.1	26.7, 89.1

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Table 2.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline						
		n	41	32	73	41	32	73
		Mean	-0.85	21.59	8.99	-0.18	3.32	1.36
		SD, SE	47.961, 7.490	42.612, 7.533	46.749, 5.472	6.521, 1.018	6.081, 1.075	6.527, 0.764
		Median	0.00	17.00	8.00	0.05	2.48	1.22
		Q1, Q3	-32.00, 28.00	-3.50, 41.50	-19.00, 34.00	-5.09, 4.35	-0.36, 6.64	-2.65, 4.48
		Min, Max	-109.0, 125.0	-82.0, 140.0	-109.0, 140.0	-15.1, 15.7	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-10.34 (10.485)	11.87 (10.691)		-1.85 (1.426)	1.84 (1.512)	
		95% CI	(-30.89, 10.21)	(-9.08, 32.83)		(-4.64, 0.95)	(-1.12, 4.81)	
		LS Mean Difference (SE)		22.22 (10.054)			3.69 (1.410)	
		95% CI		(2.51, 41.92)			(0.93, 6.46)	
		p-value		0.0271			0.0088	
		HedgesG (95% CI)		0.479 (0.010, 0.948)			0.539 (0.069, 1.010)	

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat > 62.5		N1	24	35	59	24	35	59
	Baseline	n	23	35	58	23	35	58
		Mean	316.17	334.34	327.14	46.15	48.33	47.47
		SD, SE	91.425, 19.064	114.554, 19.363	105.518, 13.855	14.052, 2.930	16.143, 2.729	15.258, 2.003
		Median	315.00	341.00	334.00	46.56	46.99	46.58
		Q1, Q3	260.00, 405.00	249.00, 416.00	260.00, 412.00	34.72, 59.40	37.88, 61.14	37.23, 60.37
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline						
		n	23	32	55	23	32	55
		Mean	316.17	330.44	324.47	46.15	47.79	47.11
		SD, SE	91.425, 19.064	118.524, 20.952	107.333, 14.473	14.052, 2.930	16.678, 2.948	15.518, 2.092
		Median	315.00	337.50	334.00	46.56	46.74	46.56
		Q1, Q3	260.00, 405.00	248.00, 425.50	249.00, 412.00	34.72, 59.40	37.56, 60.75	36.79, 60.37
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4
		Observed						
		n	23	32	55	23	32	55
		Mean	329.96	348.56	340.78	48.15	50.53	49.53
		SD, SE	93.045, 19.401	114.427, 20.228	105.497, 14.225	14.031, 2.926	16.152, 2.855	15.211, 2.051
		Median	325.00	351.00	329.00	45.26	52.96	49.25
		Q1, Q3	280.00, 383.00	305.50, 431.00	291.00, 425.00	40.98, 57.88	43.49, 59.96	41.07, 59.24
		Min, Max	170.0, 481.0	80.0, 535.0	80.0, 535.0	25.9, 73.8	11.1, 80.0	11.1, 80.0

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 2.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline						
		n	23	32	55	23	32	55
		Mean	13.78	18.13	16.31	1.99	2.74	2.43
		SD, SE	30.972, 6.458	44.833, 7.925	39.362, 5.308	4.463, 0.931	6.805, 1.203	5.902, 0.796
		Median	18.00	10.00	12.00	2.74	1.61	1.99
		Q1, Q3	-9.00, 40.00	-5.50, 44.00	-7.00, 40.00	-1.23, 5.89	-0.71, 7.00	-0.91, 6.25
		Min, Max	-54.0, 60.0	-92.0, 155.0	-92.0, 155.0	-8.5, 8.7	-14.4, 24.6	-14.4, 24.6
		GEE Estimates						
		LS Mean (SE)	3.57 (8.020)	8.18 (7.571)		0.35 (1.165)	1.16 (1.125)	
		95% CI	(-12.15, 19.29)	(-6.65, 23.02)		(-1.93, 2.63)	(-1.05, 3.36)	
		LS Mean Difference (SE)		4.62 (9.857)			0.81 (1.461)	
		95% CI		(-14.70, 23.93)			(-2.05, 3.67)	
		p-value		0.6396			0.5795	
		HedgesG (95% CI)		0.106 (-0.430, 0.642)			0.121 (-0.415, 0.658)	

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Table 2.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline						
		n	23	33	56	23	33	56
		Mean	316.17	338.36	329.25	46.15	49.00	47.83
		SD, SE	91.425, 19.064	116.112, 20.213	106.343, 14.211	14.052, 2.930	16.266, 2.832	15.327, 2.048
		Median	315.00	342.00	334.50	46.56	48.13	46.80
		Q1, Q3	260.00, 405.00	278.00, 416.00	267.00, 413.00	34.72, 59.40	42.80, 61.14	37.56, 60.75
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4
		Observed						
		n	23	33	56	23	33	56
		Mean	323.70	360.64	345.46	47.20	52.32	50.22
		SD, SE	95.671, 19.949	120.958, 21.056	111.848, 14.946	14.022, 2.924	16.888, 2.940	15.845, 2.117
		Median	336.00	356.00	338.50	48.03	53.07	49.41
		Q1, Q3	268.00, 388.00	300.00, 461.00	298.00, 435.00	35.28, 60.33	44.78, 65.54	42.89, 62.03
		Min, Max	156.0, 480.0	100.0, 587.0	100.0, 587.0	23.9, 70.0	13.8, 86.8	13.8, 86.8

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline						
		n	23	33	56	23	33	56
		Mean	7.52	22.27	16.21	1.04	3.32	2.39
		SD, SE	31.763, 6.623	55.140, 9.599	47.182, 6.305	4.601, 0.959	8.187, 1.425	6.982, 0.933
		Median	8.00	21.00	16.00	1.33	3.00	2.49
		Q1, Q3	-10.00, 38.00	-13.00, 55.00	-11.50, 45.50	-1.35, 5.46	-1.71, 8.75	-1.53, 6.48
		Min, Max	-64.0, 61.0	-147.0, 138.0	-147.0, 138.0	-10.1, 7.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-2.69 (7.886)	12.62 (9.029)		-0.60 (1.132)	1.79 (1.328)	
		95% CI	(-18.15, 12.76)	(-5.08, 30.32)		(-2.82, 1.62)	(-0.81, 4.39)	
		LS Mean Difference (SE)		15.31 (11.477)			2.39 (1.678)	
		95% CI		(-7.18, 37.81)			(-0.90, 5.68)	
		p-value		0.1821			0.1540	
		HedgesG (95% CI)		0.304 (-0.232, 0.839)			0.317 (-0.218, 0.853)	

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat <= 47.8		N1	37	30	67	37	30	67
	Baseline	n	37	29	66	37	29	66
		Mean	404.22	392.21	398.94	56.34	55.81	56.11
		SD, SE	106.034, 17.432	99.684, 18.511	102.682, 12.639	15.516, 2.551	14.757, 2.740	15.074, 1.855
		Median	394.00	364.00	387.00	56.21	54.96	55.17
		Q1, Q3	349.00, 472.00	331.00, 473.00	331.00, 473.00	46.55, 66.85	45.19, 66.03	45.19, 66.64
		Min, Max	164.0, 615.0	203.0, 643.0	164.0, 643.0	24.7, 88.4	25.9, 92.4	24.7, 92.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline						
		n	36	28	64	36	28	64
		Mean	407.69	392.21	400.92	56.79	55.83	56.37
		SD, SE	105.375, 17.563	101.513, 19.184	103.175, 12.897	15.486, 2.581	15.028, 2.840	15.174, 1.897
		Median	407.00	362.00	388.00	56.51	54.72	55.59
		Q1, Q3	351.00, 479.00	325.50, 475.00	332.50, 475.00	47.60, 68.21	44.53, 66.34	45.84, 66.75
		Min, Max	164.0, 615.0	203.0, 643.0	164.0, 643.0	24.7, 88.4	25.9, 92.4	24.7, 92.4
		Observed						
		n	36	28	64	36	28	64
		Mean	410.58	407.46	409.22	57.10	58.11	57.54
		SD, SE	99.839, 16.640	94.687, 17.894	96.864, 12.108	14.237, 2.373	14.438, 2.728	14.220, 1.777
		Median	416.00	394.00	404.00	56.78	57.87	57.14
		Q1, Q3	344.00, 468.00	354.50, 483.50	350.50, 471.50	48.33, 65.97	46.71, 67.92	48.02, 67.73
		Min, Max	175.0, 600.0	240.0, 660.0	175.0, 660.0	25.3, 84.6	30.6, 94.9	25.3, 94.9

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Table 2.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline						
		n	36	28	64	36	28	64
		Mean	2.89	15.25	8.30	0.31	2.28	1.17
		SD, SE	43.410, 7.235	38.940, 7.359	41.653, 5.207	5.870, 0.978	5.159, 0.975	5.614, 0.702
		Median	-2.50	15.50	6.00	-0.28	2.21	0.90
		Q1, Q3	-25.00, 29.00	2.00, 31.50	-9.00, 29.00	-3.50, 4.02	0.28, 4.39	-1.32, 4.04
		Min, Max	-64.0, 132.0	-136.0, 93.0	-136.0, 132.0	-9.5, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-0.22 (8.651)	9.16 (10.270)		-0.30 (1.106)	1.42 (1.360)	
		95% CI	(-17.17, 16.74)	(-10.96, 29.29)		(-2.47, 1.87)	(-1.24, 4.09)	
		LS Mean Difference (SE)		9.38 (9.574)			1.73 (1.277)	
		95% CI		(-9.38, 28.15)			(-0.78, 4.23)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
		p-value		0.3271			0.1763	
		HedgesG (95% CI)		0.289 (-0.207, 0.786)			0.343 (-0.154, 0.841)	

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Table 2.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline						
		n	37	29	66	37	29	66
		Mean	404.22	392.21	398.94	56.34	55.81	56.11
		SD, SE	106.034, 17.432	99.684, 18.511	102.682, 12.639	15.516, 2.551	14.757, 2.740	15.074, 1.855
		Median	394.00	364.00	387.00	56.21	54.96	55.17
		Q1, Q3	349.00, 472.00	331.00, 473.00	331.00, 473.00	46.55, 66.85	45.19, 66.03	45.19, 66.64
		Min, Max	164.0, 615.0	203.0, 643.0	164.0, 643.0	24.7, 88.4	25.9, 92.4	24.7, 92.4
		Observed						
		n	37	29	66	37	29	66
		Mean	407.54	411.97	409.48	56.71	58.84	57.65
		SD, SE	105.350, 17.319	88.983, 16.524	97.788, 12.037	14.747, 2.424	13.899, 2.581	14.311, 1.762
		Median	411.00	400.00	405.00	56.39	58.64	56.41
		Q1, Q3	347.00, 475.00	360.00, 452.00	360.00, 475.00	47.18, 64.69	50.39, 68.51	49.49, 68.51
		Min, Max	158.0, 617.0	231.0, 619.0	158.0, 619.0	23.9, 85.2	29.5, 89.1	23.9, 89.1

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Table 2.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline						
		n	37	29	66	37	29	66
		Mean	3.32	19.76	10.55	0.38	3.02	1.54
		SD, SE	49.904, 8.204	43.122, 8.008	47.412, 5.836	6.788, 1.116	6.046, 1.123	6.559, 0.807
		Median	8.00	19.00	12.50	1.22	2.78	2.04
		Q1, Q3	-32.00, 37.00	-4.00, 40.00	-21.00, 40.00	-5.09, 5.32	-0.42, 6.64	-2.65, 5.46
		Min, Max	-109.0, 125.0	-82.0, 140.0	-109.0, 140.0	-15.1, 15.7	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	0.46 (9.012)	15.01 (10.171)		-0.21 (1.188)	2.35 (1.415)	
		95% CI	(-17.20, 18.13)	(-4.93, 34.94)		(-2.53, 2.12)	(-0.42, 5.12)	
		LS Mean Difference (SE)		14.54 (10.528)			2.56 (1.461)	
		95% CI		(-6.09, 35.18)			(-0.31, 5.42)	

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
		p-value		0.1673			0.0804	
		HedgesG (95% CI)		0.340 (-0.150, 0.829)			0.398 (-0.093, 0.889)	

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat > 47.8		N1	29	38	67	29	38	67
	Baseline	n	28	38	66	28	38	66
		Mean	318.79	329.74	325.09	46.84	48.09	47.56
		SD, SE	77.768, 14.697	110.089, 17.859	97.163, 11.960	12.333, 2.331	15.988, 2.594	14.459, 1.780
		Median	311.50	337.50	333.50	45.94	46.95	46.58
		Q1, Q3	276.50, 375.00	249.00, 416.00	276.00, 396.00	38.60, 57.71	37.88, 61.14	37.88, 59.40
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Table 2.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline						
		n	28	36	64	28	36	64
		Mean	318.79	327.61	323.75	46.84	47.79	47.38
		SD, SE	77.768, 14.697	112.214, 18.702	98.015, 12.252	12.333, 2.331	16.276, 2.713	14.580, 1.823
		Median	311.50	337.50	333.50	45.94	46.95	46.58
		Q1, Q3	276.50, 375.00	248.00, 412.50	268.00, 391.00	38.60, 57.71	37.56, 60.75	37.56, 58.82
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4
		Observed						
		n	28	36	64	28	36	64
		Mean	319.93	347.92	335.67	47.06	50.85	49.19
		SD, SE	73.596, 13.908	108.415, 18.069	95.116, 11.889	11.806, 2.231	15.760, 2.627	14.188, 1.774
		Median	320.00	353.50	328.50	44.87	54.32	49.81
		Q1, Q3	284.50, 370.00	305.50, 425.50	288.50, 394.50	41.18, 54.66	43.49, 59.96	42.15, 57.41
		Min, Max	170.0, 481.0	80.0, 535.0	80.0, 535.0	25.9, 73.8	11.1, 80.0	11.1, 80.0

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Table 2.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline						
		n	28	36	64	28	36	64
		Mean	1.14	20.31	11.92	0.22	3.06	1.82
		SD, SE	36.440, 6.887	44.159, 7.360	41.764, 5.221	5.390, 1.019	6.699, 1.117	6.276, 0.785
		Median	-0.50	13.00	9.00	-0.03	2.08	1.34
		Q1, Q3	-12.00, 31.00	-6.50, 44.50	-10.00, 38.50	-1.73, 4.85	-0.90, 7.00	-1.36, 6.03
		Min, Max	-95.0, 60.0	-92.0, 155.0	-95.0, 155.0	-14.5, 8.7	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	-12.26 (9.101)	10.29 (6.546)		-2.01 (1.361)	1.33 (0.951)	
		95% CI	(-30.10, 5.57)	(-2.54, 23.12)		(-4.68, 0.66)	(-0.53, 3.20)	
		LS Mean Difference (SE)		22.56 (9.855)			3.35 (1.483)	
		95% CI		(3.24, 41.87)			(0.44, 6.25)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
		p-value		0.0221			0.0240	
		HedgesG (95% CI)		0.455 (-0.045, 0.955)			0.447 (-0.053, 0.947)	

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Table 2.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline						
		n	27	36	63	27	36	63
		Mean	316.67	333.17	326.10	46.44	48.69	47.73
		SD, SE	78.421, 15.092	111.479, 18.580	98.297, 12.384	12.381, 2.383	16.104, 2.684	14.558, 1.834
		Median	308.00	341.50	334.00	45.32	47.56	46.61
		Q1, Q3	276.00, 374.00	263.50, 419.50	276.00, 402.00	37.24, 57.76	40.04, 61.16	37.88, 60.01
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4
		Observed						
		n	27	36	63	27	36	63
		Mean	317.22	356.86	339.87	46.55	52.25	49.81
		SD, SE	75.063, 14.446	117.407, 19.568	102.642, 12.932	11.591, 2.231	16.892, 2.815	15.018, 1.892
		Median	323.00	351.50	337.00	48.03	53.31	49.31
		Q1, Q3	271.00, 364.00	300.00, 461.00	296.00, 400.00	40.36, 54.86	44.54, 65.24	42.46, 60.33
		Min, Max	156.0, 470.0	100.0, 587.0	100.0, 587.0	23.9, 66.5	13.8, 86.8	13.8, 86.8

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline						
		n	27	36	63	27	36	63
		Mean	0.56	23.69	13.78	0.11	3.56	2.08
		SD, SE	31.296, 6.023	53.792, 8.965	46.663, 5.879	4.509, 0.868	8.041, 1.340	6.928, 0.873
		Median	0.00	18.50	9.00	0.10	2.82	1.45
		Q1, Q3	-22.00, 26.00	-5.00, 57.00	-16.00, 40.00	-3.09, 3.83	-0.61, 8.88	-2.10, 5.83
		Min, Max	-64.0, 61.0	-147.0, 138.0	-147.0, 138.0	-10.1, 7.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-14.75 (8.581)	13.02 (7.910)		-2.42 (1.253)	1.75 (1.154)	
		95% CI	(-31.56, 2.07)	(-2.48, 28.52)		(-4.88, 0.03)	(-0.51, 4.02)	
		LS Mean Difference (SE)		27.77 (10.922)			4.18 (1.613)	
		95% CI		(6.36, 49.17)			(1.02, 7.34)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
		p-value		0.0110			0.0096	
		HedgesG (95% CI)		0.493 (-0.013, 1.000)			0.497 (-0.010, 1.003)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Pain Medication Use at BL = Yes		N1	44	47	91	44	47	91
	Baseline	n	44	46	90	44	46	90
		Mean	350.09	347.07	348.54	50.80	50.68	50.74
		SD, SE	100.990, 15.225	104.131, 15.353	102.042, 10.756	14.928, 2.250	14.986, 2.210	14.874, 1.568
		Median	342.50	338.00	338.50	49.63	50.29	50.10
		Q1, Q3	278.00, 408.50	300.00, 414.00	279.00, 412.00	40.10, 61.05	42.80, 61.14	41.09, 61.14
		Min, Max	160.0, 569.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4

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Table 2.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Pain Medication Use at BL = Yes	Week 12	Baseline						
		n	43	43	86	43	43	86
		Mean	351.74	345.05	348.40	51.06	50.44	50.75
		SD, SE	101.581, 15.491	106.935, 16.307	103.731, 11.186	15.010, 2.289	15.385, 2.346	15.112, 1.630
		Median	349.00	335.00	338.50	50.22	49.98	50.10
		Q1, Q3	277.00, 412.00	278.00, 414.00	278.00, 412.00	40.19, 62.10	42.19, 61.14	41.09, 61.14
		Min, Max	160.0, 569.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	43	43	86	43	43	86
		Mean	356.77	367.42	362.09	51.78	53.80	52.79
		SD, SE	96.311, 14.687	106.730, 16.276	101.196, 10.912	14.109, 2.152	15.339, 2.339	14.685, 1.584
		Median	340.00	360.00	355.50	50.37	54.82	51.44
		Q1, Q3	294.00, 405.00	311.00, 423.00	307.00, 420.00	43.10, 61.74	45.15, 64.13	43.49, 61.74
		Min, Max	170.0, 600.0	80.0, 660.0	80.0, 660.0	25.3, 84.6	11.1, 94.9	11.1, 94.9

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Table 2.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Pain Medication Use at BL = Yes	Week 12	Change from Baseline						
		n	43	43	86	43	43	86
		Mean	5.02	22.37	13.70	0.73	3.35	2.04
		SD, SE	36.783, 5.609	38.746, 5.909	38.555, 4.157	5.239, 0.799	5.910, 0.901	5.707, 0.615
		Median	0.00	16.00	10.00	0.05	2.40	1.53
		Q1, Q3	-15.00, 35.00	3.00, 44.00	-7.00, 37.00	-2.09, 5.75	0.46, 6.69	-0.94, 5.82
		Min, Max	-64.0, 93.0	-92.0, 155.0	-92.0, 155.0	-9.5, 11.9	-14.4, 24.6	-14.4, 24.6
		GEE Estimates						
		LS Mean (SE)	3.91 (7.582)	21.44 (6.573)		0.35 (1.012)	3.04 (0.878)	
		95% CI	(-10.95, 18.77)	(8.56, 34.33)		(-1.63, 2.33)	(1.31, 4.76)	
		LS Mean Difference (SE)		17.53 (8.057)			2.68 (1.192)	
		95% CI		(1.74, 33.33)			(0.35, 5.02)	
		p-value		0.0295			0.0243	
		HedgesG (95% CI)		0.450 (0.022, 0.878)			0.461 (0.033, 0.889)	

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 2.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Pain Medication Use at BL = Yes	Week 24	Baseline						
		n	44	44	88	44	44	88
		Mean	350.09	350.66	350.38	50.80	51.29	51.05
		SD, SE	100.990, 15.225	104.489, 15.752	102.162, 10.891	14.928, 2.250	14.940, 2.252	14.850, 1.583
		Median	342.50	344.00	344.00	49.63	50.95	50.41
		Q1, Q3	278.00, 408.50	303.50, 415.00	284.00, 413.00	40.10, 61.05	42.98, 61.16	41.31, 61.16
		Min, Max	160.0, 569.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	44	44	88	44	44	88
		Mean	352.20	371.68	361.94	51.05	54.47	52.76
		SD, SE	101.337, 15.277	105.507, 15.906	103.312, 11.013	14.383, 2.168	15.074, 2.273	14.749, 1.572
		Median	338.50	363.00	358.50	49.33	55.61	52.91
		Q1, Q3	293.00, 405.50	320.00, 436.50	303.50, 422.00	41.99, 59.64	46.55, 63.69	45.14, 61.18
		Min, Max	156.0, 617.0	100.0, 619.0	100.0, 619.0	23.9, 85.2	13.8, 89.1	13.8, 89.1

6MWT = Six Minute Walk Test.
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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Pain Medication Use at BL = Yes	Week 24	Change from Baseline						
		n	44	44	88	44	44	88
		Mean	2.11	21.02	11.57	0.25	3.18	1.72
		SD, SE	39.216, 5.912	49.327, 7.436	45.311, 4.830	5.476, 0.826	7.324, 1.104	6.596, 0.703
		Median	2.00	21.50	13.50	0.42	3.41	2.05
		Q1, Q3	-26.00, 29.00	-7.00, 49.00	-18.00, 37.50	-3.77, 4.40	-0.88, 7.56	-2.62, 5.53
		Min, Max	-68.0, 125.0	-147.0, 138.0	-147.0, 138.0	-10.1, 15.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	1.22 (7.854)	20.20 (7.606)		-0.10 (1.037)	2.88 (1.029)	
		95% CI	(-14.17, 16.61)	(5.29, 35.10)		(-2.13, 1.93)	(0.86, 4.90)	
		LS Mean Difference (SE)		18.98 (9.455)			2.98 (1.365)	
		95% CI		(0.44, 37.51)			(0.30, 5.66)	
		p-value		0.0448			0.0290	
		HedgesG (95% CI)		0.416 (-0.007, 0.838)			0.444 (0.021, 0.867)	

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Table 2.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Pain Medication Use at BL cat=No		N1	22	21	43	22	21	43
	Baseline	n	21	21	42	21	21	42
		Mean	403.71	378.05	390.88	55.27	53.08	54.17
		SD, SE	101.228, 22.090	120.219, 26.234	110.532, 17.055	14.740, 3.217	17.815, 3.887	16.187, 2.498
		Median	420.00	386.00	401.50	56.80	58.23	57.22
		Q1, Q3	364.00, 455.00	297.00, 477.00	335.00, 473.00	46.61, 61.34	42.49, 66.03	45.19, 66.00
		Min, Max	164.0, 615.0	78.0, 541.0	78.0, 615.0	24.7, 85.7	12.1, 82.4	12.1, 85.7

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Table 2.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Pain Medication Use at BL cat=No	Week 12	Baseline						
		n	21	21	42	21	21	42
		Mean	403.71	378.05	390.88	55.27	53.08	54.17
		SD, SE	101.228, 22.090	120.219, 26.234	110.532, 17.055	14.740, 3.217	17.815, 3.887	16.187, 2.498
		Median	420.00	386.00	401.50	56.80	58.23	57.22
		Q1, Q3	364.00, 455.00	297.00, 477.00	335.00, 473.00	46.61, 61.34	42.49, 66.03	45.19, 66.00
		Min, Max	164.0, 615.0	78.0, 541.0	78.0, 615.0	24.7, 85.7	12.1, 82.4	12.1, 85.7
		Observed						
		n	21	21	42	21	21	42
		Mean	399.90	387.38	393.64	54.61	54.49	54.55
		SD, SE	102.155, 22.292	106.126, 23.159	103.076, 15.905	14.089, 3.074	16.223, 3.540	15.007, 2.316
		Median	420.00	409.00	412.00	56.34	56.94	56.86
		Q1, Q3	325.00, 467.00	329.00, 462.00	325.00, 467.00	46.46, 65.48	45.69, 67.38	45.69, 66.79
		Min, Max	175.0, 560.0	103.0, 525.0	103.0, 560.0	25.9, 78.2	15.9, 80.1	15.9, 80.1

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Table 2.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Pain Medication Use at BL cat=No	Week 12	Change from Baseline						
		n	21	21	42	21	21	42
		Mean	-3.81	9.33	2.76	-0.66	1.41	0.37
		SD, SE	46.866, 10.227	46.980, 10.252	46.822, 7.225	6.366, 1.389	6.240, 1.362	6.314, 0.974
		Median	-4.00	11.00	-1.50	-0.46	1.43	-0.15
		Q1, Q3	-35.00, 13.00	-8.00, 25.00	-15.00, 25.00	-4.43, 1.71	-1.25, 3.88	-1.90, 3.88
		Min, Max	-95.0, 132.0	-136.0, 93.0	-136.0, 132.0	-14.5, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-20.05 (12.838)	-6.97 (10.065)		-2.65 (1.684)	-0.34 (1.356)	
		95% CI	(-45.21, 5.12)	(-26.69, 12.76)		(-5.95, 0.65)	(-3.00, 2.32)	
		LS Mean Difference (SE)		13.08 (13.476)			2.31 (1.782)	
		95% CI		(-13.33, 39.49)			(-1.18, 5.80)	
		p-value		0.3318			0.1950	
		HedgesG (95% CI)		0.268 (-0.339, 0.876)			0.314 (-0.295, 0.923)	

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Table 2.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Pain Medication Use at BL cat=No	Week 24	Baseline						
		n	20	21	41	20	21	41
		Mean	405.10	378.05	391.24	55.15	53.08	54.09
		SD, SE	103.653, 23.177	120.219, 26.234	111.880, 17.473	15.113, 3.379	17.815, 3.887	16.379, 2.558
		Median	425.50	386.00	417.00	56.51	58.23	56.80
		Q1, Q3	349.50, 455.00	297.00, 477.00	335.00, 473.00	46.58, 62.27	42.49, 66.03	45.19, 66.00
		Min, Max	164.0, 615.0	78.0, 541.0	78.0, 615.0	24.7, 85.7	12.1, 82.4	12.1, 85.7
		Observed						
		n	20	21	41	20	21	41
		Mean	407.35	401.90	404.56	55.44	56.70	56.08
		SD, SE	99.997, 22.360	114.297, 24.942	106.251, 16.594	14.095, 3.152	17.679, 3.858	15.845, 2.475
		Median	417.00	434.00	429.00	55.15	58.04	57.60
		Q1, Q3	364.00, 477.50	356.00, 478.00	360.00, 478.00	50.01, 67.37	44.77, 69.91	49.49, 69.91
		Min, Max	158.0, 540.0	125.0, 578.0	125.0, 578.0	23.9, 74.1	19.4, 84.4	19.4, 84.4

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Table 2.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Pain Medication Use at BL cat=No	Week 24	Change from Baseline						
		n	20	21	41	20	21	41
		Mean	2.25	23.86	13.32	0.29	3.62	1.99
		SD, SE	50.841, 11.368	49.422, 10.785	50.682, 7.915	6.880, 1.538	7.007, 1.529	7.062, 1.103
		Median	2.00	7.00	7.00	0.35	0.96	0.96
		Q1, Q3	-27.00, 37.50	-4.00, 47.00	-6.00, 42.00	-3.59, 4.91	-0.51, 7.31	-0.86, 5.57
		Min, Max	-109.0, 99.0	-82.0, 140.0	-109.0, 140.0	-15.1, 12.4	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-17.52 (13.031)	7.56 (10.614)		-2.25 (1.728)	1.87 (1.539)	
		95% CI	(-43.06, 8.02)	(-13.25, 28.36)		(-5.64, 1.14)	(-1.14, 4.89)	
		LS Mean Difference (SE)		25.07 (15.092)			4.12 (2.124)	
		95% CI		(-4.51, 54.65)			(-0.04, 8.28)	
		p-value		0.0966			0.0524	
		HedgesG (95% CI)		0.412 (-0.207, 1.031)			0.459 (-0.162, 1.079)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Opioid Pain Medication Use at BL = Yes		N1	13	17	30	13	17	30
	Baseline	n	13	17	30	13	17	30
		Mean	380.23	292.82	330.70	55.93	43.25	48.75
		SD, SE	113.619, 31.512	100.148, 24.289	113.208, 20.669	17.416, 4.830	15.200, 3.686	17.140, 3.129
		Median	353.00	312.00	336.00	53.01	44.79	48.58
		Q1, Q3	312.00, 463.00	247.00, 354.00	274.00, 405.00	42.95, 68.63	36.52, 53.65	38.96, 57.76
		Min, Max	160.0, 542.0	55.0, 450.0	55.0, 542.0	24.4, 88.4	7.6, 66.6	7.6, 88.4

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Opioid Pain Medication Use at BL = Yes	Week 12	Baseline						
		n	13	16	29	13	16	29
		Mean	380.23	286.63	328.59	55.93	42.50	48.52
		SD, SE	113.619, 31.512	100.007, 25.002	114.608, 21.282	17.416, 4.830	15.363, 3.841	17.397, 3.231
		Median	353.00	295.00	331.00	53.01	43.49	48.13
		Q1, Q3	312.00, 463.00	231.50, 350.50	274.00, 405.00	42.95, 68.63	33.83, 52.85	38.96, 57.76
		Min, Max	160.0, 542.0	55.0, 450.0	55.0, 542.0	24.4, 88.4	7.6, 66.6	7.6, 88.4
		Observed						
		n	13	16	29	13	16	29
		Mean	374.85	309.56	338.83	55.14	46.03	50.11
		SD, SE	102.432, 28.410	95.481, 23.870	102.335, 19.003	15.791, 4.380	15.044, 3.761	15.792, 2.932
		Median	365.00	340.00	352.00	50.37	48.29	49.25
		Q1, Q3	300.00, 453.00	264.50, 361.00	289.00, 405.00	45.52, 71.35	39.07, 55.35	43.48, 59.00
		Min, Max	170.0, 524.0	80.0, 440.0	80.0, 524.0	26.0, 81.8	11.1, 67.7	11.1, 81.8

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Table 2.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Opioid Pain Medication Use at BL = Yes	Week 12	Change from Baseline						
		n	13	16	29	13	16	29
		Mean	-5.38	22.94	10.24	-0.80	3.53	1.59
		SD, SE	44.601, 12.370	52.407, 13.102	50.292, 9.339	6.236, 1.730	8.198, 2.050	7.580, 1.408
		Median	0.00	19.50	10.00	0.04	2.62	1.55
		Q1, Q3	-40.00, 18.00	-2.00, 44.00	-15.00, 26.00	-6.53, 2.74	-0.28, 7.00	-2.09, 4.03
		Min, Max	-64.0, 93.0	-92.0, 155.0	-92.0, 155.0	-9.5, 11.7	-14.4, 24.6	-14.4, 24.6
		GEE Estimates						
		LS Mean (SE)	0.17 (10.739)	12.52 (12.183)		-0.01 (1.520)	2.09 (1.955)	
		95% CI	(-20.87, 21.22)	(-11.35, 36.40)		(-2.99, 2.97)	(-1.74, 5.92)	
		LS Mean Difference (SE)		12.35 (15.572)			2.10 (2.324)	
		95% CI		(-18.17, 42.87)			(-2.45, 6.66)	
		p-value		0.4278			0.3660	
		HedgesG (95% CI)		0.541 (-0.204, 1.286)			0.549 (-0.196, 1.294)	

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Table 2.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Opioid Pain Medication Use at BL = Yes	Week 24	Baseline						
		n	13	16	29	13	16	29
		Mean	380.23	297.63	334.66	55.93	44.14	49.43
		SD, SE	113.619, 31.512	101.391, 25.348	113.083, 20.999	17.416, 4.830	15.237, 3.809	17.029, 3.162
		Median	353.00	321.50	341.00	53.01	45.64	49.03
		Q1, Q3	312.00, 463.00	255.00, 357.00	278.00, 405.00	42.95, 68.63	36.66, 54.31	41.53, 57.76
		Min, Max	160.0, 542.0	55.0, 450.0	55.0, 542.0	24.4, 88.4	7.6, 66.6	7.6, 88.4
		Observed						
		n	13	16	29	13	16	29
		Mean	370.46	322.81	344.17	54.35	47.94	50.82
		SD, SE	108.794, 30.174	110.703, 27.676	110.542, 20.527	15.855, 4.397	16.611, 4.153	16.312, 3.029
		Median	370.00	345.50	357.00	54.66	49.93	52.75
		Q1, Q3	300.00, 437.00	295.50, 380.50	300.00, 420.00	45.66, 63.82	42.64, 56.51	44.78, 59.36
		Min, Max	156.0, 550.0	100.0, 522.0	100.0, 550.0	23.9, 82.9	13.8, 76.2	13.8, 82.9

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Opioid Pain Medication Use at BL = Yes	Week 24	Change from Baseline						
		n	13	16	29	13	16	29
		Mean	-9.77	25.19	9.52	-1.58	3.80	1.39
		SD, SE	49.920, 13.845	63.743, 15.936	59.647, 11.076	6.708, 1.860	9.618, 2.404	8.732, 1.622
		Median	-23.00	28.00	13.00	-3.69	4.18	2.27
		Q1, Q3	-43.00, 8.00	10.50, 62.00	-34.00, 38.00	-6.25, 1.23	1.81, 8.71	-4.99, 5.83
		Min, Max	-62.0, 125.0	-147.0, 138.0	-147.0, 138.0	-8.5, 15.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-4.21 (13.480)	16.25 (16.683)		-0.80 (1.795)	2.57 (2.511)	
		95% CI	(-30.63, 22.21)	(-16.45, 48.95)		(-4.31, 2.72)	(-2.35, 7.49)	
		LS Mean Difference (SE)		20.46 (21.206)			3.37 (2.990)	
		95% CI		(-21.11, 62.02)			(-2.49, 9.23)	
		p-value		0.3347			0.2601	
		HedgesG (95% CI)		0.565 (-0.181, 1.311)			0.597 (-0.151, 1.345)	

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Opioid Pain Medication Use at BL cat = No		N1	53	51	104	53	51	104
	Baseline	n	52	50	102	52	50	102
		Mean	364.21	378.52	371.23	51.33	54.22	52.74
		SD, SE	101.633, 14.094	104.706, 14.808	102.889, 10.188	14.246, 1.976	15.197, 2.149	14.718, 1.457
		Median	370.00	359.00	366.50	52.24	53.29	52.31
		Q1, Q3	290.00, 437.00	320.00, 470.00	300.00, 446.00	40.48, 60.13	44.69, 66.00	42.49, 62.20
		Min, Max	160.0, 615.0	78.0, 643.0	78.0, 643.0	23.1, 85.7	12.1, 92.4	12.1, 92.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 2.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Opioid Pain Medication Use at BL cat = No	Week 12	Baseline						
		n	51	48	99	51	48	99
		Mean	365.88	378.96	372.22	51.55	54.25	52.86
		SD, SE	101.920, 14.272	106.428, 15.362	103.804, 10.433	14.297, 2.002	15.430, 2.227	14.843, 1.492
		Median	371.00	359.00	367.00	52.53	53.29	52.53
		Q1, Q3	291.00, 440.00	314.00, 471.00	300.00, 455.00	40.76, 60.25	44.27, 66.01	42.49, 62.54
		Min, Max	160.0, 615.0	78.0, 643.0	78.0, 643.0	23.1, 85.7	12.1, 92.4	12.1, 92.4
		Observed						
		n	51	48	99	51	48	99
		Mean	369.92	395.44	382.29	52.09	56.69	54.32
		SD, SE	99.839, 13.980	101.485, 14.648	100.942, 10.145	13.679, 1.915	14.870, 2.146	14.382, 1.445
		Median	375.00	396.50	381.00	51.48	56.86	54.01
		Q1, Q3	304.00, 440.00	323.50, 471.00	313.00, 450.00	43.13, 61.57	45.90, 67.57	44.49, 65.13
		Min, Max	175.0, 600.0	103.0, 660.0	103.0, 660.0	25.3, 84.6	15.9, 94.9	15.9, 94.9

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Table 2.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Opioid Pain Medication Use at BL cat = No	Week 12	Change from Baseline						
		n	51	48	99	51	48	99
		Mean	4.04	16.48	10.07	0.54	2.44	1.47
		SD, SE	39.260, 5.497	38.008, 5.486	38.965, 3.916	5.487, 0.768	5.212, 0.752	5.413, 0.544
		Median	-2.00	11.50	6.00	-0.20	1.75	0.89
		Q1, Q3	-15.00, 35.00	-3.00, 37.00	-9.00, 36.00	-2.07, 4.75	-0.37, 5.28	-1.25, 4.85
		Min, Max	-95.0, 132.0	-136.0, 93.0	-136.0, 132.0	-14.5, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-2.72 (8.030)	12.59 (7.108)		-0.60 (1.069)	1.82 (0.942)	
		95% CI	(-18.46, 13.02)	(-1.34, 26.52)		(-2.70, 1.49)	(-0.02, 3.67)	
		LS Mean Difference (SE)		15.31 (7.350)			2.42 (1.027)	
		95% CI		(0.90, 29.71)			(0.41, 4.44)	
		p-value		0.0373			0.0183	
		HedgesG (95% CI)		0.316 (-0.081, 0.713)			0.349 (-0.048, 0.746)	

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Table 2.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Opioid Pain Medication Use at BL cat = No	Week 24	Baseline						
		n	51	49	100	51	49	100
		Mean	363.98	379.71	371.69	51.20	54.39	52.76
		SD, SE	102.630, 14.371	105.446, 15.064	103.794, 10.379	14.360, 2.011	15.303, 2.186	14.841, 1.484
		Median	369.00	360.00	366.50	51.95	54.48	52.31
		Q1, Q3	289.00, 440.00	320.00, 470.00	300.00, 450.50	40.19, 60.25	44.69, 66.00	42.39, 62.37
		Min, Max	160.0, 615.0	78.0, 643.0	78.0, 643.0	23.1, 85.7	12.1, 92.4	12.1, 92.4
		Observed						
		n	51	49	100	51	49	100
		Mean	369.18	400.59	384.57	51.93	57.56	54.69
		SD, SE	103.085, 14.435	101.666, 14.524	103.089, 10.309	14.041, 1.966	15.027, 2.147	14.733, 1.473
		Median	367.00	400.00	389.00	50.91	58.04	55.02
		Q1, Q3	305.00, 434.00	345.00, 478.00	319.50, 461.00	43.12, 60.74	46.85, 68.51	45.63, 64.82
		Min, Max	158.0, 617.0	125.0, 619.0	125.0, 619.0	23.9, 85.2	19.4, 89.1	19.4, 89.1

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Opioid Pain Medication Use at BL cat = No	Week 24	Change from Baseline						
		n	51	49	100	51	49	100
		Mean	5.20	20.88	12.88	0.73	3.17	1.92
		SD, SE	40.747, 5.706	43.879, 6.268	42.827, 4.283	5.646, 0.791	6.290, 0.899	6.064, 0.606
		Median	8.00	16.00	11.50	1.22	2.33	1.51
		Q1, Q3	-19.00, 34.00	-5.00, 47.00	-12.50, 40.00	-2.65, 4.48	-0.59, 7.13	-1.58, 5.52
		Min, Max	-109.0, 99.0	-82.0, 140.0	-109.0, 140.0	-15.1, 12.4	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-2.47 (8.047)	16.50 (7.235)		-0.55 (1.072)	2.48 (1.006)	
		95% CI	(-18.24, 13.30)	(2.33, 30.68)		(-2.66, 1.55)	(0.51, 4.45)	
		LS Mean Difference (SE)		18.98 (8.230)			3.03 (1.168)	
		95% CI		(2.85, 35.11)			(0.74, 5.32)	
		p-value		0.0211			0.0094	
		HedgesG (95% CI)		0.364 (-0.031, 0.759)			0.401 (0.005, 0.797)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Active fractures and pseudo-fractures at BL = Yes		N1	38	32	70	38	32	70
	Baseline	n	38	32	70	38	32	70
		Mean	338.95	362.66	349.79	48.07	51.89	49.82
		SD, SE	90.771, 14.725	104.120, 18.406	97.110, 11.607	13.122, 2.129	15.530, 2.745	14.295, 1.709
		Median	330.50	347.00	335.00	46.56	49.05	46.95
		Q1, Q3	279.00, 396.00	302.50, 458.50	289.00, 431.00	40.01, 59.75	42.34, 63.18	40.76, 61.34
		Min, Max	160.0, 517.0	78.0, 541.0	78.0, 541.0	23.1, 76.5	12.1, 82.4	12.1, 82.4

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The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Active fractures and pseudo-fractures at BL = Yes	Week 12	Baseline						
		n	37	30	67	37	30	67
		Mean	340.57	362.30	350.30	48.29	51.78	49.85
		SD, SE	91.465, 15.037	106.900, 19.517	98.503, 12.034	13.233, 2.175	15.917, 2.906	14.488, 1.770
		Median	335.00	347.00	335.00	46.56	49.05	46.99
		Q1, Q3	289.00, 396.00	297.00, 460.00	289.00, 438.00	40.19, 59.75	42.19, 63.81	40.76, 61.34
		Min, Max	160.0, 517.0	78.0, 541.0	78.0, 541.0	23.1, 76.5	12.1, 82.4	12.1, 82.4
		Observed						
		n	37	30	67	37	30	67
		Mean	351.14	386.17	366.82	49.76	55.18	52.19
		SD, SE	87.489, 14.383	105.705, 19.299	96.916, 11.840	12.252, 2.014	15.467, 2.824	13.942, 1.703
		Median	348.00	383.50	365.00	49.09	55.11	51.01
		Q1, Q3	294.00, 405.00	328.00, 480.00	304.00, 450.00	43.10, 60.96	44.91, 67.38	43.49, 62.25
		Min, Max	175.0, 490.0	103.0, 535.0	103.0, 535.0	25.3, 71.4	15.9, 80.1	15.9, 80.1

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Active fractures and pseudo-fractures at BL = Yes	Week 12	Change from Baseline						
		n	37	30	67	37	30	67
		Mean	10.57	23.87	16.52	1.47	3.40	2.33
		SD, SE	39.411, 6.479	30.741, 5.613	36.151, 4.416	5.277, 0.868	4.249, 0.776	4.905, 0.599
		Median	1.00	21.50	17.00	0.23	3.02	2.40
		Q1, Q3	-10.00, 35.00	-3.00, 43.00	-7.00, 36.00	-1.35, 4.75	-0.36, 5.97	-0.91, 5.75
		Min, Max	-64.0, 132.0	-19.0, 93.0	-64.0, 132.0	-8.7, 16.4	-2.8, 12.8	-8.7, 16.4
		GEE Estimates						
		LS Mean (SE)	2.47 (10.110)	18.85 (7.549)		0.16 (1.266)	2.63 (0.993)	
		95% CI	(-17.34, 22.29)	(4.05, 33.64)		(-2.32, 2.64)	(0.69, 4.58)	
		LS Mean Difference (SE)		16.38 (8.949)			2.47 (1.162)	
		95% CI		(-1.16, 33.92)			(0.19, 4.75)	

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Table 2.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
		p-value		0.0672			0.0335	
		HedgesG (95% CI)		0.362 (-0.124, 0.847)			0.388 (-0.098, 0.874)	

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Active fractures and pseudo-fractures at BL = Yes	Week 24	Baseline						
		n	38	30	68	38	30	68
		Mean	338.95	368.97	352.19	48.07	52.86	50.18
		SD, SE	90.771, 14.725	103.648, 18.923	97.085, 11.773	13.122, 2.129	15.412, 2.814	14.270, 1.730
		Median	330.50	349.50	335.50	46.56	50.64	47.56
		Q1, Q3	279.00, 396.00	308.00, 460.00	289.00, 434.50	40.01, 59.75	42.49, 63.81	40.93, 61.36
		Min, Max	160.0, 517.0	78.0, 541.0	78.0, 541.0	23.1, 76.5	12.1, 82.4	12.1, 82.4
		Observed						
		n	38	30	68	38	30	68
		Mean	345.21	393.80	366.65	48.90	56.44	52.22
		SD, SE	92.196, 14.956	109.448, 19.982	102.322, 12.408	12.619, 2.047	15.922, 2.907	14.557, 1.765
		Median	343.50	391.00	364.50	49.07	57.84	51.83
		Q1, Q3	286.00, 420.00	320.00, 478.00	303.50, 440.00	40.36, 58.96	46.47, 65.54	43.22, 62.03
		Min, Max	158.0, 533.0	125.0, 587.0	125.0, 587.0	23.9, 72.1	19.4, 86.8	19.4, 86.8

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Active fractures and pseudo-fractures at BL = Yes	Week 24	Change from Baseline						
		n	38	30	68	38	30	68
		Mean	6.26	24.83	14.46	0.82	3.58	2.04
		SD, SE	42.424, 6.882	57.066, 10.419	49.898, 6.051	5.715, 0.927	8.297, 1.515	7.052, 0.855
		Median	5.50	23.00	12.00	0.85	3.38	1.78
		Q1, Q3	-28.00, 31.00	-3.00, 66.00	-17.00, 39.00	-3.85, 4.36	-0.29, 10.00	-2.35, 5.59
		Min, Max	-68.0, 125.0	-147.0, 140.0	-147.0, 140.0	-9.4, 15.7	-22.0, 20.6	-22.0, 20.6
		GEE Estimates						
		LS Mean (SE)	-1.53 (9.947)	18.54 (11.789)		-0.45 (1.259)	2.67 (1.667)	
		95% CI	(-21.03, 17.96)	(-4.57, 41.65)		(-2.92, 2.01)	(-0.59, 5.94)	
		LS Mean Difference (SE)		20.07 (12.989)			3.13 (1.785)	
		95% CI		(-5.38, 45.53)			(-0.37, 6.62)	

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Table 2.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
		p-value		0.1222			0.0797	
		HedgesG (95% CI)		0.366 (-0.116, 0.849)			0.385 (-0.098, 0.868)	

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Table 2.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Active fractures and pseudo-fractures at BL = No		N1	28	36	64	28	36	64
	Baseline	n	27	35	62	27	35	62
		Mean	407.48	351.40	375.82	58.12	51.02	54.11
		SD, SE	108.374, 20.857	115.384, 19.503	114.946, 14.598	15.500, 2.983	16.312, 2.757	16.227, 2.061
		Median	405.00	351.00	375.00	57.65	52.10	54.60
		Q1, Q3	364.00, 486.00	278.00, 417.00	307.00, 450.00	51.90, 69.56	42.80, 63.76	44.94, 65.52
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	24.4, 88.4	7.6, 92.4	7.6, 92.4

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 2.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Active fractures and pseudo-fractures at BL = No	Week 12	Baseline						
		n	27	34	61	27	34	61
		Mean	407.48	350.21	375.56	58.12	50.89	54.09
		SD, SE	108.374, 20.857	116.899, 20.048	115.881, 14.837	15.500, 2.983	16.540, 2.837	16.361, 2.095
		Median	405.00	346.50	374.00	57.65	52.05	54.48
		Q1, Q3	364.00, 486.00	278.00, 417.00	307.00, 450.00	51.90, 69.56	42.80, 63.76	44.94, 65.52
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	24.4, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	27	34	61	27	34	61
		Mean	398.04	363.21	378.62	56.75	53.00	54.66
		SD, SE	110.011, 21.172	106.866, 18.327	108.765, 13.926	15.537, 2.990	15.704, 2.693	15.613, 1.999
		Median	392.00	366.50	377.00	53.75	53.49	53.75
		Q1, Q3	320.00, 474.00	310.00, 417.00	318.00, 440.00	46.46, 71.35	45.33, 64.13	45.37, 65.48
		Min, Max	170.0, 600.0	80.0, 660.0	80.0, 660.0	26.0, 84.6	11.1, 94.9	11.1, 94.9

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Table 2.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Active fractures and pseudo-fractures at BL = No	Week 12	Change from Baseline						
		n	27	34	61	27	34	61
		Mean	-9.44	13.00	3.07	-1.37	2.11	0.57
		SD, SE	39.070, 7.519	49.331, 8.460	46.111, 5.904	5.758, 1.108	7.280, 1.249	6.824, 0.874
		Median	-8.00	9.00	4.00	-0.96	1.34	0.63
		Q1, Q3	-35.00, 10.00	-4.00, 37.00	-15.00, 25.00	-4.74, 1.55	-0.51, 5.71	-1.90, 3.46
		Min, Max	-95.0, 84.0	-136.0, 155.0	-136.0, 155.0	-14.5, 11.9	-16.8, 24.6	-16.8, 24.6
		GEE Estimates						
		LS Mean (SE)	-10.03 (10.854)	3.21 (11.463)		-1.68 (1.580)	0.59 (1.644)	
		95% CI	(-31.31, 11.24)	(-19.25, 25.68)		(-4.78, 1.41)	(-2.64, 3.81)	
		LS Mean Difference (SE)		13.25 (10.881)			2.27 (1.564)	
		95% CI		(-8.08, 34.57)			(-0.79, 5.33)	

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Table 2.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
		p-value		0.2234			0.1466	
		HedgesG (95% CI)		0.483 (-0.029, 0.996)			0.508 (-0.005, 1.021)	

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Table 2.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Active fractures and pseudo-fractures at BL = No	Week 24	Baseline						
		n	26	35	61	26	35	61
		Mean	408.69	351.40	375.82	58.14	51.02	54.05
		SD, SE	110.334, 21.638	115.384, 19.503	115.900, 14.839	15.807, 3.100	16.312, 2.757	16.355, 2.094
		Median	408.50	351.00	374.00	57.49	52.10	54.48
		Q1, Q3	364.00, 486.00	278.00, 417.00	307.00, 450.00	51.90, 69.56	42.80, 63.76	44.94, 65.52
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	24.4, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	26	35	61	26	35	61
		Mean	404.85	370.86	385.34	57.58	54.12	55.59
		SD, SE	110.267, 21.625	108.062, 18.266	109.410, 14.009	15.335, 3.007	15.954, 2.697	15.659, 2.005
		Median	402.50	361.00	382.00	57.18	55.92	55.98
		Q1, Q3	337.00, 497.00	314.00, 448.00	321.00, 452.00	49.35, 70.04	46.23, 66.46	47.03, 66.46
		Min, Max	156.0, 617.0	100.0, 619.0	100.0, 619.0	23.9, 85.2	13.8, 89.1	13.8, 89.1

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Table 2.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
Active fractures and pseudo-fractures at BL = No	Week 24	Change from Baseline						
		n	26	35	61	26	35	61
		Mean	-3.85	19.46	9.52	-0.56	3.10	1.54
		SD, SE	43.391, 8.510	41.545, 7.022	43.561, 5.577	6.167, 1.209	6.162, 1.042	6.379, 0.817
		Median	-3.50	16.00	11.00	-0.34	2.64	1.49
		Q1, Q3	-24.00, 28.00	-5.00, 45.00	-16.00, 40.00	-3.69, 4.43	-0.59, 6.64	-2.20, 5.57
		Min, Max	-109.0, 61.0	-82.0, 138.0	-109.0, 138.0	-15.1, 8.5	-10.0, 21.9	-15.1, 21.9
		GEE Estimates						
		LS Mean (SE)	-6.14 (10.813)	10.69 (9.636)		-1.15 (1.562)	1.72 (1.379)	
		95% CI	(-27.33, 15.05)	(-8.20, 29.58)		(-4.21, 1.91)	(-0.98, 4.43)	
		LS Mean Difference (SE)		16.83 (10.131)			2.87 (1.444)	
		95% CI		(-3.03, 36.69)			(0.04, 5.70)	

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Table 2.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
		p-value		0.0967			0.0467	
		HedgesG (95% CI)		0.534 (0.018, 1.051)			0.577 (0.059, 1.094)	

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Table 2.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
6MWT score at BL = High		N1	29	37	66	29	37	66
	Baseline	n	29	37	66	29	37	66
		Mean	275.41	280.62	278.33	39.14	40.85	40.10
		SD, SE	55.075, 10.227	73.541, 12.090	65.641, 8.080	7.878, 1.463	11.117, 1.828	9.794, 1.206
		Median	289.00	307.00	293.50	40.19	43.16	41.80
		Q1, Q3	246.00, 312.00	247.00, 334.00	246.00, 333.00	34.72, 44.94	36.52, 48.13	34.97, 46.61
		Min, Max	160.0, 353.0	55.0, 354.0	55.0, 354.0	23.1, 53.0	7.6, 54.7	7.6, 54.7

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Table 2.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
6MWT score at BL = High	Week 12	Baseline						
		n	28	36	64	28	36	64
		Mean	275.29	279.53	277.67	39.10	40.72	40.01
		SD, SE	56.081, 10.598	74.278, 12.380	66.464, 8.308	8.021, 1.516	11.245, 1.874	9.923, 1.240
		Median	289.00	303.50	293.50	40.48	42.98	41.80
		Q1, Q3	243.00, 313.50	244.00, 334.00	243.50, 333.50	34.23, 45.13	35.75, 49.05	34.84, 46.75
		Min, Max	160.0, 353.0	55.0, 354.0	55.0, 354.0	23.1, 53.0	7.6, 54.7	7.6, 54.7
		Observed						
		n	28	36	64	28	36	64
		Mean	293.50	308.11	301.72	41.60	45.00	43.51
		SD, SE	70.460, 13.316	80.386, 13.398	75.967, 9.496	9.069, 1.714	12.441, 2.074	11.141, 1.393
		Median	297.00	320.50	311.00	43.22	45.53	44.70
		Q1, Q3	250.50, 327.00	266.00, 361.00	254.00, 352.50	37.25, 46.83	38.69, 54.32	37.91, 51.44
		Min, Max	170.0, 467.0	80.0, 425.0	80.0, 467.0	25.3, 58.0	11.1, 66.0	11.1, 66.0

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
6MWT score at BL = High	Week 12	Change from Baseline						
		n	28	36	64	28	36	64
		Mean	18.21	28.58	24.05	2.49	4.27	3.50
		SD, SE	39.108, 7.391	40.456, 6.743	39.895, 4.987	5.214, 0.985	6.213, 1.035	5.821, 0.728
		Median	14.00	21.50	17.00	2.01	3.02	2.46
		Q1, Q3	-9.50, 41.00	7.00, 46.00	0.00, 44.50	-1.29, 6.07	1.03, 7.20	0.05, 6.58
		Min, Max	-63.0, 132.0	-92.0, 155.0	-92.0, 155.0	-9.5, 16.4	-14.4, 24.6	-14.4, 24.6
		GEE Estimates						
		LS Mean (SE)	18.70 (15.515)	30.62 (13.272)		2.25 (1.991)	4.38 (1.790)	
		95% CI	(-11.71, 49.11)	(4.60, 56.63)		(-1.65, 6.15)	(0.87, 7.88)	
		LS Mean Difference (SE)		11.91 (10.545)			2.13 (1.514)	
		95% CI		(-8.75, 32.58)			(-0.84, 5.09)	
		p-value		0.2585			0.1603	
		HedgesG (95% CI)		0.253 (-0.243, 0.749)			0.298 (-0.198, 0.795)	

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
6MWT score at BL = High	Week 24	Baseline						
		n	29	35	64	29	35	64
		Mean	275.41	281.34	278.66	39.14	41.06	40.19
		SD, SE	55.075, 10.227	74.548, 12.601	66.001, 8.250	7.878, 1.463	11.227, 1.898	9.826, 1.228
		Median	289.00	307.00	293.50	40.19	43.16	41.80
		Q1, Q3	246.00, 312.00	247.00, 334.00	246.50, 333.50	34.72, 44.94	36.52, 49.97	35.10, 46.75
		Min, Max	160.0, 353.0	55.0, 354.0	55.0, 354.0	23.1, 53.0	7.6, 54.7	7.6, 54.7
		Observed						
		n	29	35	64	29	35	64
		Mean	289.31	310.43	300.86	41.00	45.44	43.43
		SD, SE	73.955, 13.733	83.867, 14.176	79.618, 9.952	9.485, 1.761	12.835, 2.169	11.569, 1.446
		Median	300.00	321.00	315.50	42.46	46.85	45.70
		Q1, Q3	244.00, 337.00	268.00, 361.00	253.00, 358.50	35.28, 48.03	39.13, 55.30	36.17, 51.53
		Min, Max	156.0, 437.0	100.0, 436.0	100.0, 437.0	23.9, 54.9	13.8, 69.9	13.8, 69.9

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 2.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
6MWT score at BL = High	Week 24	Change from Baseline						
		n	29	35	64	29	35	64
		Mean	13.90	29.09	22.20	1.87	4.38	3.24
		SD, SE	37.247, 6.917	48.134, 8.136	43.875, 5.484	4.930, 0.915	7.257, 1.227	6.389, 0.799
		Median	8.00	28.00	16.00	1.33	3.97	2.43
		Q1, Q3	-6.00, 28.00	7.00, 55.00	-1.00, 45.50	-0.86, 4.43	1.12, 8.75	-0.07, 6.68
		Min, Max	-49.0, 125.0	-147.0, 138.0	-147.0, 138.0	-7.3, 15.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	15.21 (14.605)	30.35 (14.474)		1.74 (1.873)	4.38 (1.972)	
		95% CI	(-13.41, 43.84)	(1.99, 58.72)		(-1.93, 5.41)	(0.52, 8.25)	
		LS Mean Difference (SE)		15.14 (11.265)			2.65 (1.604)	
		95% CI		(-6.94, 37.22)			(-0.50, 5.79)	
		p-value		0.1789			0.0990	
		HedgesG (95% CI)		0.339 (-0.157, 0.835)			0.387 (-0.110, 0.884)	

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Table 2.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
6MWT score at BL = Low		N1	36	30	66	36	30	66
	Baseline	n	36	30	66	36	30	66
		Mean	441.53	450.70	445.70	62.81	64.48	63.57
		SD, SE	66.813, 11.135	63.494, 11.592	64.989, 8.000	9.960, 1.660	9.892, 1.806	9.888, 1.217
		Median	432.50	453.50	439.00	60.13	64.67	62.15
		Q1, Q3	379.50, 479.00	411.00, 483.00	392.00, 483.00	56.36, 69.10	60.37, 68.65	57.65, 68.65
		Min, Max	364.0, 615.0	358.0, 643.0	358.0, 643.0	46.6, 88.4	44.7, 92.4	44.7, 92.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Table 2.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
6MWT score at BL = Low	Week 12	Baseline						
		n	36	28	64	36	28	64
		Mean	441.53	454.04	447.00	62.81	64.92	63.73
		SD, SE	66.813, 11.135	64.392, 12.169	65.545, 8.193	9.960, 1.660	10.074, 1.904	9.986, 1.248
		Median	432.50	458.50	442.00	60.13	65.76	62.37
		Q1, Q3	379.50, 479.00	412.50, 484.50	390.00, 484.50	56.36, 69.10	60.75, 68.83	57.71, 68.83
		Min, Max	364.0, 615.0	358.0, 643.0	358.0, 643.0	46.6, 88.4	44.7, 92.4	44.7, 92.4
		Observed						
		n	36	28	64	36	28	64
		Mean	431.14	458.64	443.17	61.35	65.63	63.22
		SD, SE	74.092, 12.349	68.380, 12.923	72.407, 9.051	10.795, 1.799	10.590, 2.001	10.834, 1.354
		Median	438.50	442.50	440.00	61.27	67.08	63.68
		Q1, Q3	381.50, 471.50	413.00, 499.50	389.00, 491.00	51.29, 69.03	58.83, 70.16	55.04, 69.51
		Min, Max	281.0, 600.0	356.0, 660.0	281.0, 660.0	43.1, 84.6	46.1, 94.9	43.1, 94.9

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Table 2.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
6MWT score at BL = Low	Week 12	Change from Baseline						
		n	36	28	64	36	28	64
		Mean	-10.39	4.61	-3.83	-1.46	0.71	-0.51
		SD, SE	36.908, 6.151	40.026, 7.564	38.725, 4.841	5.373, 0.895	5.265, 0.995	5.394, 0.674
		Median	-6.50	4.50	-3.00	-0.90	0.72	-0.37
		Q1, Q3	-37.50, 8.50	-9.50, 25.00	-25.00, 20.00	-5.54, 1.17	-1.34, 3.57	-3.50, 2.93
		Min, Max	-95.0, 84.0	-136.0, 84.0	-136.0, 84.0	-14.5, 11.9	-16.8, 10.5	-16.8, 11.9
		GEE Estimates						
		LS Mean (SE)	-15.74 (8.292)	2.05 (9.986)		-2.75 (1.168)	-0.03 (1.272)	
		95% CI	(-31.99, 0.51)	(-17.52, 21.63)		(-5.04, -0.46)	(-2.52, 2.46)	
		LS Mean Difference (SE)		17.80 (9.658)			2.72 (1.376)	
		95% CI		(-1.13, 36.72)			(0.02, 5.41)	
		p-value		0.0654			0.0482	
		HedgesG (95% CI)		0.381 (-0.118, 0.879)			0.396 (-0.102, 0.895)	

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Table 2.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
6MWT score at BL = Low	Week 24	Baseline						
		n	35	30	65	35	30	65
		Mean	443.40	450.70	446.77	62.96	64.48	63.66
		SD, SE	66.823, 11.295	63.494, 11.592	64.903, 8.050	10.065, 1.701	9.892, 1.806	9.937, 1.233
		Median	434.00	453.50	440.00	60.25	64.67	62.20
		Q1, Q3	380.00, 486.00	411.00, 483.00	394.00, 483.00	56.21, 69.56	60.37, 68.65	57.76, 68.65
		Min, Max	364.0, 615.0	358.0, 643.0	358.0, 643.0	46.6, 88.4	44.7, 92.4	44.7, 92.4
		Observed						
		n	35	30	65	35	30	65
		Mean	435.83	464.30	448.97	61.89	66.57	64.05
		SD, SE	72.714, 12.291	67.290, 12.286	71.171, 8.828	10.145, 1.715	10.627, 1.940	10.554, 1.309
		Median	420.00	464.50	448.00	60.74	66.03	63.41
		Q1, Q3	390.00, 480.00	405.00, 506.00	400.00, 497.00	54.67, 70.04	58.92, 70.68	56.42, 70.47
		Min, Max	310.0, 617.0	356.0, 619.0	310.0, 619.0	45.5, 85.2	44.8, 89.1	44.8, 89.1

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Table 2.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**	**Placebo (N=66)**	**KRN23 (N=68)**	**Total (N=134)**
6MWT score at BL = Low	Week 24	Change from Baseline						
		n	35	30	65	35	30	65
		Mean	-7.57	13.60	2.20	-1.07	2.09	0.39
		SD, SE	45.077, 7.619	49.460, 9.030	47.970, 5.950	6.351, 1.074	6.987, 1.276	6.787, 0.842
		Median	-4.00	5.00	-3.00	-0.41	0.95	-0.28
		Q1, Q3	-43.00, 31.00	-18.00, 31.00	-32.00, 31.00	-6.25, 4.36	-2.65, 4.47	-4.63, 4.40
		Min, Max	-109.0, 87.0	-82.0, 140.0	-109.0, 140.0	-15.1, 11.9	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-14.12 (8.757)	10.75 (10.349)		-2.54 (1.221)	1.29 (1.395)	
		95% CI	(-31.28, 3.04)	(-9.53, 31.04)		(-4.94, -0.15)	(-1.44, 4.02)	
		LS Mean Difference (SE)		24.87 (11.788)			3.83 (1.686)	
		95% CI		(1.77, 47.98)			(0.53, 7.14)	
		p-value		0.0348			0.0231	
		HedgesG (95% CI)		0.437 (-0.057, 0.930)			0.462 (-0.032, 0.956)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADXRAY.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Worst Pain at BL <= 6		N1	27	17	44	27	17	44
	Baseline	n	27	16	43	27	16	43
		Mean	417.26	383.63	404.74	59.75	55.30	58.09
		SD, SE	100.269, 19.297	112.350, 28.087	104.893, 15.996	13.242, 2.548	17.584, 4.396	14.957, 2.281
		Median	412.00	356.00	396.00	59.75	54.72	58.23
		Q1, Q3	366.00, 486.00	314.00, 455.50	334.00, 473.00	52.53, 69.56	42.13, 65.85	46.99, 68.63
		Min, Max	237.0, 615.0	203.0, 643.0	203.0, 643.0	33.5, 85.7	25.9, 92.4	25.9, 92.4

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Worst Pain at BL <= 6	Week 12	Baseline						
		n	27	16	43	27	16	43
		Mean	417.26	383.63	404.74	59.75	55.30	58.09
		SD, SE	100.269, 19.297	112.350, 28.087	104.893, 15.996	13.242, 2.548	17.584, 4.396	14.957, 2.281
		Median	412.00	356.00	396.00	59.75	54.72	58.23
		Q1, Q3	366.00, 486.00	314.00, 455.50	334.00, 473.00	52.53, 69.56	42.13, 65.85	46.99, 68.63
		Min, Max	237.0, 615.0	203.0, 643.0	203.0, 643.0	33.5, 85.7	25.9, 92.4	25.9, 92.4
		Observed						
		n	27	16	43	27	16	43
		Mean	406.41	416.44	410.14	58.38	59.97	58.97
		SD, SE	90.967, 17.507	101.140, 25.285	93.808, 14.306	12.463, 2.398	15.861, 3.965	13.660, 2.083
		Median	412.00	395.00	403.00	57.88	58.03	57.88
		Q1, Q3	348.00, 457.00	369.50, 481.00	360.00, 462.00	48.53, 68.96	52.94, 67.92	50.88, 68.07
		Min, Max	227.0, 573.0	240.0, 660.0	227.0, 660.0	32.1, 79.1	30.6, 94.9	30.6, 94.9

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Table 5.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Worst Pain at BL <= 6	Week 12	Change from Baseline						
		n	27	16	43	27	16	43
		Mean	-10.85	32.81	5.40	-1.37	4.67	0.88
		SD, SE	26.900, 5.177	33.044, 8.261	35.972, 5.486	3.948, 0.760	4.754, 1.188	5.144, 0.784
		Median	-6.00	25.00	0.00	-0.87	3.80	0.05
		Q1, Q3	-29.00, 4.00	12.50, 56.00	-16.00, 26.00	-4.32, 0.63	1.73, 8.45	-2.35, 3.99
		Min, Max	-64.0, 37.0	-16.0, 93.0	-64.0, 93.0	-8.7, 6.3	-2.4, 12.8	-8.7, 12.8
		GEE Estimates						
		LS Mean (SE)	-25.58 (6.204)	12.53 (7.993)		-3.79 (0.897)	1.55 (1.095)	
		95% CI	(-37.74, -13.42)	(-3.14, 28.20)		(-5.55, -2.03)	(-0.60, 3.69)	
		LS Mean Difference (SE)		38.11 (7.668)			5.34 (1.128)	
		95% CI		(23.08, 53.14)			(3.13, 7.55)	
		p-value		<.0001			<.0001	
		HedgesG (95% CI)		1.429 (0.740, 2.117)			1.360 (0.678, 2.042)	

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Table 5.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Worst Pain at BL <= 6	Week 24	Baseline						
		n	27	16	43	27	16	43
		Mean	417.26	383.63	404.74	59.75	55.30	58.09
		SD, SE	100.269, 19.297	112.350, 28.087	104.893, 15.996	13.242, 2.548	17.584, 4.396	14.957, 2.281
		Median	412.00	356.00	396.00	59.75	54.72	58.23
		Q1, Q3	366.00, 486.00	314.00, 455.50	334.00, 473.00	52.53, 69.56	42.13, 65.85	46.99, 68.63
		Min, Max	237.0, 615.0	203.0, 643.0	203.0, 643.0	33.5, 85.7	25.9, 92.4	25.9, 92.4
		Observed						
		n	27	16	43	27	16	43
		Mean	400.44	415.31	405.98	57.43	59.96	58.37
		SD, SE	97.746, 18.811	100.213, 25.053	97.745, 14.906	12.734, 2.451	16.167, 4.042	13.974, 2.131
		Median	400.00	394.00	400.00	58.70	59.41	59.36
		Q1, Q3	335.00, 465.00	375.50, 450.00	365.00, 452.00	49.70, 63.96	53.11, 65.61	49.70, 63.96
		Min, Max	221.0, 617.0	231.0, 619.0	221.0, 619.0	31.3, 85.2	29.5, 89.1	29.5, 89.1

6MWT = Six Minute Walk Test.
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Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Worst Pain at BL <= 6	Week 24	Change from Baseline						
		n	27	16	43	27	16	43
		Mean	-16.81	31.69	1.23	-2.32	4.66	0.27
		SD, SE	36.422, 7.009	49.976, 12.494	47.706, 7.275	5.122, 0.986	7.183, 1.796	6.806, 1.038
		Median	-18.00	28.00	-3.00	-2.59	4.01	-0.28
		Q1, Q3	-39.00, 9.00	-4.50, 74.00	-28.00, 28.00	-5.66, 1.33	-0.57, 10.39	-3.85, 3.83
		Min, Max	-109.0, 48.0	-38.0, 140.0	-109.0, 140.0	-15.1, 6.8	-5.2, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-31.54 (7.638)	11.40 (11.095)		-4.74 (1.091)	1.53 (1.588)	
		95% CI	(-46.51, -16.57)	(-10.34, 33.15)		(-6.88, -2.60)	(-1.58, 4.64)	
		LS Mean Difference (SE)		42.95 (12.539)			6.27 (1.817)	
		95% CI		(18.37, 67.52)			(2.71, 9.83)	
		p-value		0.0006			0.0006	
		HedgesG (95% CI)		1.110 (0.448, 1.771)			1.123 (0.460, 1.785)	

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Worst Pain at BL > 6		N1	39	51	90	39	51	90
	Baseline	n	38	50	88	38	50	88
		Mean	332.00	346.12	340.02	46.92	49.85	48.58
		SD, SE	91.271, 14.806	108.198, 15.302	100.925, 10.759	13.806, 2.240	15.144, 2.142	14.573, 1.553
		Median	330.50	344.50	335.50	46.56	50.29	47.51
		Q1, Q3	279.00, 376.00	283.00, 423.00	281.00, 415.00	38.96, 56.21	42.80, 61.39	39.98, 59.83
		Min, Max	160.0, 534.0	55.0, 538.0	55.0, 538.0	23.1, 88.4	7.6, 80.4	7.6, 88.4

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Table 5.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Worst Pain at BL > Week 12 6	Baseline							
		n	37	47	84	37	47	84
		Mean	333.43	344.21	339.46	47.10	49.58	48.49
		SD, SE	92.096, 15.141	110.905, 16.177	102.590, 11.193	13.947, 2.293	15.501, 2.261	14.801, 1.615
		Median	335.00	342.00	335.50	46.56	49.98	47.51
		Q1, Q3	289.00, 376.00	278.00, 437.00	280.50, 416.50	38.96, 56.21	42.49, 62.54	39.45, 59.83
		Min, Max	160.0, 534.0	55.0, 538.0	55.0, 538.0	23.1, 88.4	7.6, 80.4	7.6, 88.4
		Observed						
		n	37	47	84	37	47	84
		Mean	345.03	357.00	351.73	48.57	51.58	50.26
		SD, SE	98.685, 16.224	104.210, 15.201	101.382, 11.062	13.850, 2.277	14.856, 2.167	14.415, 1.573
		Median	328.00	356.00	345.00	48.13	51.74	49.91
		Q1, Q3	291.00, 403.00	307.00, 426.00	304.00, 421.50	41.29, 54.01	44.91, 63.43	43.24, 58.96
		Min, Max	170.0, 600.0	80.0, 542.0	80.0, 600.0	25.3, 84.6	11.1, 80.0	11.1, 84.6

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Table 5.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Worst Pain at BL > 6	Week 12	Change from Baseline						
		n	37	47	84	37	47	84
		Mean	11.59	12.79	12.26	1.47	2.00	1.77
		SD, SE	45.698, 7.513	43.796, 6.388	44.375, 4.842	6.366, 1.047	6.377, 0.930	6.339, 0.692
		Median	11.00	8.00	10.00	1.69	1.24	1.47
		Q1, Q3	-10.00, 40.00	-4.00, 33.00	-8.00, 38.50	-1.39, 5.89	-0.50, 4.51	-1.08, 5.78
		Min, Max	-95.0, 132.0	-136.0, 155.0	-136.0, 155.0	-14.5, 16.4	-16.8, 24.6	-16.8, 24.6
		GEE Estimates						
		LS Mean (SE)	3.93 (14.371)	7.15 (11.543)		0.10 (1.877)	1.07 (1.505)	
		95% CI	(-24.24, 32.10)	(-15.48, 29.77)		(-3.58, 3.78)	(-1.88, 4.02)	
		LS Mean Difference (SE)		3.22 (9.820)			0.97 (1.389)	
		95% CI		(-16.03, 22.47)			(-1.75, 3.69)	
		p-value		0.7432			0.4841	
		HedgesG (95% CI)		0.026 (-0.405, 0.457)			0.082 (-0.349, 0.513)	

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Table 5.2.7.1.24.1
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Worst Pain at BL > Week 24 6	Baseline							
		n	37	48	85	37	48	85
		Mean	330.81	349.38	341.29	46.63	50.37	48.74
		SD, SE	92.232, 15.163	108.717, 15.692	101.709, 11.032	13.878, 2.282	15.141, 2.185	14.639, 1.588
		Median	326.00	347.00	336.00	46.55	50.95	48.13
		Q1, Q3	279.00, 374.00	291.50, 430.00	283.00, 416.00	38.96, 53.01	42.98, 61.96	40.01, 60.25
		Min, Max	160.0, 534.0	55.0, 538.0	55.0, 538.0	23.1, 88.4	7.6, 80.4	7.6, 88.4
		Observed						
		n	37	48	85	37	48	85
		Mean	346.81	369.90	359.85	48.77	53.52	51.46
		SD, SE	102.749, 16.892	110.835, 15.998	107.381, 11.647	14.482, 2.381	15.751, 2.274	15.308, 1.660
		Median	340.00	360.00	357.00	48.84	53.55	50.32
		Q1, Q3	300.00, 411.00	315.50, 464.50	302.00, 437.00	42.46, 54.86	45.14, 66.03	44.29, 61.67
		Min, Max	156.0, 575.0	100.0, 587.0	100.0, 587.0	23.9, 82.9	13.8, 86.8	13.8, 86.8

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Worst Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Worst Pain at BL > Week 24 6		Change from Baseline						
		n	37	48	85	37	48	85
		Mean	16.00	20.52	18.55	2.15	3.15	2.71
		SD, SE	42.145, 6.929	47.664, 6.880	45.138, 4.896	5.761, 0.947	7.022, 1.013	6.485, 0.703
		Median	14.00	19.00	17.00	2.08	2.73	2.64
		Q1, Q3	-6.00, 40.00	-3.50, 47.00	-5.00, 45.00	-0.86, 5.73	-0.36, 6.98	-0.59, 6.32
		Min, Max	-64.0, 125.0	-147.0, 138.0	-147.0, 138.0	-10.1, 15.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	7.00 (13.671)	14.91 (11.578)		0.57 (1.781)	2.23 (1.546)	
		95% CI	(-19.80, 33.79)	(-7.79, 37.60)		(-2.92, 4.06)	(-0.80, 5.26)	
		LS Mean Difference (SE)		7.91 (10.113)			1.66 (1.437)	
		95% CI		(-11.91, 27.73)			(-1.16, 4.47)	
		p-value		0.4343			0.2490	
		HedgesG (95% CI)		0.098 (-0.331, 0.527)			0.151 (-0.278, 0.580)	

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Table 5.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Average Pain at BL <= 6		N1	49	48	97	49	48	97
	Baseline	n	49	46	95	49	46	95
		Mean	385.86	366.43	376.45	54.78	52.97	53.90
		SD, SE	106.379, 15.197	100.325, 14.792	103.403, 10.609	15.403, 2.200	14.858, 2.191	15.088, 1.548
		Median	382.00	349.50	374.00	56.50	50.95	54.48
		Q1, Q3	291.00, 455.00	300.00, 423.00	296.00, 446.00	41.53, 65.35	42.80, 63.76	42.19, 63.81
		Min, Max	164.0, 615.0	146.0, 643.0	146.0, 643.0	24.7, 88.4	22.3, 92.4	22.3, 92.4

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Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Average Pain at BL <= 6	Week 12	Baseline						
		n	48	44	92	48	44	92
		Mean	388.08	364.73	376.91	55.09	52.73	53.96
		SD, SE	106.345, 15.350	102.264, 15.417	104.500, 10.895	15.413, 2.225	15.139, 2.282	15.245, 1.589
		Median	388.00	341.00	372.50	56.65	50.29	53.74
		Q1, Q3	293.50, 459.00	298.50, 430.00	296.50, 450.50	41.53, 66.10	42.65, 63.79	42.34, 64.58
		Min, Max	164.0, 615.0	146.0, 643.0	146.0, 643.0	24.7, 88.4	22.3, 92.4	22.3, 92.4
		Observed						
		n	48	44	92	48	44	92
		Mean	390.85	381.55	386.40	55.46	55.25	55.36
		SD, SE	102.972, 14.863	97.757, 14.737	100.069, 10.433	14.632, 2.112	14.715, 2.218	14.591, 1.521
		Median	403.00	372.50	384.50	55.99	54.84	54.93
		Q1, Q3	316.50, 465.00	320.50, 424.00	319.00, 455.00	44.51, 65.58	45.14, 67.53	45.14, 65.97
		Min, Max	175.0, 600.0	160.0, 660.0	160.0, 660.0	25.3, 84.6	24.5, 94.9	24.5, 94.9

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Average Pain at BL <= 6	Week 12	Change from Baseline						
		n	48	44	92	48	44	92
		Mean	2.77	16.82	9.49	0.37	2.52	1.40
		SD, SE	40.266, 5.812	36.430, 5.492	38.914, 4.057	5.556, 0.802	4.986, 0.752	5.372, 0.560
		Median	-1.50	13.00	6.00	-0.15	2.01	0.97
		Q1, Q3	-25.00, 29.00	0.50, 37.00	-8.00, 34.00	-3.50, 4.02	0.10, 5.23	-1.10, 4.63
		Min, Max	-64.0, 132.0	-136.0, 93.0	-136.0, 132.0	-9.5, 16.4	-16.8, 12.8	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-3.21 (7.948)	9.12 (7.430)		-0.60 (1.031)	1.40 (0.974)	
		95% CI	(-18.78, 12.37)	(-5.44, 23.68)		(-2.62, 1.42)	(-0.51, 3.31)	
		LS Mean Difference (SE)		12.33 (7.613)			1.99 (1.029)	
		95% CI		(-2.59, 27.25)			(-0.02, 4.01)	
		p-value		0.1054			0.0526	
		HedgesG (95% CI)		0.358 (-0.054, 0.770)			0.399 (-0.014, 0.812)	

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Average Pain at BL <= 6	Week 24	Baseline						
		n	49	46	95	49	46	95
		Mean	385.86	366.43	376.45	54.78	52.97	53.90
		SD, SE	106.379, 15.197	100.325, 14.792	103.403, 10.609	15.403, 2.200	14.858, 2.191	15.088, 1.548
		Median	382.00	349.50	374.00	56.50	50.95	54.48
		Q1, Q3	291.00, 455.00	300.00, 423.00	296.00, 446.00	41.53, 65.35	42.80, 63.76	42.19, 63.81
		Min, Max	164.0, 615.0	146.0, 643.0	146.0, 643.0	24.7, 88.4	22.3, 92.4	22.3, 92.4
		Observed						
		n	49	46	95	49	46	95
		Mean	384.29	385.87	385.05	54.49	55.94	55.19
		SD, SE	108.251, 15.464	100.519, 14.821	104.027, 10.673	15.012, 2.145	15.234, 2.246	15.057, 1.545
		Median	400.00	378.50	390.00	54.74	56.03	55.98
		Q1, Q3	300.00, 465.00	321.00, 452.00	317.00, 452.00	43.12, 63.82	46.85, 65.60	45.51, 64.68
		Min, Max	158.0, 617.0	109.0, 619.0	109.0, 619.0	23.9, 85.2	16.7, 89.1	16.7, 89.1

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Average Pain at BL <= 6	Week 24	Change from Baseline						
		n	49	46	95	49	46	95
		Mean	-1.57	19.43	8.60	-0.29	2.96	1.29
		SD, SE	45.143, 6.449	43.095, 6.354	45.178, 4.635	6.206, 0.887	6.174, 0.910	6.371, 0.654
		Median	-1.00	15.50	8.00	-0.08	2.30	1.22
		Q1, Q3	-32.00, 24.00	-13.00, 40.00	-21.00, 31.00	-4.47, 3.83	-1.71, 6.64	-2.73, 4.43
		Min, Max	-109.0, 125.0	-82.0, 140.0	-109.0, 140.0	-15.1, 15.7	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-7.40 (8.262)	11.95 (7.776)		-1.24 (1.083)	1.86 (1.079)	
		95% CI	(-23.59, 8.79)	(-3.29, 27.19)		(-3.36, 0.88)	(-0.25, 3.98)	
		LS Mean Difference (SE)		19.35 (8.765)			3.10 (1.223)	
		95% CI		(2.17, 36.53)			(0.71, 5.50)	
		p-value		0.0273			0.0112	
		HedgesG (95% CI)		0.467 (0.059, 0.875)			0.516 (0.107, 0.925)	

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Table 5.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Average Pain at BL > 6		N1	17	20	37	17	20	37
	Baseline	n	16	20	36	16	20	36
		Mean	310.94	329.40	321.19	44.49	47.03	45.90
		SD, SE	69.991, 17.498	127.316, 28.469	104.811, 17.469	10.159, 2.540	17.485, 3.910	14.555, 2.426
		Median	320.50	344.50	335.50	46.58	48.83	46.58
		Q1, Q3	288.50, 358.50	244.00, 453.50	276.50, 366.50	40.35, 51.09	37.34, 61.86	38.92, 54.19
		Min, Max	160.0, 419.0	55.0, 487.0	55.0, 487.0	23.1, 57.8	7.6, 70.0	7.6, 70.0

6MWT = Six Minute Walk Test.
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Table 5.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Average Pain at BL > 6	Week 12	Baseline						
		n	16	19	35	16	19	35
		Mean	310.94	329.89	321.23	44.49	47.11	45.91
		SD, SE	69.991, 17.498	130.785, 30.004	106.341, 17.975	10.159, 2.540	17.961, 4.121	14.767, 2.496
		Median	320.50	347.00	336.00	46.58	52.05	46.61
		Q1, Q3	288.50, 358.50	241.00, 457.00	276.00, 369.00	40.35, 51.09	36.79, 62.54	37.88, 54.72
		Min, Max	160.0, 419.0	55.0, 487.0	55.0, 487.0	23.1, 57.8	7.6, 70.0	7.6, 70.0
		Observed						
		n	16	19	35	16	19	35
		Mean	311.13	350.21	332.34	44.47	50.16	47.56
		SD, SE	57.690, 14.422	122.747, 28.160	99.172, 16.763	7.890, 1.973	16.851, 3.866	13.640, 2.306
		Median	322.50	371.00	328.00	44.87	55.22	48.13
		Q1, Q3	292.50, 350.00	304.00, 442.00	294.00, 395.00	42.20, 49.73	45.15, 64.13	43.10, 55.70
		Min, Max	170.0, 381.0	80.0, 499.0	80.0, 499.0	26.0, 55.3	11.1, 69.1	11.1, 69.1

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Table 5.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Average Pain at BL > 6	Week 12	Change from Baseline						
		n	16	19	35	16	19	35
		Mean	0.19	20.32	11.11	-0.02	3.05	1.65
		SD, SE	41.291, 10.323	53.834, 12.350	48.887, 8.263	5.987, 1.497	8.239, 1.890	7.360, 1.244
		Median	-3.50	22.00	7.00	-0.44	3.11	0.91
		Q1, Q3	-14.50, 33.50	-12.00, 57.00	-14.00, 44.00	-2.08, 4.88	-1.59, 8.54	-1.86, 6.58
		Min, Max	-95.0, 60.0	-92.0, 155.0	-95.0, 155.0	-14.5, 8.7	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	-5.30 (13.669)	18.77 (5.617)		-1.40 (2.141)	2.36 (0.871)	
		95% CI	(-32.09, 21.49)	(7.76, 29.78)		(-5.60, 2.79)	(0.66, 4.07)	
		LS Mean Difference (SE)		24.07 (15.787)			3.77 (2.373)	
		95% CI		(-6.87, 55.01)			(-0.88, 8.42)	
		p-value		0.1273			0.1124	
		HedgesG (95% CI)		0.393 (-0.278, 1.065)			0.399 (-0.272, 1.071)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Average Pain at BL > 6	Week 24	Baseline						
		n	15	18	33	15	18	33
		Mean	306.60	336.22	322.76	43.62	48.11	46.07
		SD, SE	70.186, 18.122	131.550, 31.007	107.578, 18.727	9.869, 2.548	17.927, 4.225	14.782, 2.573
		Median	315.00	349.00	336.00	46.56	52.07	46.61
		Q1, Q3	277.00, 353.00	247.00, 457.00	277.00, 364.00	39.95, 50.22	37.88, 62.54	39.95, 53.65
		Min, Max	160.0, 419.0	55.0, 487.0	55.0, 487.0	23.1, 57.8	7.6, 70.0	7.6, 70.0
		Observed						
		n	15	18	33	15	18	33
		Mean	320.93	369.44	347.39	45.68	53.07	49.71
		SD, SE	68.034, 17.566	131.639, 31.028	108.778, 18.936	9.362, 2.417	18.035, 4.251	15.003, 2.612
		Median	340.00	360.00	347.00	48.03	54.92	49.31
		Q1, Q3	305.00, 361.00	300.00, 478.00	305.00, 400.00	43.97, 50.32	44.78, 69.45	44.78, 56.42
		Min, Max	156.0, 400.0	100.0, 524.0	100.0, 524.0	23.9, 56.4	13.8, 76.2	13.8, 76.2

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.2
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Baseline BPI Average Pain

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
BPI Average Pain at BL > 6	Week 24	Change from Baseline						
		n	15	18	33	15	18	33
		Mean	14.33	33.22	24.64	2.06	4.97	3.65
		SD, SE	32.202, 8.314	59.263, 13.968	49.099, 8.547	4.443, 1.147	8.914, 2.101	7.280, 1.267
		Median	17.00	36.50	26.00	2.52	5.00	3.71
		Q1, Q3	-6.00, 40.00	9.00, 55.00	0.00, 47.00	-0.81, 5.83	1.45, 8.75	0.10, 6.73
		Min, Max	-62.0, 61.0	-147.0, 138.0	-147.0, 138.0	-8.5, 7.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	4.81 (13.329)	31.11 (7.724)		0.05 (2.084)	4.22 (1.198)	
		95% CI	(-21.32, 30.93)	(15.97, 46.25)		(-4.04, 4.13)	(1.87, 6.57)	
		LS Mean Difference (SE)		26.30 (17.228)			4.17 (2.564)	
		95% CI		(-7.47, 60.06)			(-0.85, 9.20)	
		p-value		0.1269			0.1038	
		HedgesG (95% CI)		0.365 (-0.326, 1.056)			0.379 (-0.313, 1.070)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
North America/EU		N1	58	58	116	58	58	116
	Baseline	n	57	56	113	57	56	113
		Mean	366.11	357.34	361.76	52.35	51.62	51.99
		SD, SE	101.055, 13.385	102.412, 13.685	101.370, 9.536	14.636, 1.939	14.721, 1.967	14.617, 1.375
		Median	367.00	349.00	354.00	51.95	51.30	51.95
		Q1, Q3	291.00, 434.00	303.50, 430.00	297.00, 434.00	41.09, 60.25	42.98, 62.32	42.19, 62.10
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
North America/EU	Week 12	Baseline						
		n	56	53	109	56	53	109
		Mean	367.66	356.28	362.13	52.57	51.48	52.04
		SD, SE	101.278, 13.534	104.766, 14.391	102.669, 9.834	14.673, 1.961	15.046, 2.067	14.797, 1.417
		Median	368.00	347.00	354.00	52.30	50.60	51.95
		Q1, Q3	293.50, 437.00	300.00, 437.00	297.00, 437.00	41.31, 61.17	42.80, 62.54	42.19, 62.10
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	56	53	109	56	53	109
		Mean	369.00	378.04	373.39	52.75	54.70	53.70
		SD, SE	95.782, 12.799	101.977, 14.008	98.487, 9.433	13.678, 1.828	14.624, 2.009	14.114, 1.352
		Median	361.00	377.00	368.00	50.61	55.22	51.95
		Q1, Q3	302.00, 441.00	318.00, 437.00	311.00, 440.00	43.41, 61.99	45.37, 65.13	44.49, 63.93
		Min, Max	170.0, 600.0	80.0, 660.0	80.0, 660.0	25.3, 84.6	11.1, 94.9	11.1, 94.9

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Table 5.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
North America/EU	Week 12	Change from Baseline						
		n	56	53	109	56	53	109
		Mean	1.34	21.75	11.27	0.18	3.22	1.65
		SD, SE	38.606, 5.159	39.726, 5.457	40.299, 3.860	5.521, 0.738	5.951, 0.817	5.908, 0.566
		Median	-0.50	14.00	7.00	-0.03	2.03	1.05
		Q1, Q3	-19.50, 33.50	-2.00, 45.00	-10.00, 37.00	-2.65, 4.40	-0.27, 6.69	-1.38, 5.82
		Min, Max	-95.0, 93.0	-92.0, 155.0	-95.0, 155.0	-14.5, 11.9	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	1.23 (5.105)	20.66 (5.813)		0.12 (0.728)	3.07 (0.875)	
		95% CI	(-8.78, 11.23)	(9.27, 32.06)		(-1.30, 1.55)	(1.36, 4.79)	
		LS Mean Difference (SE)		19.44 (6.945)			2.95 (1.015)	
		95% CI		(5.83, 33.05)			(0.96, 4.93)	
		p-value		0.0051			0.0037	
		HedgesG (95% CI)		0.513 (0.131, 0.895)			0.522 (0.140, 0.904)	

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Table 5.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
North America/EU	Week 24	Baseline						
		n	56	54	110	56	54	110
		Mean	365.93	360.65	363.34	52.26	52.15	52.21
		SD, SE	101.960, 13.625	102.321, 13.924	101.702, 9.697	14.751, 1.971	14.639, 1.992	14.629, 1.395
		Median	366.50	351.50	356.00	51.93	52.03	51.98
		Q1, Q3	290.00, 437.00	307.00, 437.00	297.00, 437.00	40.93, 61.17	43.16, 62.54	42.19, 62.10
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	56	54	110	56	54	110
		Mean	368.50	387.09	377.63	52.58	56.11	54.32
		SD, SE	100.806, 13.471	105.681, 14.381	103.176, 9.837	14.031, 1.875	15.274, 2.079	14.694, 1.401
		Median	362.50	378.50	371.50	50.61	56.51	54.66
		Q1, Q3	303.50, 431.00	324.00, 461.00	314.00, 452.00	43.54, 62.03	46.63, 66.46	45.66, 63.96
		Min, Max	156.0, 617.0	100.0, 619.0	100.0, 619.0	23.9, 85.2	13.8, 89.1	13.8, 89.1

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 5.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
North America/EU	Week 24	Change from Baseline						
		n	56	54	110	56	54	110
		Mean	2.57	26.44	14.29	0.33	3.96	2.11
		SD, SE	42.103, 5.626	48.835, 6.646	46.881, 4.470	5.845, 0.781	7.206, 0.981	6.770, 0.645
		Median	5.50	21.00	14.00	0.85	3.08	2.13
		Q1, Q3	-26.00, 32.50	-3.00, 55.00	-17.00, 41.00	-3.77, 4.45	-0.29, 8.75	-2.47, 5.83
		Min, Max	-109.0, 125.0	-147.0, 140.0	-147.0, 140.0	-15.1, 15.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	1.62 (5.637)	25.46 (7.063)		0.14 (0.776)	3.84 (1.052)	
		95% CI	(-9.43, 12.67)	(11.62, 39.31)		(-1.38, 1.66)	(1.78, 5.90)	
		LS Mean Difference (SE)		23.84 (8.394)			3.70 (1.206)	
		95% CI		(7.39, 40.29)			(1.33, 6.06)	
		p-value		0.0045			0.0022	
		HedgesG (95% CI)		0.516 (0.136, 0.896)			0.546 (0.166, 0.927)	

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Asia		N1	8	10	18	8	10	18
	Baseline	n	8	10	18	8	10	18
		Mean	376.75	343.30	358.17	51.50	48.66	49.92
		SD, SE	126.322, 44.662	149.631, 47.317	136.808, 32.246	17.766, 6.281	21.714, 6.866	19.537, 4.605
		Median	401.00	333.50	358.50	54.67	48.36	51.92
		Q1, Q3	287.50, 465.00	240.00, 470.00	240.00, 470.00	36.30, 65.45	30.83, 66.03	31.07, 66.03
		Min, Max	164.0, 543.0	78.0, 541.0	78.0, 543.0	24.7, 74.4	12.1, 82.4	12.1, 82.4

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Asia	Week 12	Baseline						
		n	8	10	18	8	10	18
		Mean	376.75	343.30	358.17	51.50	48.66	49.92
		SD, SE	126.322, 44.662	149.631, 47.317	136.808, 32.246	17.766, 6.281	21.714, 6.866	19.537, 4.605
		Median	401.00	333.50	358.50	54.67	48.36	51.92
		Q1, Q3	287.50, 465.00	240.00, 470.00	240.00, 470.00	36.30, 65.45	30.83, 66.03	31.07, 66.03
		Min, Max	164.0, 543.0	78.0, 541.0	78.0, 543.0	24.7, 74.4	12.1, 82.4	12.1, 82.4
		Observed						
		n	8	10	18	8	10	18
		Mean	384.38	340.60	360.06	52.43	48.51	50.25
		SD, SE	130.013, 45.967	125.876, 39.805	125.895, 29.674	17.539, 6.201	19.216, 6.077	18.060, 4.257
		Median	426.00	339.50	390.50	57.15	47.47	52.69
		Q1, Q3	291.50, 462.00	251.00, 409.00	251.00, 457.00	39.00, 63.52	32.27, 64.75	32.27, 64.75
		Min, Max	175.0, 541.0	103.0, 525.0	103.0, 541.0	25.9, 74.2	15.9, 80.1	15.9, 80.1

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Table 5.2.7.1.24.3
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Asia	Week 12	Change from Baseline						
		n	8	10	18	8	10	18
		Mean	7.63	-2.70	1.89	0.93	-0.15	0.33
		SD, SE	52.923, 18.711	49.777, 15.741	49.929, 11.768	6.653, 2.352	6.303, 1.993	6.290, 1.483
		Median	-3.00	13.50	-0.50	-0.33	1.98	0.01
		Q1, Q3	-18.50, 6.00	-8.00, 25.00	-8.00, 21.00	-2.52, 0.96	-1.25, 3.57	-1.25, 3.20
		Min, Max	-40.0, 132.0	-136.0, 37.0	-136.0, 132.0	-5.2, 16.4	-16.8, 4.7	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	19.73 (16.389)	-1.34 (15.095)		2.34 (1.725)	0.26 (1.722)	
		95% CI	(-12.40, 51.85)	(-30.92, 28.25)		(-1.04, 5.73)	(-3.12, 3.63)	
		LS Mean Difference (SE)		-21.06 (22.701)			-2.09 (2.744)	
		95% CI		(-65.56, 23.43)			(-7.47, 3.29)	
		p-value		0.3534			0.4470	
		HedgesG (95% CI)		-0.181 (-1.113, 0.750)			-0.151 (-1.082, 0.780)	

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Asia	Week 24	Baseline						
		n	8	10	18	8	10	18
		Mean	376.75	343.30	358.17	51.50	48.66	49.92
		SD, SE	126.322, 44.662	149.631, 47.317	136.808, 32.246	17.766, 6.281	21.714, 6.866	19.537, 4.605
		Median	401.00	333.50	358.50	54.67	48.36	51.92
		Q1, Q3	287.50, 465.00	240.00, 470.00	240.00, 470.00	36.30, 65.45	30.83, 66.03	31.07, 66.03
		Min, Max	164.0, 543.0	78.0, 541.0	78.0, 543.0	24.7, 74.4	12.1, 82.4	12.1, 82.4
		Observed						
		n	8	10	18	8	10	18
		Mean	376.00	349.70	361.39	51.32	49.84	50.49
		SD, SE	127.659, 45.134	128.686, 40.694	125.133, 29.494	17.304, 6.118	19.382, 6.129	17.965, 4.234
		Median	417.00	338.00	399.50	55.15	51.41	53.83
		Q1, Q3	301.00, 437.00	247.00, 452.00	247.00, 440.00	40.36, 60.75	31.79, 64.94	31.79, 63.41
		Min, Max	158.0, 540.0	125.0, 538.0	125.0, 540.0	23.9, 74.1	19.4, 82.1	19.4, 82.1

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Region

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Asia	Week 24	Change from Baseline						
		n	8	10	18	8	10	18
		Mean	-0.75	6.40	3.22	-0.18	1.17	0.57
		SD, SE	50.239, 17.762	42.093, 13.311	44.617, 10.516	6.633, 2.345	5.776, 1.827	6.022, 1.419
		Median	-3.50	2.00	-3.00	-0.34	0.34	-0.28
		Q1, Q3	-19.00, 10.50	-14.00, 28.00	-14.00, 28.00	-2.48, 1.64	-2.05, 3.76	-2.05, 3.62
		Min, Max	-81.0, 99.0	-82.0, 73.0	-82.0, 99.0	-11.5, 12.4	-10.0, 11.1	-11.5, 12.4
		GEE Estimates						
		LS Mean (SE)	11.35 (17.018)	7.76 (13.263)		1.23 (2.008)	1.58 (1.702)	
		95% CI	(-22.00, 44.70)	(-18.23, 33.76)		(-2.71, 5.16)	(-1.75, 4.92)	
		LS Mean Difference (SE)		-3.59 (21.467)			0.36 (2.758)	
		95% CI		(-45.66, 38.48)			(-5.05, 5.76)	
		p-value		0.8672			0.8974	
		HedgesG (95% CI)		0.140 (-0.791, 1.071)			0.198 (-0.734, 1.129)	

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Table 5.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Sex = Male		N1	23	24	47	23	24	47
	Baseline	n	23	23	46	23	23	46
		Mean	386.48	370.83	378.65	51.40	49.53	50.46
		SD, SE	101.084, 21.077	108.604, 22.645	104.040, 15.340	14.490, 3.021	15.586, 3.250	14.910, 2.198
		Median	394.00	352.00	361.00	52.53	45.61	46.73
		Q1, Q3	289.00, 455.00	297.00, 470.00	296.00, 455.00	38.96, 59.12	38.71, 62.10	38.96, 61.14
		Min, Max	237.0, 615.0	203.0, 643.0	203.0, 643.0	31.1, 85.7	25.9, 92.4	25.9, 92.4

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Sex = Male	Week 12	Baseline						
		n	23	22	45	23	22	45
		Mean	386.48	373.14	379.96	51.40	49.71	50.57
		SD, SE	101.084, 21.077	110.580, 23.576	104.836, 15.628	14.490, 3.021	15.929, 3.396	15.060, 2.245
		Median	394.00	353.00	364.00	52.53	45.96	46.90
		Q1, Q3	289.00, 455.00	297.00, 470.00	296.00, 455.00	38.96, 59.12	38.71, 62.10	38.96, 61.14
		Min, Max	237.0, 615.0	203.0, 643.0	203.0, 643.0	31.1, 85.7	25.9, 92.4	25.9, 92.4
		Observed						
		n	23	22	45	23	22	45
		Mean	394.39	392.64	393.53	52.34	52.37	52.35
		SD, SE	95.367, 19.885	110.615, 23.583	101.921, 15.194	13.180, 2.748	16.185, 3.451	14.556, 2.170
		Median	405.00	385.00	398.00	50.62	50.07	50.62
		Q1, Q3	325.00, 467.00	329.00, 462.00	328.00, 462.00	43.00, 60.96	43.35, 64.75	43.35, 60.96
		Min, Max	200.0, 573.0	204.0, 660.0	200.0, 660.0	25.9, 79.1	27.5, 94.9	25.9, 94.9

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Sex = Male	Week 12	Change from Baseline						
		n	23	22	45	23	22	45
		Mean	7.91	19.50	13.58	0.94	2.66	1.78
		SD, SE	45.928, 9.577	45.675, 9.738	45.658, 6.806	5.904, 1.231	5.822, 1.241	5.862, 0.874
		Median	-1.00	17.00	11.00	-0.10	2.47	1.44
		Q1, Q3	-21.00, 36.00	6.00, 37.00	-8.00, 36.00	-2.92, 4.75	0.83, 4.74	-0.96, 4.74
		Min, Max	-55.0, 132.0	-136.0, 93.0	-136.0, 132.0	-7.6, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-3.08 (14.997)	7.35 (14.681)		-0.86 (1.892)	0.80 (1.869)	
		95% CI	(-32.47, 26.32)	(-21.42, 36.13)		(-4.56, 2.85)	(-2.86, 4.47)	
		LS Mean Difference (SE)		10.43 (12.818)			1.66 (1.623)	
		95% CI		(-14.69, 35.55)			(-1.52, 4.84)	
		p-value		0.4158			0.3066	
		HedgesG (95% CI)		0.243 (-0.344, 0.830)			0.283 (-0.305, 0.870)	

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Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Sex = Male	Week 24	Baseline						
		n	23	21	44	23	21	44
		Mean	386.48	380.62	383.68	51.40	50.69	51.06
		SD, SE	101.084, 21.077	107.452, 23.448	102.989, 15.526	14.490, 3.021	15.624, 3.409	14.869, 2.242
		Median	394.00	354.00	367.50	52.53	46.49	46.95
		Q1, Q3	289.00, 455.00	331.00, 470.00	296.50, 455.00	38.96, 59.12	42.07, 62.10	40.03, 61.16
		Min, Max	237.0, 615.0	203.0, 643.0	203.0, 643.0	31.1, 85.7	25.9, 92.4	25.9, 92.4
		Observed						
		n	23	21	44	23	21	44
		Mean	392.26	403.57	397.66	52.07	53.88	52.93
		SD, SE	101.480, 21.160	103.071, 22.492	101.206, 15.257	13.847, 2.887	15.484, 3.379	14.507, 2.187
		Median	405.00	425.00	415.00	51.88	55.92	52.81
		Q1, Q3	310.00, 443.00	345.00, 461.00	321.50, 456.50	42.46, 61.67	44.29, 62.70	43.22, 62.19
		Min, Max	208.0, 617.0	231.0, 619.0	208.0, 619.0	27.0, 85.2	29.5, 89.1	27.0, 89.1

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The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Sex = Male	Week 24	Change from Baseline						
		n	23	21	44	23	21	44
		Mean	5.78	22.95	13.98	0.67	3.19	1.87
		SD, SE	56.780, 11.839	51.044, 11.139	54.190, 8.169	7.500, 1.564	6.883, 1.502	7.241, 1.092
		Median	7.00	19.00	10.00	0.97	2.69	1.35
		Q1, Q3	-32.00, 42.00	-4.00, 34.00	-19.50, 41.50	-4.09, 5.57	-0.42, 4.47	-2.62, 5.52
		Min, Max	-109.0, 125.0	-82.0, 140.0	-109.0, 140.0	-15.1, 15.7	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-5.21 (15.841)	9.89 (14.406)		-1.12 (2.039)	1.21 (1.887)	
		95% CI	(-36.25, 25.84)	(-18.35, 38.13)		(-5.12, 2.87)	(-2.49, 4.91)	
		LS Mean Difference (SE)		15.10 (14.957)			2.33 (1.996)	
		95% CI		(-14.22, 44.41)			(-1.58, 6.25)	
		p-value		0.3128			0.2424	
		HedgesG (95% CI)		0.304 (-0.291, 0.899)			0.335 (-0.261, 0.931)	

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Sex = Female		N1	43	44	87	43	44	87
	Baseline	n	42	43	85	42	43	85
		Mean	356.98	346.86	351.86	52.71	52.05	52.38
		SD, SE	104.373, 16.105	110.403, 16.836	106.946, 11.600	15.275, 2.357	16.033, 2.445	15.573, 1.689
		Median	365.00	342.00	351.00	52.30	52.10	52.10
		Q1, Q3	291.00, 412.00	283.00, 417.00	291.00, 416.00	41.53, 62.20	43.16, 65.52	42.49, 62.54
		Min, Max	160.0, 543.0	55.0, 541.0	55.0, 543.0	23.1, 88.4	7.6, 82.4	7.6, 88.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 5.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Sex = Female	Week 12	Baseline						
		n	41	41	82	41	41	82
		Mean	358.88	344.07	351.48	53.02	51.74	52.38
		SD, SE	104.930, 16.387	112.338, 17.544	108.281, 11.958	15.331, 2.394	16.351, 2.554	15.764, 1.741
		Median	366.00	341.00	350.00	52.64	52.05	52.07
		Q1, Q3	300.00, 412.00	283.00, 417.00	291.00, 417.00	42.30, 62.20	43.16, 65.52	42.49, 63.20
		Min, Max	160.0, 543.0	55.0, 541.0	55.0, 543.0	23.1, 88.4	7.6, 82.4	7.6, 88.4
		Observed						
		n	41	41	82	41	41	82
		Mean	357.76	361.07	359.41	52.92	54.44	53.68
		SD, SE	100.585, 15.709	102.949, 16.078	101.157, 11.171	14.677, 2.292	15.169, 2.369	14.853, 1.640
		Median	340.00	365.00	361.00	51.01	55.70	54.41
		Q1, Q3	294.00, 437.00	311.00, 420.00	304.00, 426.00	43.48, 62.25	45.69, 65.13	45.15, 65.13
		Min, Max	170.0, 600.0	80.0, 535.0	80.0, 600.0	25.3, 84.6	11.1, 80.1	11.1, 84.6

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The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Sex = Female	Week 12	Change from Baseline						
		n	41	41	82	41	41	82
		Mean	-1.12	17.00	7.94	-0.10	2.69	1.30
		SD, SE	36.827, 5.751	40.465, 6.320	39.515, 4.364	5.495, 0.858	6.290, 0.982	6.035, 0.667
		Median	-2.00	10.00	3.50	-0.20	1.51	0.59
		Q1, Q3	-18.00, 26.00	-4.00, 43.00	-10.00, 35.00	-2.38, 3.94	-0.51, 6.59	-1.39, 5.71
		Min, Max	-95.0, 84.0	-92.0, 155.0	-95.0, 155.0	-14.5, 11.9	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	-3.52 (6.771)	13.40 (6.275)		-0.54 (1.019)	2.16 (0.968)	
		95% CI	(-16.79, 9.75)	(1.11, 25.70)		(-2.54, 1.46)	(0.26, 4.05)	
		LS Mean Difference (SE)		16.92 (7.824)			2.70 (1.208)	
		95% CI		(1.59, 32.26)			(0.33, 5.06)	
		p-value		0.0306			0.0256	
		HedgesG (95% CI)		0.458 (0.020, 0.897)			0.463 (0.024, 0.902)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Sex = Female	Week 24	Baseline						
		n	41	43	84	41	43	84
		Mean	356.51	346.86	351.57	52.59	52.05	52.32
		SD, SE	105.625, 16.496	110.403, 16.836	107.555, 11.735	15.445, 2.412	16.033, 2.445	15.656, 1.708
		Median	364.00	342.00	350.00	51.95	52.10	52.07
		Q1, Q3	291.00, 412.00	283.00, 417.00	287.00, 416.50	41.53, 62.20	43.16, 65.52	42.39, 62.87
		Min, Max	160.0, 543.0	55.0, 541.0	55.0, 543.0	23.1, 88.4	7.6, 82.4	7.6, 88.4
		Observed						
		n	41	43	84	41	43	84
		Mean	356.63	370.35	363.65	52.62	55.74	54.22
		SD, SE	103.455, 16.157	111.773, 17.045	107.366, 11.715	14.759, 2.305	16.355, 2.494	15.582, 1.700
		Median	361.00	373.00	362.50	52.75	56.29	54.80
		Q1, Q3	302.00, 405.00	320.00, 461.00	307.50, 422.00	45.66, 62.39	47.03, 69.38	46.43, 65.11
		Min, Max	156.0, 575.0	100.0, 587.0	100.0, 587.0	23.9, 82.9	13.8, 86.8	13.8, 86.8

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.4
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Gender

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Sex = Female	Week 24	Change from Baseline						
		n	41	43	84	41	43	84
		Mean	0.12	23.49	12.08	0.03	3.69	1.91
		SD, SE	33.106, 5.170	47.213, 7.200	42.359, 4.622	4.862, 0.759	7.183, 1.095	6.394, 0.698
		Median	0.00	21.00	13.00	0.10	3.00	2.07
		Q1, Q3	-23.00, 26.00	-4.00, 53.00	-11.50, 39.00	-3.50, 3.83	-0.51, 7.99	-1.53, 5.78
		Min, Max	-81.0, 59.0	-147.0, 138.0	-147.0, 138.0	-11.5, 8.5	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-3.26 (6.839)	20.28 (7.480)		-0.57 (1.018)	3.21 (1.132)	
		95% CI	(-16.66, 10.14)	(5.62, 34.94)		(-2.57, 1.42)	(0.99, 5.42)	
		LS Mean Difference (SE)		23.54 (8.494)			3.78 (1.283)	
		95% CI		(6.89, 40.19)			(1.26, 6.29)	
		p-value		0.0056			0.0033	
		HedgesG (95% CI)		0.559 (0.123, 0.995)			0.581 (0.145, 1.018)	

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Race = White		N1	53	55	108	53	55	108
	Baseline	n	52	53	105	52	53	105
		Mean	369.37	359.26	364.27	52.82	52.02	52.42
		SD, SE	103.623, 14.370	100.992, 13.872	101.936, 9.948	14.931, 2.071	14.353, 1.972	14.577, 1.423
		Median	370.00	351.00	358.00	52.30	52.01	52.01
		Q1, Q3	293.50, 443.00	308.00, 423.00	300.00, 437.00	41.31, 61.17	43.86, 62.10	42.80, 62.10
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Race = White	Week 12	Baseline						
		n	52	50	102	52	50	102
		Mean	369.37	358.26	363.92	52.82	51.90	52.37
		SD, SE	103.623, 14.370	103.459, 14.631	103.180, 10.216	14.931, 2.071	14.689, 2.077	14.747, 1.460
		Median	370.00	349.00	356.00	52.30	51.30	51.98
		Q1, Q3	293.50, 443.00	307.00, 437.00	300.00, 438.00	41.31, 61.17	43.16, 62.54	42.30, 62.10
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	52	50	102	52	50	102
		Mean	370.15	381.40	375.67	52.93	55.32	54.10
		SD, SE	97.395, 13.506	99.736, 14.105	98.223, 9.725	13.849, 1.921	14.093, 1.993	13.951, 1.381
		Median	363.50	378.50	373.00	50.75	55.46	52.93
		Q1, Q3	302.00, 441.00	323.00, 437.00	313.00, 440.00	43.41, 61.99	46.10, 65.13	45.15, 63.93
		Min, Max	170.0, 600.0	80.0, 660.0	80.0, 660.0	25.3, 84.6	11.1, 94.9	11.1, 94.9

6MWT = Six Minute Walk Test.
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Table 5.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Race = White	Week 12	Change from Baseline						
		n	52	50	102	52	50	102
		Mean	0.79	23.14	11.75	0.11	3.42	1.73
		SD, SE	38.503, 5.339	40.432, 5.718	40.838, 4.044	5.522, 0.766	6.061, 0.857	5.999, 0.594
		Median	-0.50	15.50	7.50	-0.03	2.28	1.14
		Q1, Q3	-19.50, 29.50	0.00, 45.00	-10.00, 37.00	-2.65, 4.02	0.05, 7.10	-1.35, 5.82
		Min, Max	-95.0, 93.0	-92.0, 155.0	-95.0, 155.0	-14.5, 11.9	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	1.14 (5.368)	22.15 (6.070)		0.12 (0.775)	3.30 (0.913)	
		95% CI	(-9.38, 11.66)	(10.25, 34.05)		(-1.40, 1.64)	(1.51, 5.09)	
		LS Mean Difference (SE)		21.01 (7.142)			3.18 (1.044)	
		95% CI		(7.01, 35.01)			(1.14, 5.23)	
		p-value		0.0033			0.0023	
		HedgesG (95% CI)		0.557 (0.161, 0.952)			0.561 (0.165, 0.957)	

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Race = White	Week 24	Baseline						
		n	51	52	103	51	52	103
		Mean	369.24	360.02	364.58	52.73	52.15	52.44
		SD, SE	104.650, 14.654	101.826, 14.121	102.830, 10.132	15.064, 2.109	14.465, 2.006	14.695, 1.448
		Median	369.00	351.50	358.00	51.95	52.03	52.01
		Q1, Q3	291.00, 446.00	307.50, 430.00	300.00, 438.00	41.09, 62.10	43.51, 62.32	42.30, 62.10
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	51	52	103	51	52	103
		Mean	370.88	387.46	379.25	52.93	56.26	54.61
		SD, SE	102.790, 14.394	105.510, 14.632	103.995, 10.247	14.232, 1.993	15.134, 2.099	14.718, 1.450
		Median	367.00	378.50	375.00	51.88	56.51	54.74
		Q1, Q3	305.00, 437.00	329.50, 461.00	319.00, 452.00	43.97, 62.39	46.74, 66.03	46.23, 63.96
		Min, Max	156.0, 617.0	100.0, 619.0	100.0, 619.0	23.9, 85.2	13.8, 89.1	13.8, 89.1

6MWT = Six Minute Walk Test.
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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Race = White	Week 24	Change from Baseline						
		n	51	52	103	51	52	103
		Mean	1.65	27.44	14.67	0.20	4.11	2.17
		SD, SE	42.664, 5.974	49.503, 6.865	47.807, 4.711	5.931, 0.831	7.305, 1.013	6.913, 0.681
		Median	7.00	21.50	15.00	0.97	3.41	2.27
		Q1, Q3	-30.00, 31.00	-2.50, 57.00	-17.00, 41.00	-4.47, 4.43	-0.23, 8.88	-2.47, 5.83
		Min, Max	-109.0, 125.0	-147.0, 140.0	-147.0, 140.0	-15.1, 15.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	0.98 (6.002)	26.85 (7.305)		0.05 (0.833)	4.05 (1.087)	
		95% CI	(-10.79, 12.74)	(12.53, 41.16)		(-1.58, 1.69)	(1.92, 6.18)	
		LS Mean Difference (SE)		25.87 (8.677)			3.99 (1.245)	
		95% CI		(8.86, 42.87)			(1.55, 6.43)	
		p-value		0.0029			0.0013	
		HedgesG (95% CI)		0.548 (0.155, 0.942)			0.577 (0.183, 0.971)	

6MWT = Six Minute Walk Test.
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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Race = Non-White		N1	13	13	26	13	13	26
	Baseline	n	13	13	26	13	13	26
		Mean	359.62	338.69	349.15	49.94	47.70	48.82
		SD, SE	106.363, 29.500	142.958, 39.649	123.911, 24.301	15.151, 4.202	21.071, 5.844	18.017, 3.533
		Median	364.00	333.00	334.50	52.53	45.42	48.93
		Q1, Q3	279.00, 434.00	240.00, 470.00	264.00, 444.00	40.01, 61.34	30.83, 66.03	33.70, 63.20
		Min, Max	164.0, 543.0	78.0, 541.0	78.0, 543.0	24.7, 74.4	12.1, 82.4	12.1, 82.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 5.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Race = Non-White	Week 12	Baseline						
		n	12	13	25	12	13	25
		Mean	366.33	338.69	351.96	50.77	47.70	49.18
		SD, SE	108.174, 31.227	142.958, 39.649	125.620, 25.124	15.515, 4.479	21.071, 5.844	18.297, 3.659
		Median	373.00	333.00	335.00	52.66	45.42	51.30
		Q1, Q3	292.00, 439.00	240.00, 470.00	264.00, 444.00	38.13, 62.27	30.83, 66.03	33.70, 63.20
		Min, Max	164.0, 543.0	78.0, 541.0	78.0, 543.0	24.7, 74.4	12.1, 82.4	12.1, 82.4
		Observed						
		n	12	13	25	12	13	25
		Mean	374.25	336.31	354.52	51.73	47.55	49.56
		SD, SE	113.063, 32.639	124.753, 34.600	118.385, 23.677	15.516, 4.479	19.174, 5.318	17.283, 3.457
		Median	397.50	329.00	350.00	53.96	45.69	49.25
		Q1, Q3	307.00, 462.00	251.00, 409.00	275.00, 457.00	42.89, 63.52	32.27, 64.75	35.13, 64.75
		Min, Max	175.0, 541.0	103.0, 525.0	103.0, 541.0	25.9, 74.2	15.9, 80.1	15.9, 80.1

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Table 5.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Race = Non-White	Week 12	Change from Baseline						
		n	12	13	25	12	13	25
		Mean	7.92	-2.38	2.56	0.96	-0.16	0.38
		SD, SE	48.388, 13.968	43.372, 12.029	45.180, 9.036	6.239, 1.801	5.493, 1.524	5.767, 1.153
		Median	-3.00	11.00	-2.00	-0.33	1.43	-0.20
		Q1, Q3	-21.50, 25.50	-8.00, 21.00	-12.00, 21.00	-3.08, 3.79	-1.25, 3.20	-1.59, 3.20
		Min, Max	-44.0, 132.0	-136.0, 37.0	-136.0, 132.0	-6.3, 16.4	-16.8, 4.7	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	6.58 (11.523)	-5.24 (13.301)		0.78 (1.417)	-0.40 (1.578)	
		95% CI	(-16.01, 29.16)	(-31.31, 20.83)		(-2.00, 3.55)	(-3.49, 2.70)	
		LS Mean Difference (SE)		-11.82 (17.348)			-1.17 (2.142)	
		95% CI		(-45.82, 22.18)			(-5.37, 3.03)	
		p-value		0.4956			0.5840	
		HedgesG (95% CI)		-0.208 (-0.995, 0.578)			-0.177 (-0.963, 0.609)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Race = Non-White	Week 24	Baseline						
		n	13	12	25	13	12	25
		Mean	359.62	348.92	354.48	49.94	49.26	49.61
		SD, SE	106.363, 29.500	144.265, 41.646	123.391, 24.678	15.151, 4.202	21.216, 6.125	17.922, 3.584
		Median	364.00	333.50	335.00	52.53	48.36	51.30
		Q1, Q3	279.00, 434.00	252.00, 480.00	276.00, 444.00	40.01, 61.34	32.26, 67.52	34.72, 63.20
		Min, Max	164.0, 543.0	78.0, 541.0	78.0, 543.0	24.7, 74.4	12.1, 82.4	12.1, 82.4
		Observed						
		n	13	12	25	13	12	25
		Mean	363.77	354.33	359.24	50.45	50.26	50.36
		SD, SE	109.757, 30.441	125.882, 36.339	115.366, 23.073	15.120, 4.194	19.181, 5.537	16.821, 3.364
		Median	394.00	338.00	356.00	53.75	51.41	53.56
		Q1, Q3	302.00, 434.00	257.50, 469.50	268.00, 440.00	42.46, 58.08	33.03, 66.73	37.36, 63.41
		Min, Max	158.0, 540.0	125.0, 538.0	125.0, 540.0	23.9, 74.1	19.4, 82.1	19.4, 82.1

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.5
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Race

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Race = Non-White	Week 24	Change from Baseline						
		n	13	12	25	13	12	25
		Mean	4.15	5.42	4.76	0.51	1.00	0.74
		SD, SE	44.875, 12.446	38.173, 11.020	40.929, 8.186	5.978, 1.658	5.244, 1.514	5.526, 1.105
		Median	-4.00	0.50	-3.00	-0.41	0.14	-0.28
		Q1, Q3	-19.00, 12.00	-9.00, 28.00	-14.00, 28.00	-2.65, 2.07	-1.28, 3.69	-2.05, 3.62
		Min, Max	-81.0, 99.0	-82.0, 73.0	-82.0, 99.0	-11.5, 12.4	-10.0, 11.1	-11.5, 12.4
		GEE Estimates						
		LS Mean (SE)	4.74 (11.249)	1.76 (12.038)		0.58 (1.437)	0.64 (1.578)	
		95% CI	(-17.30, 26.79)	(-21.84, 25.35)		(-2.23, 3.40)	(-2.45, 3.74)	
		LS Mean Difference (SE)		-2.99 (15.749)			0.06 (2.053)	
		95% CI		(-33.86, 27.88)			(-3.96, 4.08)	
		p-value		0.8495			0.9771	
		HedgesG (95% CI)		0.028 (-0.757, 0.813)			0.082 (-0.703, 0.866)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Age <= 41 Years		N1	36	31	67	36	31	67
	Baseline	n	36	30	66	36	30	66
		Mean	374.11	368.33	371.48	51.11	50.45	50.81
		SD, SE	97.877, 16.313	105.575, 19.275	100.696, 12.395	14.097, 2.349	15.090, 2.755	14.447, 1.778
		Median	370.00	359.00	364.00	51.06	48.48	50.10
		Q1, Q3	300.50, 449.50	307.00, 470.00	301.00, 455.00	40.39, 60.61	42.80, 62.54	41.54, 62.10
		Min, Max	160.0, 543.0	55.0, 534.0	55.0, 543.0	23.1, 76.5	7.6, 71.2	7.6, 76.5

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Table 5.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Age <= 41 Years	Week 12	Baseline						
		n	35	28	63	35	28	63
		Mean	376.83	365.79	371.92	51.43	49.88	50.74
		SD, SE	97.918, 16.551	108.904, 20.581	102.242, 12.881	14.171, 2.395	15.457, 2.921	14.655, 1.846
		Median	371.00	356.00	364.00	51.90	46.74	49.98
		Q1, Q3	301.00, 455.00	303.50, 471.50	301.00, 457.00	40.76, 62.10	42.44, 64.03	41.54, 62.54
		Min, Max	160.0, 543.0	55.0, 534.0	55.0, 543.0	23.1, 76.5	7.6, 71.2	7.6, 76.5
		Observed						
		n	35	28	63	35	28	63
		Mean	386.57	380.79	384.00	52.72	51.99	52.39
		SD, SE	95.103, 16.075	100.530, 18.998	96.796, 12.195	13.515, 2.284	14.514, 2.743	13.858, 1.746
		Median	392.00	392.50	392.00	51.57	50.18	51.01
		Q1, Q3	325.00, 457.00	310.50, 442.50	320.00, 453.00	43.89, 61.74	45.03, 63.78	44.90, 62.25
		Min, Max	179.0, 600.0	80.0, 535.0	80.0, 600.0	25.3, 84.6	11.1, 79.1	11.1, 84.6

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Table 5.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Age <= 41 Years	Week 12	Change from Baseline						
		n	35	28	63	35	28	63
		Mean	9.74	15.00	12.08	1.29	2.10	1.65
		SD, SE	42.847, 7.243	42.996, 8.126	42.647, 5.373	5.712, 0.965	5.616, 1.061	5.638, 0.710
		Median	-2.00	10.50	6.00	-0.20	1.44	0.89
		Q1, Q3	-15.00, 40.00	-1.50, 40.50	-10.00, 40.00	-2.09, 5.82	-0.16, 5.36	-1.35, 5.82
		Min, Max	-64.0, 132.0	-136.0, 93.0	-136.0, 132.0	-8.7, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-0.57 (10.225)	3.72 (11.877)		-0.22 (1.299)	0.44 (1.506)	
		95% CI	(-20.61, 19.47)	(-19.56, 27.00)		(-2.77, 2.32)	(-2.51, 3.40)	
		LS Mean Difference (SE)		4.29 (10.062)			0.67 (1.334)	
		95% CI		(-15.43, 24.01)			(-1.95, 3.28)	
		p-value		0.6701			0.6163	
		HedgesG (95% CI)		0.119 (-0.378, 0.616)			0.140 (-0.358, 0.637)	

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Table 5.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Age <= 41 Years	Week 24	Baseline						
		n	36	30	66	36	30	66
		Mean	374.11	368.33	371.48	51.11	50.45	50.81
		SD, SE	97.877, 16.313	105.575, 19.275	100.696, 12.395	14.097, 2.349	15.090, 2.755	14.447, 1.778
		Median	370.00	359.00	364.00	51.06	48.48	50.10
		Q1, Q3	300.50, 449.50	307.00, 470.00	301.00, 455.00	40.39, 60.61	42.80, 62.54	41.54, 62.10
		Min, Max	160.0, 543.0	55.0, 534.0	55.0, 543.0	23.1, 76.5	7.6, 71.2	7.6, 76.5
		Observed						
		n	36	30	66	36	30	66
		Mean	387.53	394.27	390.59	52.94	54.14	53.49
		SD, SE	95.709, 15.951	105.221, 19.211	99.415, 12.237	13.410, 2.235	15.464, 2.823	14.279, 1.758
		Median	402.50	390.00	400.50	53.25	54.73	53.64
		Q1, Q3	336.50, 452.50	324.00, 478.00	336.00, 470.00	46.87, 62.03	45.49, 65.54	46.23, 63.96
		Min, Max	174.0, 575.0	100.0, 587.0	100.0, 587.0	25.2, 81.2	13.8, 86.8	13.8, 86.8

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Table 5.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Age <= 41 Years	Week 24	Change from Baseline						
		n	36	30	66	36	30	66
		Mean	13.42	25.93	19.11	1.82	3.69	2.67
		SD, SE	41.781, 6.964	41.299, 7.540	41.718, 5.135	5.585, 0.931	5.585, 1.020	5.620, 0.692
		Median	13.00	20.00	16.50	1.81	2.89	2.43
		Q1, Q3	-11.00, 40.50	4.00, 53.00	-4.00, 45.00	-1.41, 5.52	0.57, 7.99	-0.41, 6.24
		Min, Max	-81.0, 125.0	-82.0, 105.0	-82.0, 125.0	-11.5, 15.7	-10.0, 15.7	-11.5, 15.7
		GEE Estimates						
		LS Mean (SE)	3.65 (9.882)	15.35 (10.942)		0.38 (1.252)	2.12 (1.410)	
		95% CI	(-15.72, 23.01)	(-6.10, 36.79)		(-2.07, 2.84)	(-0.64, 4.89)	
		LS Mean Difference (SE)		11.70 (9.649)			1.74 (1.302)	
		95% CI		(-7.21, 30.61)			(-0.81, 4.29)	
		p-value		0.2253			0.1812	
		HedgesG (95% CI)		0.293 (-0.194, 0.780)			0.326 (-0.162, 0.814)	

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Age > 41 Years		N1	30	37	67	30	37	67
	Baseline	n	29	36	65	29	36	65
		Mean	359.10	344.28	350.89	53.65	51.78	52.61
		SD, SE	111.075, 20.626	113.051, 18.842	111.545, 13.835	15.983, 2.968	16.564, 2.761	16.208, 2.010
		Median	367.00	334.50	342.00	56.50	51.66	53.01
		Q1, Q3	289.00, 412.00	278.00, 414.00	278.00, 412.00	41.53, 61.34	42.34, 62.45	42.19, 61.34
		Min, Max	160.0, 615.0	78.0, 643.0	78.0, 643.0	24.4, 88.4	12.1, 92.4	12.1, 92.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 5.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Age > 41 Years	Week 12	Baseline						
		n	29	35	64	29	35	64
		Mean	359.10	344.97	351.38	53.65	51.95	52.72
		SD, SE	111.075, 20.626	114.624, 19.375	112.358, 14.045	15.983, 2.968	16.772, 2.835	16.312, 2.039
		Median	367.00	335.00	344.50	56.50	52.01	53.33
		Q1, Q3	289.00, 412.00	278.00, 417.00	278.00, 414.50	41.53, 61.34	42.19, 63.76	41.86, 61.77
		Min, Max	160.0, 615.0	78.0, 643.0	78.0, 643.0	24.4, 88.4	12.1, 92.4	12.1, 92.4
		Observed						
		n	29	35	64	29	35	64
		Mean	352.03	365.14	359.20	52.70	55.10	54.01
		SD, SE	103.186, 19.161	110.942, 18.753	106.855, 13.357	14.921, 2.771	16.205, 2.739	15.560, 1.945
		Median	333.00	365.00	357.50	50.37	54.99	54.32
		Q1, Q3	286.00, 403.00	311.00, 417.00	291.50, 414.50	43.33, 63.93	45.69, 67.38	43.49, 65.41
		Min, Max	170.0, 573.0	103.0, 660.0	103.0, 660.0	26.0, 81.8	15.9, 94.9	15.9, 94.9

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Table 5.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Age > 41 Years	Week 12	Change from Baseline						
		n	29	35	64	29	35	64
		Mean	-7.07	20.17	7.83	-0.96	3.15	1.29
		SD, SE	35.332, 6.561	41.680, 7.045	40.978, 5.122	5.349, 0.993	6.477, 1.095	6.292, 0.786
		Median	0.00	16.00	7.00	0.04	2.40	1.14
		Q1, Q3	-29.00, 17.00	-4.00, 43.00	-11.00, 29.50	-4.32, 2.40	-0.50, 6.69	-1.49, 4.27
		Min, Max	-95.0, 44.0	-92.0, 155.0	-95.0, 155.0	-14.5, 6.5	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	-15.63 (8.918)	11.63 (8.941)		-2.15 (1.381)	1.97 (1.416)	
		95% CI	(-33.11, 1.85)	(-5.90, 29.15)		(-4.86, 0.55)	(-0.80, 4.75)	
		LS Mean Difference (SE)		27.26 (8.710)			4.13 (1.349)	
		95% CI		(10.19, 44.33)			(1.48, 6.77)	
		p-value		0.0017			0.0022	
		HedgesG (95% CI)		0.680 (0.174, 1.186)			0.665 (0.160, 1.171)	

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Table 5.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Age > 41 Years	Week 24	Baseline						
		n	28	34	62	28	34	62
		Mean	358.50	348.76	353.16	53.51	52.63	53.03
		SD, SE	113.065, 21.367	114.096, 19.567	112.804, 14.326	16.257, 3.072	16.537, 2.836	16.283, 2.068
		Median	366.50	338.00	344.50	55.70	52.03	53.33
		Q1, Q3	281.50, 415.50	278.00, 417.00	278.00, 417.00	41.31, 61.77	42.49, 63.76	42.19, 62.20
		Min, Max	160.0, 615.0	78.0, 643.0	78.0, 643.0	24.4, 88.4	12.1, 92.4	12.1, 92.4
		Observed						
		n	28	34	62	28	34	62
		Mean	346.18	369.76	359.11	51.76	56.00	54.09
		SD, SE	109.855, 20.761	113.100, 19.396	111.363, 14.143	15.658, 2.959	16.596, 2.846	16.188, 2.056
		Median	330.50	367.00	358.50	49.36	57.16	55.08
		Q1, Q3	269.50, 397.00	317.00, 436.00	300.00, 424.00	40.94, 61.87	46.85, 66.46	43.32, 63.82
		Min, Max	156.0, 617.0	109.0, 619.0	109.0, 619.0	23.9, 85.2	16.7, 89.1	16.7, 89.1

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.6
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Age

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Age > 41 Years	Week 24	Change from Baseline						
		n	28	34	62	28	34	62
		Mean	-12.32	21.00	5.95	-1.75	3.38	1.06
		SD, SE	40.235, 7.604	53.904, 9.244	50.675, 6.436	5.762, 1.089	8.188, 1.404	7.588, 0.964
		Median	-11.00	20.50	1.50	-1.53	3.17	0.34
		Q1, Q3	-33.00, 12.50	-14.00, 47.00	-24.00, 30.00	-5.26, 2.02	-2.05, 7.31	-3.50, 4.47
		Min, Max	-109.0, 87.0	-147.0, 140.0	-147.0, 140.0	-15.1, 11.9	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-22.78 (10.477)	12.03 (10.733)		-3.24 (1.548)	2.15 (1.666)	
		95% CI	(-43.32, -2.25)	(-9.01, 33.07)		(-6.27, -0.20)	(-1.11, 5.42)	
		LS Mean Difference (SE)		34.81 (11.443)			5.39 (1.711)	
		95% CI		(12.39, 57.24)			(2.03, 8.74)	
		p-value		0.0023			0.0016	
		HedgesG (95% CI)		0.671 (0.157, 1.185)			0.692 (0.177, 1.207)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat <= 62.5		N1	41	39	80	41	39	80
	Baseline	n	40	38	78	40	38	78
		Mean	386.85	372.00	379.62	54.73	53.48	54.12
		SD, SE	99.419, 15.720	102.092, 16.562	100.352, 11.363	14.748, 2.332	14.956, 2.426	14.766, 1.672
		Median	379.50	351.50	365.00	53.95	52.05	52.90
		Q1, Q3	300.50, 449.50	307.00, 457.00	301.00, 455.00	41.31, 65.03	44.79, 66.00	42.30, 66.00
		Min, Max	164.0, 615.0	146.0, 643.0	146.0, 643.0	24.7, 88.4	22.3, 92.4	22.3, 92.4

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The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline						
		n	39	38	77	39	38	77
		Mean	389.62	372.00	380.92	55.10	53.48	54.30
		SD, SE	99.148, 15.876	102.092, 16.562	100.340, 11.435	14.744, 2.361	14.956, 2.426	14.774, 1.684
		Median	380.00	351.50	366.00	54.90	52.05	53.01
		Q1, Q3	301.00, 455.00	307.00, 457.00	307.00, 455.00	41.53, 66.85	44.79, 66.00	42.49, 66.00
		Min, Max	164.0, 615.0	146.0, 643.0	146.0, 643.0	24.7, 88.4	22.3, 92.4	22.3, 92.4
		Observed						
		n	39	38	77	39	38	77
		Mean	389.36	384.66	387.04	54.96	55.37	55.16
		SD, SE	93.211, 14.926	97.393, 15.799	94.697, 10.792	13.391, 2.144	14.543, 2.359	13.880, 1.582
		Median	383.00	380.50	381.00	51.95	55.59	54.87
		Q1, Q3	313.00, 457.00	318.00, 425.00	318.00, 450.00	43.49, 63.93	45.69, 66.79	45.37, 65.13
		Min, Max	175.0, 600.0	160.0, 660.0	160.0, 660.0	26.4, 84.6	24.5, 94.9	24.5, 94.9

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Table 5.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline						
		n	39	38	77	39	38	77
		Mean	-0.26	12.66	6.12	-0.14	1.89	0.86
		SD, SE	45.572, 7.297	40.768, 6.614	43.472, 4.954	6.308, 1.010	5.691, 0.923	6.059, 0.690
		Median	-2.00	14.00	7.00	-0.24	2.10	1.05
		Q1, Q3	-29.00, 26.00	-3.00, 37.00	-14.00, 33.00	-4.32, 3.94	-0.36, 5.71	-1.86, 4.51
		Min, Max	-95.0, 132.0	-136.0, 93.0	-136.0, 132.0	-14.5, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-9.00 (10.294)	1.92 (10.503)		-1.64 (1.348)	0.22 (1.417)	
		95% CI	(-29.17, 11.18)	(-18.67, 22.50)		(-4.28, 1.00)	(-2.56, 3.00)	
		LS Mean Difference (SE)		10.91 (8.976)			1.86 (1.229)	
		95% CI		(-6.68, 28.51)			(-0.55, 4.27)	
		p-value		0.2241			0.1303	
		HedgesG (95% CI)		0.292 (-0.158, 0.741)			0.329 (-0.120, 0.779)	

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline						
		n	39	38	77	39	38	77
		Mean	387.13	372.00	379.66	54.65	53.48	54.07
		SD, SE	100.703, 16.125	102.092, 16.562	101.009, 11.511	14.933, 2.391	14.956, 2.426	14.858, 1.693
		Median	380.00	351.50	364.00	53.01	52.05	52.79
		Q1, Q3	300.00, 455.00	307.00, 457.00	301.00, 455.00	41.09, 66.85	44.79, 66.00	42.30, 66.00
		Min, Max	164.0, 615.0	146.0, 643.0	146.0, 643.0	24.7, 88.4	22.3, 92.4	22.3, 92.4
		Observed						
		n	39	38	77	39	38	77
		Mean	387.87	392.32	390.06	54.69	56.56	55.61
		SD, SE	94.089, 15.066	100.034, 16.228	96.452, 10.992	13.354, 2.138	15.072, 2.445	14.164, 1.614
		Median	390.00	380.00	388.00	54.66	56.95	55.98
		Q1, Q3	323.00, 465.00	346.00, 452.00	326.00, 452.00	45.66, 63.82	47.03, 65.60	46.85, 63.96
		Min, Max	158.0, 575.0	109.0, 619.0	109.0, 619.0	23.9, 82.9	16.7, 89.1	16.7, 89.1

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline						
		n	39	38	77	39	38	77
		Mean	0.74	20.32	10.40	0.04	3.08	1.54
		SD, SE	46.320, 7.417	37.150, 6.027	42.915, 4.891	6.324, 1.013	5.204, 0.844	5.960, 0.679
		Median	4.00	20.00	9.00	0.73	2.89	1.34
		Q1, Q3	-28.00, 31.00	-3.00, 40.00	-12.00, 34.00	-3.85, 4.48	-0.28, 6.64	-1.46, 4.70
		Min, Max	-109.0, 125.0	-82.0, 105.0	-109.0, 125.0	-15.1, 15.7	-10.0, 15.7	-15.1, 15.7
		GEE Estimates						
		LS Mean (SE)	-9.51 (10.301)	9.57 (9.621)		-1.69 (1.350)	1.41 (1.310)	
		95% CI	(-29.70, 10.68)	(-9.28, 28.43)		(-4.34, 0.95)	(-1.16, 3.98)	
		LS Mean Difference (SE)		19.09 (9.082)			3.10 (1.249)	
		95% CI		(1.29, 36.89)			(0.66, 5.55)	
		p-value		0.0356			0.0130	
		HedgesG (95% CI)		0.455 (0.002, 0.907)			0.512 (0.058, 0.966)	

6MWT = Six Minute Walk Test.
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Table 5.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat > 62.5		N1	25	29	54	25	29	54
	Baseline	n	25	28	53	25	28	53
		Mean	336.32	332.43	334.26	48.28	48.05	48.16
		SD, SE	104.004, 20.801	116.926, 22.097	109.977, 15.107	14.563, 2.913	16.648, 3.146	15.550, 2.136
		Median	335.00	338.00	335.00	46.61	47.80	46.61
		Q1, Q3	276.00, 382.00	248.00, 419.50	249.00, 416.00	35.23, 59.75	37.56, 61.28	37.23, 60.25
		Min, Max	160.0, 569.0	55.0, 538.0	55.0, 569.0	23.1, 78.4	7.6, 80.4	7.6, 80.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline						
		n	25	25	50	25	25	50
		Mean	336.32	327.20	331.76	48.28	47.32	47.80
		SD, SE	104.004, 20.801	122.094, 24.419	112.342, 15.888	14.563, 2.913	17.360, 3.472	15.866, 2.244
		Median	335.00	334.00	334.50	46.61	45.42	46.58
		Q1, Q3	276.00, 382.00	247.00, 423.00	247.00, 423.00	35.23, 59.75	37.23, 61.18	36.79, 60.25
		Min, Max	160.0, 569.0	55.0, 538.0	55.0, 569.0	23.1, 78.4	7.6, 80.4	7.6, 80.4
		Observed						
		n	25	25	50	25	25	50
		Mean	342.16	353.00	347.58	49.19	51.21	50.20
		SD, SE	104.176, 20.835	117.098, 23.420	109.825, 15.532	14.610, 2.922	16.684, 3.337	15.554, 2.200
		Median	333.00	352.00	339.00	49.09	53.82	50.04
		Q1, Q3	289.00, 403.00	311.00, 437.00	294.00, 426.00	41.29, 61.57	43.62, 64.13	43.00, 63.43
		Min, Max	170.0, 573.0	80.0, 542.0	80.0, 573.0	25.3, 79.1	11.1, 80.0	11.1, 80.0

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Table 5.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline						
		n	25	25	50	25	25	50
		Mean	5.84	25.80	15.82	0.91	3.89	2.40
		SD, SE	30.532, 6.106	43.443, 8.689	38.505, 5.445	4.385, 0.877	6.569, 1.314	5.729, 0.810
		Median	0.00	12.00	5.00	0.05	1.99	0.76
		Q1, Q3	-10.00, 35.00	-3.00, 57.00	-10.00, 36.00	-1.39, 5.75	-0.37, 8.54	-1.35, 5.82
		Min, Max	-54.0, 60.0	-46.0, 155.0	-54.0, 155.0	-8.5, 8.7	-6.6, 24.6	-8.5, 24.6
		GEE Estimates						
		LS Mean (SE)	-3.18 (7.462)	14.51 (6.917)		-0.45 (1.112)	2.25 (1.005)	
		95% CI	(-17.81, 11.44)	(0.95, 28.07)		(-2.63, 1.73)	(0.28, 4.22)	
		LS Mean Difference (SE)		17.69 (9.517)			2.69 (1.414)	
		95% CI		(-0.96, 36.35)			(-0.08, 5.46)	
		p-value		0.0630			0.0569	
		HedgesG (95% CI)		0.513 (-0.051, 1.076)			0.514 (-0.049, 1.078)	

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Table 5.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline						
		n	25	26	51	25	26	51
		Mean	336.32	337.38	336.86	48.28	48.87	48.58
		SD, SE	104.004, 20.801	119.128, 23.363	110.852, 15.522	14.563, 2.913	16.852, 3.305	15.617, 2.187
		Median	335.00	344.50	342.00	46.61	50.64	49.03
		Q1, Q3	276.00, 382.00	249.00, 423.00	249.00, 423.00	35.23, 59.75	37.88, 61.39	37.23, 61.18
		Min, Max	160.0, 569.0	55.0, 538.0	55.0, 569.0	23.1, 78.4	7.6, 80.4	7.6, 80.4
		Observed						
		n	25	26	51	25	26	51
		Mean	340.68	365.08	353.12	48.90	53.05	51.02
		SD, SE	112.369, 22.474	121.829, 23.893	116.764, 16.350	15.341, 3.068	17.303, 3.393	16.342, 2.288
		Median	337.00	364.50	356.00	50.32	52.62	50.91
		Q1, Q3	271.00, 405.00	300.00, 478.00	296.00, 425.00	40.36, 57.96	44.29, 66.46	42.46, 63.41
		Min, Max	156.0, 617.0	100.0, 578.0	100.0, 617.0	23.9, 85.2	13.8, 84.4	13.8, 85.2

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Table 5.2.7.1.24.7
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Stiffness at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline						
		n	25	26	51	25	26	51
		Mean	4.36	27.69	16.25	0.61	4.18	2.43
		SD, SE	37.367, 7.473	61.264, 12.015	51.823, 7.257	5.260, 1.052	9.159, 1.796	7.647, 1.071
		Median	0.00	22.00	15.00	0.05	3.23	2.18
		Q1, Q3	-18.00, 30.00	-14.00, 62.00	-16.00, 47.00	-2.59, 4.36	-2.05, 9.29	-2.20, 6.77
		Min, Max	-64.0, 87.0	-147.0, 140.0	-147.0, 140.0	-10.1, 11.9	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-4.66 (8.597)	16.79 (10.394)		-0.74 (1.255)	2.60 (1.558)	
		95% CI	(-21.51, 12.19)	(-3.59, 37.16)		(-3.20, 1.72)	(-0.46, 5.65)	
		LS Mean Difference (SE)		21.45 (13.263)			3.34 (1.945)	
		95% CI		(-4.55, 47.45)			(-0.47, 7.15)	
		p-value		0.1058			0.0859	
		HedgesG (95% CI)		0.442 (-0.114, 0.997)			0.459 (-0.097, 1.015)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat <= 47.8		N1	37	30	67	37	30	67
	Baseline	n	37	29	66	37	29	66
		Mean	404.22	395.93	400.58	56.34	56.29	56.31
		SD, SE	106.034, 17.432	98.400, 18.272	102.054, 12.562	15.516, 2.551	14.668, 2.724	15.034, 1.851
		Median	394.00	392.00	393.00	56.21	55.38	55.80
		Q1, Q3	349.00, 472.00	331.00, 473.00	334.00, 473.00	46.55, 66.85	46.49, 66.03	46.49, 66.64
		Min, Max	164.0, 615.0	203.0, 643.0	164.0, 643.0	24.7, 88.4	25.9, 92.4	24.7, 92.4

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline						
		n	36	27	63	36	27	63
		Mean	407.69	395.33	402.40	56.79	56.13	56.51
		SD, SE	105.375, 17.563	102.034, 19.637	103.307, 13.015	15.486, 2.581	15.187, 2.923	15.238, 1.920
		Median	407.00	364.00	394.00	56.51	54.96	56.21
		Q1, Q3	351.00, 479.00	331.00, 477.00	334.00, 477.00	47.60, 68.21	45.19, 66.64	46.49, 66.85
		Min, Max	164.0, 615.0	203.0, 643.0	164.0, 643.0	24.7, 88.4	25.9, 92.4	24.7, 92.4
		Observed						
		n	36	27	63	36	27	63
		Mean	410.58	412.44	411.38	57.10	58.69	57.78
		SD, SE	99.839, 16.640	93.367, 17.969	96.351, 12.139	14.237, 2.373	14.447, 2.780	14.234, 1.793
		Median	416.00	398.00	405.00	56.78	58.67	57.22
		Q1, Q3	344.00, 468.00	356.00, 487.00	355.00, 474.00	48.33, 65.97	47.33, 68.07	48.13, 67.77
		Min, Max	175.0, 600.0	240.0, 660.0	175.0, 660.0	25.3, 84.6	30.6, 94.9	25.3, 94.9

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline						
		n	36	27	63	36	27	63
		Mean	2.89	17.11	8.98	0.31	2.56	1.28
		SD, SE	43.410, 7.235	39.852, 7.670	42.192, 5.316	5.870, 0.978	5.295, 1.019	5.698, 0.718
		Median	-2.50	17.00	6.00	-0.28	2.53	0.91
		Q1, Q3	-25.00, 29.00	6.00, 37.00	-10.00, 36.00	-3.50, 4.02	0.83, 5.71	-1.39, 4.74
		Min, Max	-64.0, 132.0	-136.0, 93.0	-136.0, 132.0	-9.5, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-1.71 (8.637)	11.05 (10.383)		-0.49 (1.106)	1.72 (1.375)	
		95% CI	(-18.64, 15.22)	(-9.30, 31.40)		(-2.66, 1.68)	(-0.97, 4.42)	
		LS Mean Difference (SE)		12.76 (9.602)			2.21 (1.292)	
		95% CI		(-6.06, 31.58)			(-0.32, 4.75)	

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
		p-value		0.1839			0.0866	
		HedgesG (95% CI)		0.330 (-0.173, 0.832)			0.389 (-0.115, 0.893)	

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Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline						
		n	37	29	66	37	29	66
		Mean	404.22	395.93	400.58	56.34	56.29	56.31
		SD, SE	106.034, 17.432	98.400, 18.272	102.054, 12.562	15.516, 2.551	14.668, 2.724	15.034, 1.851
		Median	394.00	392.00	393.00	56.21	55.38	55.80
		Q1, Q3	349.00, 472.00	331.00, 473.00	334.00, 473.00	46.55, 66.85	46.49, 66.03	46.49, 66.64
		Min, Max	164.0, 615.0	203.0, 643.0	164.0, 643.0	24.7, 88.4	25.9, 92.4	24.7, 92.4
		Observed						
		n	37	29	66	37	29	66
		Mean	407.54	416.00	411.26	56.71	59.34	57.87
		SD, SE	105.350, 17.319	89.257, 16.575	97.963, 12.058	14.747, 2.424	14.004, 2.600	14.375, 1.769
		Median	411.00	401.00	408.00	56.39	59.36	56.41
		Q1, Q3	347.00, 475.00	361.00, 478.00	360.00, 478.00	47.18, 64.69	50.39, 68.91	49.49, 68.91
		Min, Max	158.0, 617.0	231.0, 619.0	158.0, 619.0	23.9, 85.2	29.5, 89.1	23.9, 89.1

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Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline						
		n	37	29	66	37	29	66
		Mean	3.32	20.07	10.68	0.38	3.05	1.55
		SD, SE	49.904, 8.204	43.743, 8.123	47.683, 5.869	6.788, 1.116	6.131, 1.139	6.596, 0.812
		Median	8.00	19.00	12.00	1.22	2.69	1.78
		Q1, Q3	-32.00, 37.00	-4.00, 43.00	-21.00, 41.00	-5.09, 5.32	-0.42, 6.64	-2.65, 5.46
		Min, Max	-109.0, 125.0	-82.0, 140.0	-109.0, 140.0	-15.1, 15.7	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-1.03 (9.042)	14.35 (10.239)		-0.40 (1.193)	2.25 (1.423)	
		95% CI	(-18.76, 16.69)	(-5.72, 34.42)		(-2.74, 1.94)	(-0.54, 5.04)	
		LS Mean Difference (SE)		15.38 (10.646)			2.65 (1.481)	
		95% CI		(-5.48, 36.25)			(-0.25, 5.55)	

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
		p-value		0.1485			0.0736	
		HedgesG (95% CI)		0.344 (-0.145, 0.834)			0.400 (-0.091, 0.891)	

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Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat > 47.8		N1	29	38	67	29	38	67
	Baseline	n	28	37	65	28	37	65
		Mean	318.79	323.30	321.35	46.84	47.17	47.03
		SD, SE	77.768, 14.697	108.416, 17.823	95.750, 11.876	12.333, 2.331	15.688, 2.579	14.235, 1.766
		Median	311.50	334.00	326.00	45.94	45.61	45.61
		Q1, Q3	276.50, 375.00	249.00, 386.00	276.00, 376.00	38.60, 57.71	37.88, 58.23	37.88, 57.76
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
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Table 5.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline						
		n	28	36	64	28	36	64
		Mean	318.79	323.39	321.38	46.84	47.21	47.05
		SD, SE	77.768, 14.697	109.952, 18.325	96.507, 12.063	12.333, 2.331	15.909, 2.651	14.346, 1.793
		Median	311.50	334.00	329.50	45.94	46.16	45.99
		Q1, Q3	276.50, 375.00	248.00, 394.00	268.00, 381.00	38.60, 57.71	37.56, 59.30	37.56, 58.00
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4
		Observed						
		n	28	36	64	28	36	64
		Mean	319.93	341.83	332.25	47.06	49.98	48.71
		SD, SE	73.596, 13.908	105.773, 17.629	93.042, 11.630	11.806, 2.231	15.277, 2.546	13.839, 1.730
		Median	320.00	344.00	327.00	44.87	51.92	49.17
		Q1, Q3	284.50, 370.00	305.50, 424.00	288.50, 388.50	41.18, 54.66	43.49, 58.96	42.15, 56.86
		Min, Max	170.0, 481.0	80.0, 535.0	80.0, 535.0	25.9, 73.8	11.1, 80.0	11.1, 80.0

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline						
		n	28	36	64	28	36	64
		Mean	1.14	18.44	10.88	0.22	2.77	1.66
		SD, SE	36.440, 6.887	44.103, 7.350	41.527, 5.191	5.390, 1.019	6.687, 1.114	6.238, 0.780
		Median	-0.50	10.50	6.00	-0.03	1.47	0.89
		Q1, Q3	-12.00, 31.00	-6.50, 44.50	-10.00, 36.00	-1.73, 4.85	-0.90, 6.95	-1.36, 5.78
		Min, Max	-95.0, 60.0	-92.0, 155.0	-95.0, 155.0	-14.5, 8.7	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	-11.32 (8.945)	8.13 (6.449)		-1.87 (1.335)	1.01 (0.938)	
		95% CI	(-28.86, 6.21)	(-4.51, 20.77)		(-4.49, 0.75)	(-0.83, 2.84)	
		LS Mean Difference (SE)		19.45 (9.796)			2.88 (1.470)	
		95% CI		(0.25, 38.65)			(-0.01, 5.76)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
		p-value		0.0470			0.0505	
		HedgesG (95% CI)		0.411 (-0.088, 0.910)			0.403 (-0.096, 0.901)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline						
		n	27	35	62	27	35	62
		Mean	316.67	326.46	322.19	46.44	47.73	47.17
		SD, SE	78.421, 15.092	109.982, 18.590	96.888, 12.305	12.381, 2.383	15.829, 2.676	14.332, 1.820
		Median	308.00	334.00	329.50	45.32	46.90	45.99
		Q1, Q3	276.00, 374.00	249.00, 402.00	276.00, 386.00	37.24, 57.76	37.88, 60.37	37.88, 58.23
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4
		Observed						
		n	27	35	62	27	35	62
		Mean	317.22	352.46	337.11	46.55	51.65	49.43
		SD, SE	75.063, 14.446	117.029, 19.781	101.713, 12.918	11.591, 2.231	16.848, 2.848	14.899, 1.892
		Median	323.00	346.00	336.50	48.03	53.07	49.05
		Q1, Q3	271.00, 364.00	300.00, 461.00	296.00, 390.00	40.36, 54.86	44.29, 64.94	42.46, 58.70
		Min, Max	156.0, 470.0	100.0, 587.0	100.0, 587.0	23.9, 66.5	13.8, 86.8	13.8, 86.8

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline						
		n	27	35	62	27	35	62
		Mean	0.56	26.00	14.92	0.11	3.92	2.26
		SD, SE	31.296, 6.023	51.905, 8.774	45.617, 5.793	4.509, 0.868	7.772, 1.314	6.780, 0.861
		Median	0.00	21.00	12.50	0.10	3.17	1.76
		Q1, Q3	-22.00, 26.00	-5.00, 55.00	-14.00, 40.00	-3.09, 3.83	-0.59, 8.75	-2.05, 5.83
		Min, Max	-64.0, 61.0	-147.0, 138.0	-147.0, 138.0	-10.1, 7.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-13.94 (8.435)	15.42 (7.702)		-2.30 (1.229)	2.13 (1.125)	
		95% CI	(-30.47, 2.60)	(0.33, 30.52)		(-4.71, 0.11)	(-0.08, 4.33)	
		LS Mean Difference (SE)		29.36 (10.768)			4.43 (1.592)	
		95% CI		(8.25, 50.46)			(1.31, 7.55)	

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Table 5.2.7.1.24.8
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Physical Function at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
		p-value		0.0064			0.0054	
		HedgesG (95% CI)		0.560 (0.048, 1.071)			0.565 (0.053, 1.077)	

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Table 5.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat <= 62.5		N1	42	32	74	42	32	74
	Baseline	n	42	32	74	42	32	74
		Mean	395.48	381.31	389.35	55.58	54.83	55.26
		SD, SE	99.636, 15.374	99.643, 17.615	99.206, 11.532	14.437, 2.228	14.997, 2.651	14.584, 1.695
		Median	379.50	360.00	375.00	53.95	53.29	53.74
		Q1, Q3	312.00, 471.00	310.00, 461.00	312.00, 471.00	42.95, 65.35	43.18, 66.01	42.95, 66.00
		Min, Max	189.0, 615.0	203.0, 643.0	189.0, 643.0	26.7, 88.4	25.9, 92.4	25.9, 92.4

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline						
		n	41	32	73	41	32	73
		Mean	398.32	381.31	390.86	55.96	54.83	55.47
		SD, SE	99.136, 15.483	99.643, 17.615	99.031, 11.591	14.402, 2.249	14.997, 2.651	14.574, 1.706
		Median	380.00	360.00	376.00	54.90	53.29	54.48
		Q1, Q3	335.00, 471.00	310.00, 461.00	320.00, 471.00	44.94, 65.35	43.18, 66.01	43.86, 66.00
		Min, Max	189.0, 615.0	203.0, 643.0	189.0, 643.0	26.7, 88.4	25.9, 92.4	25.9, 92.4
		Observed						
		n	41	32	73	41	32	73
		Mean	393.90	399.38	396.30	55.27	57.52	56.26
		SD, SE	96.675, 15.098	91.949, 16.255	94.021, 11.004	13.570, 2.119	14.236, 2.517	13.814, 1.617
		Median	394.00	388.00	392.00	51.57	57.00	54.99
		Q1, Q3	320.00, 457.00	354.50, 451.00	333.00, 457.00	46.46, 65.00	47.68, 67.86	46.46, 66.26
		Min, Max	179.0, 600.0	240.0, 660.0	179.0, 660.0	25.3, 84.6	30.6, 94.9	25.3, 94.9

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline						
		n	41	32	73	41	32	73
		Mean	-4.41	18.06	5.44	-0.70	2.69	0.79
		SD, SE	43.553, 6.802	39.055, 6.904	42.856, 5.016	6.012, 0.939	5.277, 0.933	5.911, 0.692
		Median	-4.00	17.00	3.00	-0.46	2.47	0.55
		Q1, Q3	-34.00, 13.00	0.50, 37.00	-10.00, 26.00	-4.43, 1.71	0.14, 5.23	-1.39, 3.99
		Min, Max	-95.0, 132.0	-136.0, 93.0	-136.0, 132.0	-14.5, 16.4	-16.8, 12.8	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-12.48 (10.271)	8.34 (10.486)		-2.15 (1.382)	1.22 (1.422)	
		95% CI	(-32.61, 7.65)	(-12.21, 28.89)		(-4.86, 0.56)	(-1.57, 4.00)	
		LS Mean Difference (SE)		20.82 (8.983)			3.36 (1.220)	
		95% CI		(3.21, 38.43)			(0.97, 5.75)	
		p-value		0.0205			0.0059	
		HedgesG (95% CI)		0.527 (0.056, 0.997)			0.580 (0.108, 1.051)	

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline						
		n	41	32	73	41	32	73
		Mean	395.95	381.31	389.53	55.53	54.83	55.22
		SD, SE	100.825, 15.746	99.643, 17.615	99.880, 11.690	14.612, 2.282	14.997, 2.651	14.683, 1.718
		Median	380.00	360.00	374.00	53.01	53.29	53.01
		Q1, Q3	312.00, 471.00	310.00, 461.00	312.00, 471.00	42.95, 65.35	43.18, 66.01	42.95, 66.00
		Min, Max	189.0, 615.0	203.0, 643.0	189.0, 643.0	26.7, 88.4	25.9, 92.4	25.9, 92.4
		Observed						
		n	41	32	73	41	32	73
		Mean	395.10	402.91	398.52	55.36	58.15	56.58
		SD, SE	99.611, 15.557	90.822, 16.055	95.285, 11.152	13.810, 2.157	14.385, 2.543	14.036, 1.643
		Median	400.00	380.00	400.00	54.66	58.12	55.98
		Q1, Q3	326.00, 443.00	360.00, 452.00	346.00, 452.00	47.07, 63.41	48.26, 67.48	47.07, 64.68
		Min, Max	189.0, 617.0	231.0, 619.0	189.0, 619.0	26.7, 85.2	29.5, 89.1	26.7, 89.1

6MWT = Six Minute Walk Test.
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Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline						
		n	41	32	73	41	32	73
		Mean	-0.85	21.59	8.99	-0.18	3.32	1.36
		SD, SE	47.961, 7.490	42.612, 7.533	46.749, 5.472	6.521, 1.018	6.081, 1.075	6.527, 0.764
		Median	0.00	17.00	8.00	0.05	2.48	1.22
		Q1, Q3	-32.00, 28.00	-3.50, 41.50	-19.00, 34.00	-5.09, 4.35	-0.36, 6.64	-2.65, 4.48
		Min, Max	-109.0, 125.0	-82.0, 140.0	-109.0, 140.0	-15.1, 15.7	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-10.34 (10.485)	11.87 (10.691)		-1.85 (1.426)	1.84 (1.512)	
		95% CI	(-30.89, 10.21)	(-9.08, 32.83)		(-4.64, 0.95)	(-1.12, 4.81)	
		LS Mean Difference (SE)		22.22 (10.054)			3.69 (1.410)	
		95% CI		(2.51, 41.92)			(0.93, 6.46)	
		p-value		0.0271			0.0088	
		HedgesG (95% CI)		0.479 (0.010, 0.948)			0.539 (0.069, 1.010)	

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Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat > 62.5		N1	24	35	59	24	35	59
	Baseline	n	23	34	57	23	34	57
		Mean	316.17	330.65	324.81	46.15	47.74	47.10
		SD, SE	91.425, 19.064	114.139, 19.575	104.939, 13.899	14.052, 2.930	15.988, 2.742	15.127, 2.004
		Median	315.00	337.50	334.00	46.56	46.74	46.56
		Q1, Q3	260.00, 405.00	249.00, 414.00	260.00, 405.00	34.72, 59.40	37.88, 60.37	37.23, 59.40
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4

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Table 5.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline						
		n	23	31	54	23	31	54
		Mean	316.17	326.26	321.96	46.15	47.12	46.71
		SD, SE	91.425, 19.064	118.062, 21.204	106.699, 14.520	14.052, 2.930	16.506, 2.965	15.376, 2.092
		Median	315.00	334.00	333.50	46.56	46.49	46.53
		Q1, Q3	260.00, 405.00	247.00, 414.00	249.00, 405.00	34.72, 59.40	37.23, 60.37	36.79, 59.40
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4
		Observed						
		n	23	31	54	23	31	54
		Mean	329.96	343.94	337.98	48.15	49.79	49.09
		SD, SE	93.045, 19.401	113.235, 20.338	104.404, 14.208	14.031, 2.926	15.857, 2.848	14.990, 2.040
		Median	325.00	350.00	328.50	45.26	52.10	49.17
		Q1, Q3	280.00, 383.00	304.00, 425.00	291.00, 423.00	40.98, 57.88	43.35, 59.24	41.07, 58.67
		Min, Max	170.0, 481.0	80.0, 535.0	80.0, 535.0	25.9, 73.8	11.1, 80.0	11.1, 80.0

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Table 5.2.7.1.24.9
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline						
		n	23	31	54	23	31	54
		Mean	13.78	17.68	16.02	1.99	2.67	2.38
		SD, SE	30.972, 6.458	45.501, 8.172	39.672, 5.399	4.463, 0.931	6.907, 1.240	5.948, 0.809
		Median	18.00	8.00	11.50	2.74	1.24	1.84
		Q1, Q3	-9.00, 40.00	-7.00, 45.00	-7.00, 40.00	-1.23, 5.89	-0.91, 7.31	-0.91, 6.25
		Min, Max	-54.0, 60.0	-92.0, 155.0	-92.0, 155.0	-8.5, 8.7	-14.4, 24.6	-14.4, 24.6
		GEE Estimates						
		LS Mean (SE)	3.52 (7.995)	7.29 (7.648)		0.37 (1.157)	1.04 (1.138)	
		95% CI	(-12.15, 19.20)	(-7.70, 22.28)		(-1.90, 2.63)	(-1.19, 3.27)	
		LS Mean Difference (SE)		3.77 (9.975)			0.67 (1.478)	
		95% CI		(-15.78, 23.32)			(-2.22, 3.57)	
		p-value		0.7058			0.6493	
		HedgesG (95% CI)		0.094 (-0.446, 0.634)			0.109 (-0.431, 0.649)	

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline						
		n	23	32	55	23	32	55
		Mean	316.17	334.56	326.87	46.15	48.39	47.45
		SD, SE	91.425, 19.064	115.865, 20.482	105.811, 14.268	14.052, 2.930	16.133, 2.852	15.202, 2.050
		Median	315.00	341.50	334.00	46.56	47.56	46.61
		Q1, Q3	260.00, 405.00	263.50, 415.00	260.00, 412.00	34.72, 59.40	40.34, 60.75	37.23, 60.37
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4
		Observed						
		n	23	32	55	23	32	55
		Mean	323.70	359.59	344.58	47.20	52.12	50.06
		SD, SE	95.671, 19.949	122.743, 21.698	112.682, 15.194	14.022, 2.924	17.116, 3.026	15.946, 2.150
		Median	336.00	350.50	337.00	48.03	51.73	49.35
		Q1, Q3	268.00, 388.00	300.00, 464.50	296.00, 436.00	35.28, 60.33	44.54, 65.57	42.46, 62.39
		Min, Max	156.0, 480.0	100.0, 587.0	100.0, 587.0	23.9, 70.0	13.8, 86.8	13.8, 86.8

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Pain Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline						
		n	23	32	55	23	32	55
		Mean	7.52	25.03	17.71	1.04	3.73	2.61
		SD, SE	31.763, 6.623	53.659, 9.486	46.259, 6.238	4.601, 0.959	7.971, 1.409	6.847, 0.923
		Median	8.00	21.50	16.00	1.33	3.32	2.64
		Q1, Q3	-10.00, 38.00	-9.00, 57.00	-10.00, 46.00	-1.35, 5.46	-1.15, 8.88	-1.35, 6.73
		Min, Max	-64.0, 61.0	-147.0, 138.0	-147.0, 138.0	-10.1, 7.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-2.74 (7.859)	14.97 (8.917)		-0.58 (1.126)	2.15 (1.313)	
		95% CI	(-18.14, 12.67)	(-2.51, 32.44)		(-2.79, 1.62)	(-0.42, 4.72)	
		LS Mean Difference (SE)		17.70 (11.400)			2.73 (1.669)	
		95% CI		(-4.64, 40.05)			(-0.54, 6.01)	
		p-value		0.1205			0.1015	
		HedgesG (95% CI)		0.369 (-0.171, 0.910)			0.384 (-0.157, 0.924)	

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Table 5.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat <= 47.8		N1	37	30	67	37	30	67
	Baseline	n	37	29	66	37	29	66
		Mean	404.22	392.21	398.94	56.34	55.81	56.11
		SD, SE	106.034, 17.432	99.684, 18.511	102.682, 12.639	15.516, 2.551	14.757, 2.740	15.074, 1.855
		Median	394.00	364.00	387.00	56.21	54.96	55.17
		Q1, Q3	349.00, 472.00	331.00, 473.00	331.00, 473.00	46.55, 66.85	45.19, 66.03	45.19, 66.64
		Min, Max	164.0, 615.0	203.0, 643.0	164.0, 643.0	24.7, 88.4	25.9, 92.4	24.7, 92.4

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline						
		n	36	28	64	36	28	64
		Mean	407.69	392.21	400.92	56.79	55.83	56.37
		SD, SE	105.375, 17.563	101.513, 19.184	103.175, 12.897	15.486, 2.581	15.028, 2.840	15.174, 1.897
		Median	407.00	362.00	388.00	56.51	54.72	55.59
		Q1, Q3	351.00, 479.00	325.50, 475.00	332.50, 475.00	47.60, 68.21	44.53, 66.34	45.84, 66.75
		Min, Max	164.0, 615.0	203.0, 643.0	164.0, 643.0	24.7, 88.4	25.9, 92.4	24.7, 92.4
		Observed						
		n	36	28	64	36	28	64
		Mean	410.58	407.46	409.22	57.10	58.11	57.54
		SD, SE	99.839, 16.640	94.687, 17.894	96.864, 12.108	14.237, 2.373	14.438, 2.728	14.220, 1.777
		Median	416.00	394.00	404.00	56.78	57.87	57.14
		Q1, Q3	344.00, 468.00	354.50, 483.50	350.50, 471.50	48.33, 65.97	46.71, 67.92	48.02, 67.73
		Min, Max	175.0, 600.0	240.0, 660.0	175.0, 660.0	25.3, 84.6	30.6, 94.9	25.3, 94.9

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline						
		n	36	28	64	36	28	64
		Mean	2.89	15.25	8.30	0.31	2.28	1.17
		SD, SE	43.410, 7.235	38.940, 7.359	41.653, 5.207	5.870, 0.978	5.159, 0.975	5.614, 0.702
		Median	-2.50	15.50	6.00	-0.28	2.21	0.90
		Q1, Q3	-25.00, 29.00	2.00, 31.50	-9.00, 29.00	-3.50, 4.02	0.28, 4.39	-1.32, 4.04
		Min, Max	-64.0, 132.0	-136.0, 93.0	-136.0, 132.0	-9.5, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-0.22 (8.651)	9.16 (10.270)		-0.30 (1.106)	1.42 (1.360)	
		95% CI	(-17.17, 16.74)	(-10.96, 29.29)		(-2.47, 1.87)	(-1.24, 4.09)	
		LS Mean Difference (SE)		9.38 (9.574)			1.73 (1.277)	
		95% CI		(-9.38, 28.15)			(-0.78, 4.23)	

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
		p-value		0.3271			0.1763	
		HedgesG (95% CI)		0.289 (-0.207, 0.786)			0.343 (-0.154, 0.841)	

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Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline						
		n	37	29	66	37	29	66
		Mean	404.22	392.21	398.94	56.34	55.81	56.11
		SD, SE	106.034, 17.432	99.684, 18.511	102.682, 12.639	15.516, 2.551	14.757, 2.740	15.074, 1.855
		Median	394.00	364.00	387.00	56.21	54.96	55.17
		Q1, Q3	349.00, 472.00	331.00, 473.00	331.00, 473.00	46.55, 66.85	45.19, 66.03	45.19, 66.64
		Min, Max	164.0, 615.0	203.0, 643.0	164.0, 643.0	24.7, 88.4	25.9, 92.4	24.7, 92.4
		Observed						
		n	37	29	66	37	29	66
		Mean	407.54	411.97	409.48	56.71	58.84	57.65
		SD, SE	105.350, 17.319	88.983, 16.524	97.788, 12.037	14.747, 2.424	13.899, 2.581	14.311, 1.762
		Median	411.00	400.00	405.00	56.39	58.64	56.41
		Q1, Q3	347.00, 475.00	360.00, 452.00	360.00, 475.00	47.18, 64.69	50.39, 68.51	49.49, 68.51
		Min, Max	158.0, 617.0	231.0, 619.0	158.0, 619.0	23.9, 85.2	29.5, 89.1	23.9, 89.1

6MWT = Six Minute Walk Test.
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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline						
		n	37	29	66	37	29	66
		Mean	3.32	19.76	10.55	0.38	3.02	1.54
		SD, SE	49.904, 8.204	43.122, 8.008	47.412, 5.836	6.788, 1.116	6.046, 1.123	6.559, 0.807
		Median	8.00	19.00	12.50	1.22	2.78	2.04
		Q1, Q3	-32.00, 37.00	-4.00, 40.00	-21.00, 40.00	-5.09, 5.32	-0.42, 6.64	-2.65, 5.46
		Min, Max	-109.0, 125.0	-82.0, 140.0	-109.0, 140.0	-15.1, 15.7	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	0.46 (9.012)	15.01 (10.171)		-0.21 (1.188)	2.35 (1.415)	
		95% CI	(-17.20, 18.13)	(-4.93, 34.94)		(-2.53, 2.12)	(-0.42, 5.12)	
		LS Mean Difference (SE)		14.54 (10.528)			2.56 (1.461)	
		95% CI		(-6.09, 35.18)			(-0.31, 5.42)	

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Table 5.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
		p-value		0.1673			0.0804	
		HedgesG (95% CI)		0.340 (-0.150, 0.829)			0.398 (-0.093, 0.889)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat > 47.8		N1	29	38	67	29	38	67
	Baseline	n	28	37	65	28	37	65
		Mean	318.79	326.22	323.02	46.84	47.54	47.24
		SD, SE	77.768, 14.697	109.417, 17.988	96.434, 11.961	12.333, 2.331	15.832, 2.603	14.328, 1.777
		Median	311.50	334.00	333.00	45.94	46.90	46.56
		Q1, Q3	276.50, 375.00	249.00, 402.00	276.00, 386.00	38.60, 57.71	37.88, 60.37	37.88, 58.23
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
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Table 5.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline						
		n	28	35	63	28	35	63
		Mean	318.79	323.83	321.59	46.84	47.20	47.04
		SD, SE	77.768, 14.697	111.500, 18.847	97.251, 12.252	12.333, 2.331	16.110, 2.723	14.443, 1.820
		Median	311.50	334.00	333.00	45.94	46.90	46.56
		Q1, Q3	276.50, 375.00	247.00, 402.00	260.00, 386.00	38.60, 57.71	37.23, 60.37	37.24, 58.23
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4
		Observed						
		n	28	35	63	28	35	63
		Mean	319.93	343.80	333.19	47.06	50.20	48.81
		SD, SE	73.596, 13.908	107.105, 18.104	93.769, 11.814	11.806, 2.231	15.498, 2.620	13.960, 1.759
		Median	320.00	352.00	328.00	44.87	53.82	49.25
		Q1, Q3	284.50, 370.00	304.00, 425.00	288.00, 394.00	41.18, 54.66	43.35, 59.24	41.29, 56.94
		Min, Max	170.0, 481.0	80.0, 535.0	80.0, 535.0	25.9, 73.8	11.1, 80.0	11.1, 80.0

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline						
		n	28	35	63	28	35	63
		Mean	1.14	19.97	11.60	0.22	3.01	1.77
		SD, SE	36.440, 6.887	44.757, 7.565	42.021, 5.294	5.390, 1.019	6.790, 1.148	6.315, 0.796
		Median	-0.50	12.00	8.00	-0.03	1.99	1.24
		Q1, Q3	-12.00, 31.00	-9.00, 45.00	-10.00, 40.00	-1.73, 4.85	-1.30, 7.31	-1.38, 6.25
		Min, Max	-95.0, 60.0	-92.0, 155.0	-95.0, 155.0	-14.5, 8.7	-14.4, 24.6	-14.5, 24.6
		GEE Estimates						
		LS Mean (SE)	-12.35 (9.070)	9.55 (6.554)		-2.01 (1.354)	1.23 (0.956)	
		95% CI	(-30.13, 5.42)	(-3.29, 22.40)		(-4.66, 0.65)	(-0.64, 3.11)	
		LS Mean Difference (SE)		21.90 (9.938)			3.24 (1.492)	
		95% CI		(2.42, 41.38)			(0.32, 6.17)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
		p-value		0.0275			0.0298	
		HedgesG (95% CI)		0.443 (-0.060, 0.946)			0.436 (-0.067, 0.938)	

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Table 5.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline						
		n	27	35	62	27	35	62
		Mean	316.67	329.54	323.94	46.44	48.12	47.39
		SD, SE	78.421, 15.092	110.935, 18.751	97.581, 12.393	12.381, 2.383	15.966, 2.699	14.427, 1.832
		Median	308.00	341.00	333.50	45.32	46.99	46.58
		Q1, Q3	276.00, 374.00	249.00, 416.00	276.00, 396.00	37.24, 57.76	37.88, 61.14	37.88, 59.40
		Min, Max	160.0, 463.0	55.0, 538.0	55.0, 538.0	23.1, 68.6	7.6, 80.4	7.6, 80.4
		Observed						
		n	27	35	62	27	35	62
		Mean	317.22	355.80	339.00	46.55	52.06	49.66
		SD, SE	75.063, 14.446	118.945, 20.105	103.243, 13.112	11.591, 2.231	17.100, 2.890	15.095, 1.917
		Median	323.00	346.00	336.50	48.03	53.07	49.28
		Q1, Q3	271.00, 364.00	300.00, 461.00	296.00, 400.00	40.36, 54.86	44.29, 65.54	42.46, 60.33
		Min, Max	156.0, 470.0	100.0, 587.0	100.0, 587.0	23.9, 66.5	13.8, 86.8	13.8, 86.8

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Table 5.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline						
		n	27	35	62	27	35	62
		Mean	0.56	26.26	15.06	0.11	3.94	2.27
		SD, SE	31.296, 6.023	52.300, 8.840	45.903, 5.830	4.509, 0.868	7.824, 1.322	6.817, 0.866
		Median	0.00	21.00	10.00	0.10	3.00	1.47
		Q1, Q3	-22.00, 26.00	-5.00, 59.00	-14.00, 40.00	-3.09, 3.83	-0.59, 9.01	-2.05, 5.83
		Min, Max	-64.0, 61.0	-147.0, 138.0	-147.0, 138.0	-10.1, 7.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-14.97 (8.586)	15.07 (7.788)		-2.44 (1.253)	2.07 (1.138)	
		95% CI	(-31.80, 1.86)	(-0.19, 30.34)		(-4.89, 0.02)	(-0.16, 4.30)	
		LS Mean Difference (SE)		30.04 (10.896)			4.51 (1.609)	
		95% CI		(8.68, 51.40)			(1.35, 7.66)	

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Table 5.2.7.1.24.10
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
WOMAC Total Score at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
		p-value		0.0058			0.0051	
		HedgesG (95% CI)		0.562 (0.050, 1.074)			0.565 (0.054, 1.077)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Pain Medication Use at BL = Yes		N1	44	47	91	44	47	91
	Baseline	n	44	45	89	44	45	89
		Mean	350.09	344.56	347.29	50.80	50.28	50.54
		SD, SE	100.990, 15.225	103.892, 15.487	101.922, 10.804	14.928, 2.250	14.906, 2.222	14.834, 1.572
		Median	342.50	335.00	336.00	49.63	49.98	49.98
		Q1, Q3	278.00, 408.50	300.00, 411.00	279.00, 411.00	40.10, 61.05	42.80, 60.37	41.09, 60.37
		Min, Max	160.0, 569.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Pain Medication Use at BL = Yes	Week 12	Baseline						
		n	43	42	85	43	42	85
		Mean	351.74	342.31	347.08	51.06	50.01	50.54
		SD, SE	101.581, 15.491	106.696, 16.464	103.626, 11.240	15.010, 2.289	15.304, 2.361	15.075, 1.635
		Median	349.00	334.50	336.00	50.22	49.98	49.98
		Q1, Q3	277.00, 412.00	278.00, 411.00	278.00, 411.00	40.19, 62.10	42.19, 60.37	41.09, 60.37
		Min, Max	160.0, 569.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	43	42	85	43	42	85
		Mean	356.77	364.45	360.56	51.78	53.33	52.55
		SD, SE	96.311, 14.687	106.214, 16.389	100.793, 10.933	14.109, 2.152	15.209, 2.347	14.596, 1.583
		Median	340.00	358.00	355.00	50.37	54.32	51.41
		Q1, Q3	294.00, 405.00	311.00, 420.00	307.00, 417.00	43.10, 61.74	45.15, 59.24	43.49, 59.76
		Min, Max	170.0, 600.0	80.0, 660.0	80.0, 660.0	25.3, 84.6	11.1, 94.9	11.1, 94.9

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Pain Medication Use at BL = Yes	Week 12	Change from Baseline						
		n	43	42	85	43	42	85
		Mean	5.02	22.14	13.48	0.73	3.32	2.01
		SD, SE	36.783, 5.609	39.186, 6.047	38.732, 4.201	5.239, 0.799	5.977, 0.922	5.732, 0.622
		Median	0.00	15.00	10.00	0.05	2.28	1.51
		Q1, Q3	-15.00, 35.00	3.00, 44.00	-7.00, 37.00	-2.09, 5.75	0.46, 6.69	-0.94, 5.82
		Min, Max	-64.0, 93.0	-92.0, 155.0	-92.0, 155.0	-9.5, 11.9	-14.4, 24.6	-14.4, 24.6
		GEE Estimates						
		LS Mean (SE)	3.55 (7.558)	20.63 (6.514)		0.31 (1.011)	2.92 (0.873)	
		95% CI	(-11.26, 18.36)	(7.86, 33.39)		(-1.67, 2.29)	(1.21, 4.63)	
		LS Mean Difference (SE)		17.08 (8.119)			2.61 (1.201)	
		95% CI		(1.16, 32.99)			(0.25, 4.96)	
		p-value		0.0354			0.0299	
		HedgesG (95% CI)		0.441 (0.011, 0.872)			0.452 (0.022, 0.883)	

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Pain Medication Use at BL = Yes	Week 24	Baseline						
		n	44	43	87	44	43	87
		Mean	350.09	348.12	349.11	50.80	50.89	50.85
		SD, SE	100.990, 15.225	104.339, 15.912	102.065, 10.942	14.928, 2.250	14.872, 2.268	14.813, 1.588
		Median	342.50	341.00	341.00	49.63	50.60	50.22
		Q1, Q3	278.00, 408.50	300.00, 414.00	279.00, 412.00	40.10, 61.05	42.80, 61.14	41.09, 61.14
		Min, Max	160.0, 569.0	55.0, 643.0	55.0, 643.0	23.1, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	44	43	87	44	43	87
		Mean	352.20	371.16	361.57	51.05	54.37	52.69
		SD, SE	101.337, 15.277	106.698, 16.271	103.853, 11.134	14.383, 2.168	15.237, 2.324	14.819, 1.589
		Median	338.50	361.00	357.00	49.33	55.30	52.75
		Q1, Q3	293.00, 405.50	320.00, 448.00	302.00, 424.00	41.99, 59.64	46.47, 64.68	44.78, 61.61
		Min, Max	156.0, 617.0	100.0, 619.0	100.0, 619.0	23.9, 85.2	13.8, 89.1	13.8, 89.1

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Table 5.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Pain Medication Use at BL = Yes	Week 24	Change from Baseline						
		n	44	43	87	44	43	87
		Mean	2.11	23.05	12.46	0.25	3.48	1.85
		SD, SE	39.216, 5.912	48.027, 7.324	44.791, 4.802	5.476, 0.826	7.132, 1.088	6.517, 0.699
		Median	2.00	22.00	14.00	0.42	3.65	2.08
		Q1, Q3	-26.00, 29.00	-1.00, 53.00	-18.00, 38.00	-3.77, 4.40	-0.05, 7.99	-2.59, 5.73
		Min, Max	-68.0, 125.0	-147.0, 138.0	-147.0, 138.0	-10.1, 15.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	0.88 (7.826)	21.65 (7.503)		-0.14 (1.036)	3.10 (1.016)	
		95% CI	(-14.46, 16.22)	(6.95, 36.36)		(-2.17, 1.89)	(1.11, 5.09)	
		LS Mean Difference (SE)		20.78 (9.382)			3.24 (1.356)	
		95% CI		(2.39, 39.16)			(0.58, 5.90)	
		p-value		0.0268			0.0169	
		HedgesG (95% CI)		0.468 (0.042, 0.894)			0.499 (0.072, 0.925)	

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Table 5.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Pain Medication Use at BL cat=No		N1	22	21	43	22	21	43
	Baseline	n	21	21	42	21	21	42
		Mean	403.71	378.05	390.88	55.27	53.08	54.17
		SD, SE	101.228, 22.090	120.219, 26.234	110.532, 17.055	14.740, 3.217	17.815, 3.887	16.187, 2.498
		Median	420.00	386.00	401.50	56.80	58.23	57.22
		Q1, Q3	364.00, 455.00	297.00, 477.00	335.00, 473.00	46.61, 61.34	42.49, 66.03	45.19, 66.00
		Min, Max	164.0, 615.0	78.0, 541.0	78.0, 615.0	24.7, 85.7	12.1, 82.4	12.1, 85.7

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The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Pain Medication Use at BL cat=No	Week 12	Baseline						
		n	21	21	42	21	21	42
		Mean	403.71	378.05	390.88	55.27	53.08	54.17
		SD, SE	101.228, 22.090	120.219, 26.234	110.532, 17.055	14.740, 3.217	17.815, 3.887	16.187, 2.498
		Median	420.00	386.00	401.50	56.80	58.23	57.22
		Q1, Q3	364.00, 455.00	297.00, 477.00	335.00, 473.00	46.61, 61.34	42.49, 66.03	45.19, 66.00
		Min, Max	164.0, 615.0	78.0, 541.0	78.0, 615.0	24.7, 85.7	12.1, 82.4	12.1, 85.7
		Observed						
		n	21	21	42	21	21	42
		Mean	399.90	387.38	393.64	54.61	54.49	54.55
		SD, SE	102.155, 22.292	106.126, 23.159	103.076, 15.905	14.089, 3.074	16.223, 3.540	15.007, 2.316
		Median	420.00	409.00	412.00	56.34	56.94	56.86
		Q1, Q3	325.00, 467.00	329.00, 462.00	325.00, 467.00	46.46, 65.48	45.69, 67.38	45.69, 66.79
		Min, Max	175.0, 560.0	103.0, 525.0	103.0, 560.0	25.9, 78.2	15.9, 80.1	15.9, 80.1

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Table 5.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Pain Medication Use at BL cat=No	Week 12	Change from Baseline						
		n	21	21	42	21	21	42
		Mean	-3.81	9.33	2.76	-0.66	1.41	0.37
		SD, SE	46.866, 10.227	46.980, 10.252	46.822, 7.225	6.366, 1.389	6.240, 1.362	6.314, 0.974
		Median	-4.00	11.00	-1.50	-0.46	1.43	-0.15
		Q1, Q3	-35.00, 13.00	-8.00, 25.00	-15.00, 25.00	-4.43, 1.71	-1.25, 3.88	-1.90, 3.88
		Min, Max	-95.0, 132.0	-136.0, 93.0	-136.0, 132.0	-14.5, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-20.05 (12.838)	-6.97 (10.065)		-2.65 (1.684)	-0.34 (1.356)	
		95% CI	(-45.21, 5.12)	(-26.69, 12.76)		(-5.95, 0.65)	(-3.00, 2.32)	
		LS Mean Difference (SE)		13.08 (13.476)			2.31 (1.782)	
		95% CI		(-13.33, 39.49)			(-1.18, 5.80)	
		p-value		0.3318			0.1950	
		HedgesG (95% CI)		0.268 (-0.339, 0.876)			0.314 (-0.295, 0.923)	

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Table 5.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Pain Medication Use at BL cat=No	Week 24	Baseline						
		n	20	21	41	20	21	41
		Mean	405.10	378.05	391.24	55.15	53.08	54.09
		SD, SE	103.653, 23.177	120.219, 26.234	111.880, 17.473	15.113, 3.379	17.815, 3.887	16.379, 2.558
		Median	425.50	386.00	417.00	56.51	58.23	56.80
		Q1, Q3	349.50, 455.00	297.00, 477.00	335.00, 473.00	46.58, 62.27	42.49, 66.03	45.19, 66.00
		Min, Max	164.0, 615.0	78.0, 541.0	78.0, 615.0	24.7, 85.7	12.1, 82.4	12.1, 85.7
		Observed						
		n	20	21	41	20	21	41
		Mean	407.35	401.90	404.56	55.44	56.70	56.08
		SD, SE	99.997, 22.360	114.297, 24.942	106.251, 16.594	14.095, 3.152	17.679, 3.858	15.845, 2.475
		Median	417.00	434.00	429.00	55.15	58.04	57.60
		Q1, Q3	364.00, 477.50	356.00, 478.00	360.00, 478.00	50.01, 67.37	44.77, 69.91	49.49, 69.91
		Min, Max	158.0, 540.0	125.0, 578.0	125.0, 578.0	23.9, 74.1	19.4, 84.4	19.4, 84.4

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Table 5.2.7.1.24.11
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Pain Medication Use at BL cat=No	Week 24	Change from Baseline						
		n	20	21	41	20	21	41
		Mean	2.25	23.86	13.32	0.29	3.62	1.99
		SD, SE	50.841, 11.368	49.422, 10.785	50.682, 7.915	6.880, 1.538	7.007, 1.529	7.062, 1.103
		Median	2.00	7.00	7.00	0.35	0.96	0.96
		Q1, Q3	-27.00, 37.50	-4.00, 47.00	-6.00, 42.00	-3.59, 4.91	-0.51, 7.31	-0.86, 5.57
		Min, Max	-109.0, 99.0	-82.0, 140.0	-109.0, 140.0	-15.1, 12.4	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-17.52 (13.031)	7.56 (10.614)		-2.25 (1.728)	1.87 (1.539)	
		95% CI	(-43.06, 8.02)	(-13.25, 28.36)		(-5.64, 1.14)	(-1.14, 4.89)	
		LS Mean Difference (SE)		25.07 (15.092)			4.12 (2.124)	
		95% CI		(-4.51, 54.65)			(-0.04, 8.28)	
		p-value		0.0966			0.0524	
		HedgesG (95% CI)		0.412 (-0.207, 1.031)			0.459 (-0.162, 1.079)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Opioid Pain Medication Use at BL = Yes		N1	13	17	30	13	17	30
	Baseline	n	13	17	30	13	17	30
		Mean	380.23	292.82	330.70	55.93	43.25	48.75
		SD, SE	113.619, 31.512	100.148, 24.289	113.208, 20.669	17.416, 4.830	15.200, 3.686	17.140, 3.129
		Median	353.00	312.00	336.00	53.01	44.79	48.58
		Q1, Q3	312.00, 463.00	247.00, 354.00	274.00, 405.00	42.95, 68.63	36.52, 53.65	38.96, 57.76
		Min, Max	160.0, 542.0	55.0, 450.0	55.0, 542.0	24.4, 88.4	7.6, 66.6	7.6, 88.4

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Opioid Pain Medication Use at BL = Yes	Week 12	Baseline						
		n	13	16	29	13	16	29
		Mean	380.23	286.63	328.59	55.93	42.50	48.52
		SD, SE	113.619, 31.512	100.007, 25.002	114.608, 21.282	17.416, 4.830	15.363, 3.841	17.397, 3.231
		Median	353.00	295.00	331.00	53.01	43.49	48.13
		Q1, Q3	312.00, 463.00	231.50, 350.50	274.00, 405.00	42.95, 68.63	33.83, 52.85	38.96, 57.76
		Min, Max	160.0, 542.0	55.0, 450.0	55.0, 542.0	24.4, 88.4	7.6, 66.6	7.6, 88.4
		Observed						
		n	13	16	29	13	16	29
		Mean	374.85	309.56	338.83	55.14	46.03	50.11
		SD, SE	102.432, 28.410	95.481, 23.870	102.335, 19.003	15.791, 4.380	15.044, 3.761	15.792, 2.932
		Median	365.00	340.00	352.00	50.37	48.29	49.25
		Q1, Q3	300.00, 453.00	264.50, 361.00	289.00, 405.00	45.52, 71.35	39.07, 55.35	43.48, 59.00
		Min, Max	170.0, 524.0	80.0, 440.0	80.0, 524.0	26.0, 81.8	11.1, 67.7	11.1, 81.8

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Table 5.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Opioid Pain Medication Use at BL = Yes	Week 12	Change from Baseline						
		n	13	16	29	13	16	29
		Mean	-5.38	22.94	10.24	-0.80	3.53	1.59
		SD, SE	44.601, 12.370	52.407, 13.102	50.292, 9.339	6.236, 1.730	8.198, 2.050	7.580, 1.408
		Median	0.00	19.50	10.00	0.04	2.62	1.55
		Q1, Q3	-40.00, 18.00	-2.00, 44.00	-15.00, 26.00	-6.53, 2.74	-0.28, 7.00	-2.09, 4.03
		Min, Max	-64.0, 93.0	-92.0, 155.0	-92.0, 155.0	-9.5, 11.7	-14.4, 24.6	-14.4, 24.6
		GEE Estimates						
		LS Mean (SE)	0.17 (10.739)	12.52 (12.183)		-0.01 (1.520)	2.09 (1.955)	
		95% CI	(-20.87, 21.22)	(-11.35, 36.40)		(-2.99, 2.97)	(-1.74, 5.92)	
		LS Mean Difference (SE)		12.35 (15.572)			2.10 (2.324)	
		95% CI		(-18.17, 42.87)			(-2.45, 6.66)	
		p-value		0.4278			0.3660	
		HedgesG (95% CI)		0.541 (-0.204, 1.286)			0.549 (-0.196, 1.294)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Opioid Pain Medication Use at BL = Yes	Week 24	Baseline						
		n	13	16	29	13	16	29
		Mean	380.23	297.63	334.66	55.93	44.14	49.43
		SD, SE	113.619, 31.512	101.391, 25.348	113.083, 20.999	17.416, 4.830	15.237, 3.809	17.029, 3.162
		Median	353.00	321.50	341.00	53.01	45.64	49.03
		Q1, Q3	312.00, 463.00	255.00, 357.00	278.00, 405.00	42.95, 68.63	36.66, 54.31	41.53, 57.76
		Min, Max	160.0, 542.0	55.0, 450.0	55.0, 542.0	24.4, 88.4	7.6, 66.6	7.6, 88.4
		Observed						
		n	13	16	29	13	16	29
		Mean	370.46	322.81	344.17	54.35	47.94	50.82
		SD, SE	108.794, 30.174	110.703, 27.676	110.542, 20.527	15.855, 4.397	16.611, 4.153	16.312, 3.029
		Median	370.00	345.50	357.00	54.66	49.93	52.75
		Q1, Q3	300.00, 437.00	295.50, 380.50	300.00, 420.00	45.66, 63.82	42.64, 56.51	44.78, 59.36
		Min, Max	156.0, 550.0	100.0, 522.0	100.0, 550.0	23.9, 82.9	13.8, 76.2	13.8, 82.9

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Table 5.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Opioid Pain Medication Use at BL = Yes	Week 24	Change from Baseline						
		n	13	16	29	13	16	29
		Mean	-9.77	25.19	9.52	-1.58	3.80	1.39
		SD, SE	49.920, 13.845	63.743, 15.936	59.647, 11.076	6.708, 1.860	9.618, 2.404	8.732, 1.622
		Median	-23.00	28.00	13.00	-3.69	4.18	2.27
		Q1, Q3	-43.00, 8.00	10.50, 62.00	-34.00, 38.00	-6.25, 1.23	1.81, 8.71	-4.99, 5.83
		Min, Max	-62.0, 125.0	-147.0, 138.0	-147.0, 138.0	-8.5, 15.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	-4.21 (13.480)	16.25 (16.683)		-0.80 (1.795)	2.57 (2.511)	
		95% CI	(-30.63, 22.21)	(-16.45, 48.95)		(-4.31, 2.72)	(-2.35, 7.49)	
		LS Mean Difference (SE)		20.46 (21.206)			3.37 (2.990)	
		95% CI		(-21.11, 62.02)			(-2.49, 9.23)	
		p-value		0.3347			0.2601	
		HedgesG (95% CI)		0.565 (-0.181, 1.311)			0.597 (-0.151, 1.345)	

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Table 5.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Opioid Pain Medication Use at BL cat = No		N1	53	51	104	53	51	104
	Baseline	n	52	49	101	52	49	101
		Mean	364.21	376.86	370.35	51.33	53.92	52.58
		SD, SE	101.633, 14.094	105.122, 15.017	103.017, 10.251	14.246, 1.976	15.209, 2.173	14.705, 1.463
		Median	370.00	358.00	366.00	52.24	52.10	52.10
		Q1, Q3	290.00, 437.00	320.00, 470.00	300.00, 444.00	40.48, 60.13	44.69, 63.81	42.49, 62.10
		Min, Max	160.0, 615.0	78.0, 643.0	78.0, 643.0	23.1, 85.7	12.1, 92.4	12.1, 92.4

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Opioid Pain Medication Use at BL cat = No	Week 12	Baseline						
		n	51	47	98	51	47	98
		Mean	365.88	377.23	371.33	51.55	53.94	52.69
		SD, SE	101.920, 14.272	106.898, 15.593	103.952, 10.501	14.297, 2.002	15.449, 2.253	14.832, 1.498
		Median	371.00	358.00	366.50	52.53	52.10	52.31
		Q1, Q3	291.00, 440.00	308.00, 472.00	300.00, 446.00	40.76, 60.25	43.86, 66.00	42.49, 62.20
		Min, Max	160.0, 615.0	78.0, 643.0	78.0, 643.0	23.1, 85.7	12.1, 92.4	12.1, 92.4
		Observed						
		n	51	47	98	51	47	98
		Mean	369.92	393.38	381.17	52.09	56.33	54.13
		SD, SE	99.839, 13.980	101.568, 14.815	100.842, 10.187	13.679, 1.915	14.820, 2.162	14.323, 1.447
		Median	375.00	395.00	381.00	51.48	56.79	53.91
		Q1, Q3	304.00, 440.00	318.00, 462.00	313.00, 443.00	43.13, 61.57	45.69, 67.38	44.49, 65.00
		Min, Max	175.0, 600.0	103.0, 660.0	103.0, 660.0	25.3, 84.6	15.9, 94.9	15.9, 94.9

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Table 5.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Opioid Pain Medication Use at BL cat = No	Week 12	Change from Baseline						
		n	51	47	98	51	47	98
		Mean	4.04	16.15	9.85	0.54	2.39	1.43
		SD, SE	39.260, 5.497	38.349, 5.594	39.101, 3.950	5.487, 0.768	5.256, 0.767	5.430, 0.548
		Median	-2.00	11.00	5.00	-0.20	1.51	0.76
		Q1, Q3	-15.00, 35.00	-3.00, 37.00	-9.00, 36.00	-2.07, 4.75	-0.37, 5.71	-1.25, 4.75
		Min, Max	-95.0, 132.0	-136.0, 93.0	-136.0, 132.0	-14.5, 16.4	-16.8, 12.2	-16.8, 16.4
		GEE Estimates						
		LS Mean (SE)	-2.92 (8.041)	11.94 (7.105)		-0.62 (1.070)	1.73 (0.940)	
		95% CI	(-18.68, 12.84)	(-1.98, 25.87)		(-2.72, 1.48)	(-0.11, 3.57)	
		LS Mean Difference (SE)		14.87 (7.401)			2.35 (1.031)	
		95% CI		(0.36, 29.37)			(0.33, 4.37)	
		p-value		0.0446			0.0228	
		HedgesG (95% CI)		0.306 (-0.092, 0.705)			0.338 (-0.061, 0.737)	

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Table 5.2.7.1.24.12
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Opioid Pain Medication Use at BL cat = No	Week 24	Baseline						
		n	51	48	99	51	48	99
		Mean	363.98	378.04	370.80	51.20	54.09	52.60
		SD, SE	102.630, 14.371	105.903, 15.286	103.936, 10.446	14.360, 2.011	15.321, 2.211	14.829, 1.490
		Median	369.00	359.00	366.00	51.95	53.29	52.10
		Q1, Q3	289.00, 440.00	314.00, 471.00	300.00, 446.00	40.19, 60.25	44.27, 64.91	42.30, 62.20
		Min, Max	160.0, 615.0	78.0, 643.0	78.0, 643.0	23.1, 85.7	12.1, 92.4	12.1, 92.4
		Observed						
		n	51	48	99	51	48	99
		Mean	369.18	400.73	384.47	51.93	57.53	54.65
		SD, SE	103.085, 14.435	102.737, 14.829	103.610, 10.413	14.041, 1.966	15.185, 2.192	14.801, 1.488
		Median	367.00	400.50	388.00	50.91	57.84	54.74
		Q1, Q3	305.00, 434.00	334.50, 478.00	319.00, 461.00	43.12, 60.74	46.74, 68.94	45.51, 64.94
		Min, Max	158.0, 617.0	125.0, 619.0	125.0, 619.0	23.9, 85.2	19.4, 89.1	19.4, 89.1

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Opioid Pain Medication Use at Baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Opioid Pain Medication Use at BL cat = No	Week 24	Change from Baseline						
		n	51	48	99	51	48	99
		Mean	5.20	22.69	13.68	0.73	3.43	2.04
		SD, SE	40.747, 5.706	42.455, 6.128	42.293, 4.251	5.646, 0.791	6.066, 0.875	5.979, 0.601
		Median	8.00	17.50	12.00	1.22	2.51	1.54
		Q1, Q3	-19.00, 34.00	-4.50, 47.00	-12.00, 40.00	-2.65, 4.48	-0.55, 7.22	-1.46, 5.57
		Min, Max	-109.0, 99.0	-82.0, 140.0	-109.0, 140.0	-15.1, 12.4	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-2.72 (8.060)	17.99 (7.150)		-0.58 (1.074)	2.70 (0.991)	
		95% CI	(-18.52, 13.08)	(3.97, 32.00)		(-2.68, 1.53)	(0.76, 4.64)	
		LS Mean Difference (SE)		20.70 (8.145)			3.28 (1.155)	
		95% CI		(4.74, 36.67)			(1.01, 5.54)	
		p-value		0.0110			0.0045	
		HedgesG (95% CI)		0.413 (0.015, 0.811)			0.454 (0.055, 0.853)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Active fractures and pseudo-fractures at BL = Yes		N1	38	32	70	38	32	70
	Baseline	n	38	31	69	38	31	69
		Mean	338.95	359.52	348.19	48.07	51.35	49.54
		SD, SE	90.771, 14.725	104.289, 18.731	96.891, 11.664	13.122, 2.129	15.478, 2.780	14.215, 1.711
		Median	330.50	347.00	335.00	46.56	48.13	46.90
		Q1, Q3	279.00, 396.00	297.00, 457.00	289.00, 423.00	40.01, 59.75	42.19, 62.54	40.76, 61.18
		Min, Max	160.0, 517.0	78.0, 541.0	78.0, 541.0	23.1, 76.5	12.1, 82.4	12.1, 82.4

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Active fractures and pseudo-fractures at BL = Yes	Week 12	Baseline						
		n	37	29	66	37	29	66
		Mean	340.57	358.93	348.64	48.29	51.20	49.57
		SD, SE	91.465, 15.037	107.159, 19.899	98.307, 12.101	13.233, 2.175	15.871, 2.947	14.409, 1.774
		Median	335.00	347.00	335.00	46.56	48.13	46.95
		Q1, Q3	289.00, 396.00	297.00, 457.00	289.00, 431.00	40.19, 59.75	42.19, 62.54	40.76, 61.18
		Min, Max	160.0, 517.0	78.0, 541.0	78.0, 541.0	23.1, 76.5	12.1, 82.4	12.1, 82.4
		Observed						
		n	37	29	66	37	29	66
		Mean	351.14	382.52	364.92	49.76	54.55	51.86
		SD, SE	87.489, 14.383	105.635, 19.616	96.398, 11.866	12.252, 2.014	15.342, 2.849	13.794, 1.698
		Median	348.00	381.00	363.50	49.09	54.99	50.95
		Q1, Q3	294.00, 405.00	328.00, 462.00	304.00, 443.00	43.10, 60.96	44.91, 66.79	43.49, 61.74
		Min, Max	175.0, 490.0	103.0, 535.0	103.0, 535.0	25.3, 71.4	15.9, 80.1	15.9, 80.1

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Active fractures and pseudo-fractures at BL = Yes	Week 12	Change from Baseline						
		n	37	29	66	37	29	66
		Mean	10.57	23.59	16.29	1.47	3.35	2.30
		SD, SE	39.411, 6.479	31.246, 5.802	36.376, 4.478	5.277, 0.868	4.315, 0.801	4.933, 0.607
		Median	1.00	21.00	16.50	0.23	2.83	2.37
		Q1, Q3	-10.00, 35.00	-3.00, 43.00	-7.00, 36.00	-1.35, 4.75	-0.36, 5.97	-0.91, 5.75
		Min, Max	-64.0, 132.0	-19.0, 93.0	-64.0, 132.0	-8.7, 16.4	-2.8, 12.8	-8.7, 16.4
		GEE Estimates						
		LS Mean (SE)	2.37 (10.143)	18.15 (7.477)		0.17 (1.270)	2.53 (0.978)	
		95% CI	(-17.51, 22.25)	(3.49, 32.80)		(-2.32, 2.66)	(0.61, 4.44)	
		LS Mean Difference (SE)		15.78 (9.016)			2.36 (1.168)	
		95% CI		(-1.90, 33.45)			(0.07, 4.65)	

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Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
		p-value		0.0802			0.0436	
		HedgesG (95% CI)		0.351 (-0.139, 0.841)			0.375 (-0.115, 0.866)	

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Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Active fractures and pseudo-fractures at BL = Yes	Week 24	Baseline						
		n	38	29	67	38	29	67
		Mean	338.95	365.83	350.58	48.07	52.31	49.91
		SD, SE	90.771, 14.725	104.021, 19.316	96.900, 11.838	13.122, 2.129	15.389, 2.858	14.194, 1.734
		Median	330.50	347.00	335.00	46.56	49.97	46.99
		Q1, Q3	279.00, 396.00	308.00, 457.00	289.00, 431.00	40.01, 59.75	42.49, 62.54	40.76, 61.34
		Min, Max	160.0, 517.0	78.0, 541.0	78.0, 541.0	23.1, 76.5	12.1, 82.4	12.1, 82.4
		Observed						
		n	38	29	67	38	29	67
		Mean	345.21	393.79	366.24	48.90	56.35	52.12
		SD, SE	92.196, 14.956	111.385, 20.684	103.038, 12.588	12.619, 2.047	16.197, 3.008	14.644, 1.789
		Median	343.50	388.00	364.00	49.07	57.64	50.91
		Q1, Q3	286.00, 420.00	320.00, 478.00	302.00, 443.00	40.36, 58.96	46.47, 65.54	43.12, 62.39
		Min, Max	158.0, 533.0	125.0, 587.0	125.0, 587.0	23.9, 72.1	19.4, 86.8	19.4, 86.8

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Table 5.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Active fractures and pseudo-fractures at BL = Yes	Week 24	Change from Baseline						
		n	38	29	67	38	29	67
		Mean	6.26	27.97	15.66	0.82	4.04	2.22
		SD, SE	42.424, 6.882	55.390, 10.286	49.274, 6.020	5.715, 0.927	8.047, 1.494	6.954, 0.850
		Median	5.50	25.00	12.00	0.85	3.76	2.03
		Q1, Q3	-28.00, 31.00	-3.00, 66.00	-16.00, 40.00	-3.85, 4.36	-0.28, 10.00	-2.10, 5.73
		Min, Max	-68.0, 125.0	-147.0, 140.0	-147.0, 140.0	-9.4, 15.7	-22.0, 20.6	-22.0, 20.6
		GEE Estimates						
		LS Mean (SE)	-1.60 (9.972)	21.15 (11.701)		-0.44 (1.262)	3.06 (1.656)	
		95% CI	(-21.14, 17.95)	(-1.78, 44.09)		(-2.91, 2.03)	(-0.19, 6.30)	
		LS Mean Difference (SE)		22.75 (12.940)			3.50 (1.783)	
		95% CI		(-2.61, 48.12)			(0.00, 6.99)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
		p-value		0.0787			0.0497	
		HedgesG (95% CI)		0.436 (-0.053, 0.925)			0.459 (-0.030, 0.949)	

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Table 5.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Active fractures and pseudo-fractures at BL = No		N1	28	36	64	28	36	64
	Baseline	n	27	35	62	27	35	62
		Mean	407.48	351.40	375.82	58.12	51.02	54.11
		SD, SE	108.374, 20.857	115.384, 19.503	114.946, 14.598	15.500, 2.983	16.312, 2.757	16.227, 2.061
		Median	405.00	351.00	375.00	57.65	52.10	54.60
		Q1, Q3	364.00, 486.00	278.00, 417.00	307.00, 450.00	51.90, 69.56	42.80, 63.76	44.94, 65.52
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	24.4, 88.4	7.6, 92.4	7.6, 92.4

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Table 5.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Active fractures and pseudo-fractures at BL = No	Week 12	Baseline						
		n	27	34	61	27	34	61
		Mean	407.48	350.21	375.56	58.12	50.89	54.09
		SD, SE	108.374, 20.857	116.899, 20.048	115.881, 14.837	15.500, 2.983	16.540, 2.837	16.361, 2.095
		Median	405.00	346.50	374.00	57.65	52.05	54.48
		Q1, Q3	364.00, 486.00	278.00, 417.00	307.00, 450.00	51.90, 69.56	42.80, 63.76	44.94, 65.52
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	24.4, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	27	34	61	27	34	61
		Mean	398.04	363.21	378.62	56.75	53.00	54.66
		SD, SE	110.011, 21.172	106.866, 18.327	108.765, 13.926	15.537, 2.990	15.704, 2.693	15.613, 1.999
		Median	392.00	366.50	377.00	53.75	53.49	53.75
		Q1, Q3	320.00, 474.00	310.00, 417.00	318.00, 440.00	46.46, 71.35	45.33, 64.13	45.37, 65.48
		Min, Max	170.0, 600.0	80.0, 660.0	80.0, 660.0	26.0, 84.6	11.1, 94.9	11.1, 94.9

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Active fractures and pseudo-fractures at BL = No	Week 12	Change from Baseline						
		n	27	34	61	27	34	61
		Mean	-9.44	13.00	3.07	-1.37	2.11	0.57
		SD, SE	39.070, 7.519	49.331, 8.460	46.111, 5.904	5.758, 1.108	7.280, 1.249	6.824, 0.874
		Median	-8.00	9.00	4.00	-0.96	1.34	0.63
		Q1, Q3	-35.00, 10.00	-4.00, 37.00	-15.00, 25.00	-4.74, 1.55	-0.51, 5.71	-1.90, 3.46
		Min, Max	-95.0, 84.0	-136.0, 155.0	-136.0, 155.0	-14.5, 11.9	-16.8, 24.6	-16.8, 24.6
		GEE Estimates						
		LS Mean (SE)	-10.03 (10.854)	3.21 (11.463)		-1.68 (1.580)	0.59 (1.644)	
		95% CI	(-31.31, 11.24)	(-19.25, 25.68)		(-4.78, 1.41)	(-2.64, 3.81)	
		LS Mean Difference (SE)		13.25 (10.881)			2.27 (1.564)	
		95% CI		(-8.08, 34.57)			(-0.79, 5.33)	

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
		p-value		0.2234			0.1466	
		HedgesG (95% CI)		0.483 (-0.029, 0.996)			0.508 (-0.005, 1.021)	

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Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Active fractures and pseudo-fractures at BL = No	Week 24	Baseline						
		n	26	35	61	26	35	61
		Mean	408.69	351.40	375.82	58.14	51.02	54.05
		SD, SE	110.334, 21.638	115.384, 19.503	115.900, 14.839	15.807, 3.100	16.312, 2.757	16.355, 2.094
		Median	408.50	351.00	374.00	57.49	52.10	54.48
		Q1, Q3	364.00, 486.00	278.00, 417.00	307.00, 450.00	51.90, 69.56	42.80, 63.76	44.94, 65.52
		Min, Max	160.0, 615.0	55.0, 643.0	55.0, 643.0	24.4, 88.4	7.6, 92.4	7.6, 92.4
		Observed						
		n	26	35	61	26	35	61
		Mean	404.85	370.86	385.34	57.58	54.12	55.59
		SD, SE	110.267, 21.625	108.062, 18.266	109.410, 14.009	15.335, 3.007	15.954, 2.697	15.659, 2.005
		Median	402.50	361.00	382.00	57.18	55.92	55.98
		Q1, Q3	337.00, 497.00	314.00, 448.00	321.00, 452.00	49.35, 70.04	46.23, 66.46	47.03, 66.46
		Min, Max	156.0, 617.0	100.0, 619.0	100.0, 619.0	23.9, 85.2	13.8, 89.1	13.8, 89.1

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Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
Active fractures and pseudo-fractures at BL = No	Week 24	Change from Baseline						
		n	26	35	61	26	35	61
		Mean	-3.85	19.46	9.52	-0.56	3.10	1.54
		SD, SE	43.391, 8.510	41.545, 7.022	43.561, 5.577	6.167, 1.209	6.162, 1.042	6.379, 0.817
		Median	-3.50	16.00	11.00	-0.34	2.64	1.49
		Q1, Q3	-24.00, 28.00	-5.00, 45.00	-16.00, 40.00	-3.69, 4.43	-0.59, 6.64	-2.20, 5.57
		Min, Max	-109.0, 61.0	-82.0, 138.0	-109.0, 138.0	-15.1, 8.5	-10.0, 21.9	-15.1, 21.9
		GEE Estimates						
		LS Mean (SE)	-6.14 (10.813)	10.69 (9.636)		-1.15 (1.562)	1.72 (1.379)	
		95% CI	(-27.33, 15.05)	(-8.20, 29.58)		(-4.21, 1.91)	(-0.98, 4.43)	
		LS Mean Difference (SE)		16.83 (10.131)			2.87 (1.444)	
		95% CI		(-3.03, 36.69)			(0.04, 5.70)	

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Table 5.2.7.1.24.14
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
Active fractures and pseudo-fractures at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
		p-value		0.0967			0.0467	
		HedgesG (95% CI)		0.534 (0.018, 1.051)			0.577 (0.059, 1.094)	

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
6MWT score at BL = High		N1	29	37	66	29	37	66
	Baseline	n	29	37	66	29	37	66
		Mean	275.41	280.62	278.33	39.14	40.85	40.10
		SD, SE	55.075, 10.227	73.541, 12.090	65.641, 8.080	7.878, 1.463	11.117, 1.828	9.794, 1.206
		Median	289.00	307.00	293.50	40.19	43.16	41.80
		Q1, Q3	246.00, 312.00	247.00, 334.00	246.00, 333.00	34.72, 44.94	36.52, 48.13	34.97, 46.61
		Min, Max	160.0, 353.0	55.0, 354.0	55.0, 354.0	23.1, 53.0	7.6, 54.7	7.6, 54.7

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
6MWT score at BL = High	Week 12	Baseline						
		n	28	36	64	28	36	64
		Mean	275.29	279.53	277.67	39.10	40.72	40.01
		SD, SE	56.081, 10.598	74.278, 12.380	66.464, 8.308	8.021, 1.516	11.245, 1.874	9.923, 1.240
		Median	289.00	303.50	293.50	40.48	42.98	41.80
		Q1, Q3	243.00, 313.50	244.00, 334.00	243.50, 333.50	34.23, 45.13	35.75, 49.05	34.84, 46.75
		Min, Max	160.0, 353.0	55.0, 354.0	55.0, 354.0	23.1, 53.0	7.6, 54.7	7.6, 54.7
		Observed						
		n	28	36	64	28	36	64
		Mean	293.50	308.11	301.72	41.60	45.00	43.51
		SD, SE	70.460, 13.316	80.386, 13.398	75.967, 9.496	9.069, 1.714	12.441, 2.074	11.141, 1.393
		Median	297.00	320.50	311.00	43.22	45.53	44.70
		Q1, Q3	250.50, 327.00	266.00, 361.00	254.00, 352.50	37.25, 46.83	38.69, 54.32	37.91, 51.44
		Min, Max	170.0, 467.0	80.0, 425.0	80.0, 467.0	25.3, 58.0	11.1, 66.0	11.1, 66.0

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
6MWT score at BL = High	Week 12	Change from Baseline						
		n	28	36	64	28	36	64
		Mean	18.21	28.58	24.05	2.49	4.27	3.50
		SD, SE	39.108, 7.391	40.456, 6.743	39.895, 4.987	5.214, 0.985	6.213, 1.035	5.821, 0.728
		Median	14.00	21.50	17.00	2.01	3.02	2.46
		Q1, Q3	-9.50, 41.00	7.00, 46.00	0.00, 44.50	-1.29, 6.07	1.03, 7.20	0.05, 6.58
		Min, Max	-63.0, 132.0	-92.0, 155.0	-92.0, 155.0	-9.5, 16.4	-14.4, 24.6	-14.4, 24.6
		GEE Estimates						
		LS Mean (SE)	18.70 (15.515)	30.62 (13.272)		2.25 (1.991)	4.38 (1.790)	
		95% CI	(-11.71, 49.11)	(4.60, 56.63)		(-1.65, 6.15)	(0.87, 7.88)	
		LS Mean Difference (SE)		11.91 (10.545)			2.13 (1.514)	
		95% CI		(-8.75, 32.58)			(-0.84, 5.09)	
		p-value		0.2585			0.1603	
		HedgesG (95% CI)		0.253 (-0.243, 0.749)			0.298 (-0.198, 0.795)	

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
6MWT score at BL = High	Week 24	Baseline						
		n	29	35	64	29	35	64
		Mean	275.41	281.34	278.66	39.14	41.06	40.19
		SD, SE	55.075, 10.227	74.548, 12.601	66.001, 8.250	7.878, 1.463	11.227, 1.898	9.826, 1.228
		Median	289.00	307.00	293.50	40.19	43.16	41.80
		Q1, Q3	246.00, 312.00	247.00, 334.00	246.50, 333.50	34.72, 44.94	36.52, 49.97	35.10, 46.75
		Min, Max	160.0, 353.0	55.0, 354.0	55.0, 354.0	23.1, 53.0	7.6, 54.7	7.6, 54.7
		Observed						
		n	29	35	64	29	35	64
		Mean	289.31	310.43	300.86	41.00	45.44	43.43
		SD, SE	73.955, 13.733	83.867, 14.176	79.618, 9.952	9.485, 1.761	12.835, 2.169	11.569, 1.446
		Median	300.00	321.00	315.50	42.46	46.85	45.70
		Q1, Q3	244.00, 337.00	268.00, 361.00	253.00, 358.50	35.28, 48.03	39.13, 55.30	36.17, 51.53
		Min, Max	156.0, 437.0	100.0, 436.0	100.0, 437.0	23.9, 54.9	13.8, 69.9	13.8, 69.9

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
6MWT score at BL = High	Week 24	Change from Baseline						
		n	29	35	64	29	35	64
		Mean	13.90	29.09	22.20	1.87	4.38	3.24
		SD, SE	37.247, 6.917	48.134, 8.136	43.875, 5.484	4.930, 0.915	7.257, 1.227	6.389, 0.799
		Median	8.00	28.00	16.00	1.33	3.97	2.43
		Q1, Q3	-6.00, 28.00	7.00, 55.00	-1.00, 45.50	-0.86, 4.43	1.12, 8.75	-0.07, 6.68
		Min, Max	-49.0, 125.0	-147.0, 138.0	-147.0, 138.0	-7.3, 15.7	-22.0, 21.9	-22.0, 21.9
		GEE Estimates						
		LS Mean (SE)	15.21 (14.605)	30.35 (14.474)		1.74 (1.873)	4.38 (1.972)	
		95% CI	(-13.41, 43.84)	(1.99, 58.72)		(-1.93, 5.41)	(0.52, 8.25)	
		LS Mean Difference (SE)		15.14 (11.265)			2.65 (1.604)	
		95% CI		(-6.94, 37.22)			(-0.50, 5.79)	
		p-value		0.1789			0.0990	
		HedgesG (95% CI)		0.339 (-0.157, 0.835)			0.387 (-0.110, 0.884)	

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The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
6MWT score at BL = Low		N1	36	30	66	36	30	66
	Baseline	n	36	29	65	36	29	65
		Mean	441.53	450.38	445.48	62.81	64.34	63.49
		SD, SE	66.813, 11.135	64.593, 11.995	65.469, 8.120	9.960, 1.660	10.036, 1.864	9.945, 1.233
		Median	432.50	450.00	438.00	60.13	63.81	62.10
		Q1, Q3	379.50, 479.00	411.00, 483.00	392.00, 483.00	56.36, 69.10	60.37, 67.89	57.65, 68.63
		Min, Max	364.0, 615.0	358.0, 643.0	358.0, 643.0	46.6, 88.4	44.7, 92.4	44.7, 92.4

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
6MWT score at BL = Low	Week 12	Baseline						
		n	36	27	63	36	27	63
		Mean	441.53	453.81	446.79	62.81	64.78	63.65
		SD, SE	66.813, 11.135	65.608, 12.626	66.050, 8.322	9.960, 1.660	10.239, 1.970	10.046, 1.266
		Median	432.50	457.00	440.00	60.13	65.52	62.20
		Q1, Q3	379.50, 479.00	411.00, 486.00	386.00, 486.00	56.36, 69.10	60.37, 69.02	57.65, 69.02
		Min, Max	364.0, 615.0	358.0, 643.0	358.0, 643.0	46.6, 88.4	44.7, 92.4	44.7, 92.4
		Observed						
		n	36	27	63	36	27	63
		Mean	431.14	457.41	442.40	61.35	65.34	63.06
		SD, SE	74.092, 12.349	69.363, 13.349	72.721, 9.162	10.795, 1.799	10.677, 2.055	10.842, 1.366
		Median	438.50	442.00	440.00	61.27	66.79	63.43
		Q1, Q3	381.50, 471.50	409.00, 500.00	386.00, 490.00	51.29, 69.03	58.67, 69.92	54.87, 69.11
		Min, Max	281.0, 600.0	356.0, 660.0	281.0, 660.0	43.1, 84.6	46.1, 94.9	43.1, 94.9

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 5.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
6MWT score at BL = Low	Week 12	Change from Baseline						
		n	36	27	63	36	27	63
		Mean	-10.39	3.59	-4.40	-1.46	0.56	-0.59
		SD, SE	36.908, 6.151	40.420, 7.779	38.765, 4.884	5.373, 0.895	5.301, 1.020	5.394, 0.680
		Median	-6.50	3.00	-3.00	-0.90	0.55	-0.37
		Q1, Q3	-37.50, 8.50	-10.00, 24.00	-29.00, 18.00	-5.54, 1.17	-1.39, 3.56	-4.09, 2.74
		Min, Max	-95.0, 84.0	-136.0, 84.0	-136.0, 84.0	-14.5, 11.9	-16.8, 10.5	-16.8, 11.9
		GEE Estimates						
		LS Mean (SE)	-16.25 (8.317)	0.67 (10.045)		-2.80 (1.173)	-0.23 (1.277)	
		95% CI	(-32.55, 0.05)	(-19.01, 20.36)		(-5.10, -0.50)	(-2.73, 2.28)	
		LS Mean Difference (SE)		16.92 (9.815)			2.57 (1.393)	
		95% CI		(-2.32, 36.16)			(-0.16, 5.30)	
		p-value		0.0847			0.0647	
		HedgesG (95% CI)		0.353 (-0.149, 0.856)			0.367 (-0.136, 0.870)	

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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
6MWT score at BL = Low	Week 24	Baseline						
		n	35	29	64	35	29	64
		Mean	443.40	450.38	446.56	62.96	64.34	63.58
		SD, SE	66.823, 11.295	64.593, 11.995	65.395, 8.174	10.065, 1.701	10.036, 1.864	9.996, 1.249
		Median	434.00	450.00	439.00	60.25	63.81	62.15
		Q1, Q3	380.00, 486.00	411.00, 483.00	393.00, 484.50	56.21, 69.56	60.37, 67.89	57.28, 68.83
		Min, Max	364.0, 615.0	358.0, 643.0	358.0, 643.0	46.6, 88.4	44.7, 92.4	44.7, 92.4
		Observed						
		n	35	29	64	35	29	64
		Mean	435.83	466.72	449.83	61.89	66.84	64.13
		SD, SE	72.714, 12.291	67.135, 12.467	71.393, 8.924	10.145, 1.715	10.715, 1.990	10.618, 1.327
		Median	420.00	468.00	450.00	60.74	66.46	63.62
		Q1, Q3	390.00, 480.00	413.00, 506.00	400.00, 497.50	54.67, 70.04	59.36, 70.68	56.41, 70.58
		Min, Max	310.0, 617.0	356.0, 619.0	310.0, 619.0	45.5, 85.2	44.8, 89.1	44.8, 89.1

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The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 5.2.7.1.24.15
Subgroup Analysis: Change from baseline in distance traveled and percent predicted of the distance traveled during 6 minutes (meters)
Primary Analysis Set_24 Weeks Analysis - Excluding subject 139-305 for incorrect baseline measurement
6MWT at baseline

			6MWT Total Distance Walked (meters)			6MWT Percent Predicted Distance		
Subgroup	**Visit**	**Statistics**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**	**Placebo (N=66)**	**KRN23 (N=67)**	**Total (N=133)**
6MWT score at BL = Low	Week 24	Change from Baseline						
		n	35	29	64	35	29	64
		Mean	-7.57	16.34	3.27	-1.07	2.50	0.55
		SD, SE	45.077, 7.619	47.954, 8.905	47.567, 5.946	6.351, 1.074	6.738, 1.251	6.719, 0.840
		Median	-4.00	13.00	-3.00	-0.41	2.18	-0.28
		Q1, Q3	-43.00, 31.00	-13.00, 31.00	-30.00, 31.00	-6.25, 4.36	-1.71, 4.47	-4.24, 4.43
		Min, Max	-109.0, 87.0	-82.0, 140.0	-109.0, 140.0	-15.1, 11.9	-10.0, 20.6	-15.1, 20.6
		GEE Estimates						
		LS Mean (SE)	-14.75 (8.813)	13.25 (10.201)		-2.61 (1.232)	1.67 (1.368)	
		95% CI	(-32.02, 2.53)	(-6.74, 33.24)		(-5.03, -0.20)	(-1.01, 4.35)	
		LS Mean Difference (SE)		28.00 (11.696)			4.28 (1.674)	
		95% CI		(5.07, 50.92)			(1.00, 7.56)	
		p-value		0.0167			0.0105	
		HedgesG (95% CI)		0.501 (0.001, 1.001)			0.531 (0.030, 1.032)	

6MWT = Six Minute Walk Test.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the change from baseline for each 6MWT endpoint as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of each 6MWT endpoint as a covariate, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADWALK.sas7bdat, ADSL.sas7bdat Program source: s-walk-dist.sas

Table 2.2.3.3.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6		N_1	27	17	44
	Baseline	n	27	17	44
		Mean	4.01	3.82	3.94
		SD, SE	1.711, 0.329	1.697, 0.412	1.688, 0.254
		Median	3.56	3.78	3.56
		Q1, Q3	2.78, 5.56	2.67, 5.11	2.78, 5.39
		Min, Max	0.7, 7.6	1.3, 6.8	0.7, 7.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Baseline			
		n	27	17	44
		Mean	4.01	3.82	3.94
		SD, SE	1.711, 0.329	1.697, 0.412	1.688, 0.254
		Median	3.56	3.78	3.56
		Q1, Q3	2.78, 5.56	2.67, 5.11	2.78, 5.39
		Min, Max	0.7, 7.6	1.3, 6.8	0.7, 7.6
		Observed			
		n	27	17	44
		Mean	3.06	2.80	2.96
		SD, SE	1.947, 0.375	1.650, 0.400	1.822, 0.275
		Median	2.56	2.11	2.44
		Q1, Q3	1.33, 4.56	1.89, 3.22	1.56, 4.00
		Min, Max	0.3, 6.9	0.8, 6.9	0.3, 6.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Change from Baseline			
		n	27	17	44
		Mean	-0.95	-1.03	-0.98
		SD, SE	1.784, 0.343	1.604, 0.389	1.698, 0.256
		Median	-0.67	-0.67	-0.67
		Q1, Q3	-1.78, -0.22	-1.89, 0.11	-1.78, 0.11
		Min, Max	-6.2, 2.1	-4.4, 1.1	-6.2, 2.1
		GEE Estimates			
		LS Mean (SE)	0.57 (0.223)	0.47 (0.335)	
		95% CI	(0.14, 1.01)	(-0.19, 1.13)	
		LS Mean Difference (SE)		-0.10 (0.452)	
		95% CI		(-0.99, 0.78)	
		p-value		0.8194	
		HedgesG (95% CI)		-0.042 (-0.649, 0.565)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Baseline			
		n	27	17	44
		Mean	4.01	3.82	3.94
		SD, SE	1.711, 0.329	1.697, 0.412	1.688, 0.254
		Median	3.56	3.78	3.56
		Q1, Q3	2.78, 5.56	2.67, 5.11	2.78, 5.39
		Min, Max	0.7, 7.6	1.3, 6.8	0.7, 7.6
		Observed			
		n	27	17	44
		Mean	3.33	3.48	3.38
		SD, SE	1.813, 0.349	1.888, 0.458	1.822, 0.275
		Median	3.22	3.33	3.22
		Q1, Q3	2.00, 4.78	1.78, 5.00	2.00, 4.94
		Min, Max	0.0, 7.3	0.8, 6.3	0.0, 7.3

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Change from Baseline			
		n	27	17	44
		Mean	-0.68	-0.35	-0.55
		SD, SE	1.719, 0.331	1.302, 0.316	1.564, 0.236
		Median	-0.67	-0.22	-0.50
		Q1, Q3	-1.56, 0.11	-1.11, 0.11	-1.39, 0.11
		Min, Max	-5.1, 3.3	-3.6, 1.7	-5.1, 3.3
		GEE Estimates			
		LS Mean (SE)	0.84 (0.288)	1.15 (0.333)	
		95% CI	(0.28, 1.40)	(0.50, 1.80)	
		LS Mean Difference (SE)		0.31 (0.415)	
		95% CI		(-0.50, 1.12)	
		p-value		0.4562	
		HedgesG (95% CI)		0.205 (-0.403, 0.814)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6		N_1	39	51	90
	Baseline	n	39	51	90
		Mean	5.45	5.89	5.70
		SD, SE	1.874, 0.300	1.894, 0.265	1.888, 0.199
		Median	5.44	5.89	5.67
		Q1, Q3	4.00, 6.89	4.44, 7.33	4.44, 7.11
		Min, Max	2.0, 9.0	1.2, 8.8	1.2, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Baseline			
		n	39	51	90
		Mean	5.45	5.89	5.70
		SD, SE	1.874, 0.300	1.894, 0.265	1.888, 0.199
		Median	5.44	5.89	5.67
		Q1, Q3	4.00, 6.89	4.44, 7.33	4.44, 7.11
		Min, Max	2.0, 9.0	1.2, 8.8	1.2, 9.0
		Observed			
		n	39	51	90
		Mean	4.93	5.04	4.99
		SD, SE	2.259, 0.362	2.280, 0.319	2.259, 0.238
		Median	4.89	5.44	5.39
		Q1, Q3	3.56, 6.67	3.11, 6.78	3.22, 6.67
		Min, Max	1.1, 9.0	0.0, 8.8	0.0, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Change from Baseline			
		n	39	51	90
		Mean	-0.52	-0.85	-0.71
		SD, SE	1.538, 0.246	1.847, 0.259	1.718, 0.181
		Median	-0.33	-0.56	-0.56
		Q1, Q3	-1.44, 0.78	-1.44, 0.33	-1.44, 0.44
		Min, Max	-3.7, 3.7	-7.9, 2.8	-7.9, 3.7
		GEE Estimates			
		LS Mean (SE)	0.16 (0.373)	-0.10 (0.311)	
		95% CI	(-0.57, 0.90)	(-0.70, 0.51)	
		LS Mean Difference (SE)		-0.26 (0.337)	
		95% CI		(-0.92, 0.40)	
		p-value		0.4412	
		HedgesG (95% CI)		-0.190 (-0.608, 0.228)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Baseline			
		n	38	50	88
		Mean	5.39	5.84	5.64
		SD, SE	1.863, 0.302	1.875, 0.265	1.872, 0.200
		Median	5.39	5.83	5.67
		Q1, Q3	4.00, 6.56	4.44, 7.33	4.33, 7.11
		Min, Max	2.0, 9.0	1.2, 8.8	1.2, 9.0
		Observed			
		n	38	50	88
		Mean	4.82	5.08	4.97
		SD, SE	2.493, 0.404	2.308, 0.326	2.379, 0.254
		Median	4.72	5.56	5.28
		Q1, Q3	2.89, 6.78	3.44, 6.89	3.00, 6.83
		Min, Max	0.0, 9.1	0.3, 9.4	0.0, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Change from Baseline			
		n	38	50	88
		Mean	-0.57	-0.75	-0.67
		SD, SE	1.760, 0.286	1.955, 0.276	1.865, 0.199
		Median	-0.33	-0.89	-0.61
		Q1, Q3	-1.44, 0.44	-2.00, 0.33	-1.83, 0.44
		Min, Max	-5.0, 2.9	-6.8, 4.0	-6.8, 4.0
		GEE Estimates			
		LS Mean (SE)	0.07 (0.400)	-0.02 (0.340)	
		95% CI	(-0.71, 0.86)	(-0.68, 0.65)	
		LS Mean Difference (SE)		-0.09 (0.379)	
		95% CI		(-0.83, 0.66)	
		p-value		0.8199	
		HedgesG (95% CI)		-0.097 (-0.519, 0.325)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6		N_1	49	48	97
	Baseline	n	49	48	97
		Mean	4.27	4.70	4.48
		SD, SE	1.679, 0.240	1.898, 0.274	1.794, 0.182
		Median	4.00	4.78	4.44
		Q1, Q3	2.89, 5.44	3.39, 6.00	3.11, 5.78
		Min, Max	0.7, 8.8	1.2, 8.1	0.7, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Baseline			
		n	49	48	97
		Mean	4.27	4.70	4.48
		SD, SE	1.679, 0.240	1.898, 0.274	1.794, 0.182
		Median	4.00	4.78	4.44
		Q1, Q3	2.89, 5.44	3.39, 6.00	3.11, 5.78
		Min, Max	0.7, 8.8	1.2, 8.1	0.7, 8.8
		Observed			
		n	49	48	97
		Mean	3.55	3.83	3.69
		SD, SE	2.116, 0.302	2.183, 0.315	2.143, 0.218
		Median	3.22	3.22	3.22
		Q1, Q3	1.89, 4.89	2.00, 5.67	2.00, 5.44
		Min, Max	0.3, 9.0	0.0, 8.8	0.0, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Change from Baseline			
		n	49	48	97
		Mean	-0.72	-0.87	-0.79
		SD, SE	1.726, 0.247	1.604, 0.232	1.660, 0.169
		Median	-0.44	-0.61	-0.44
		Q1, Q3	-1.67, 0.33	-1.78, 0.50	-1.78, 0.44
		Min, Max	-6.2, 3.7	-4.4, 1.6	-6.2, 3.7
		GEE Estimates			
		LS Mean (SE)	-0.29 (0.308)	-0.33 (0.275)	
		95% CI	(-0.89, 0.32)	(-0.86, 0.21)	
		LS Mean Difference (SE)		-0.04 (0.319)	
		95% CI		(-0.67, 0.59)	
		p-value		0.9012	
		HedgesG (95% CI)		-0.085 (-0.483, 0.313)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Baseline			
		n	49	48	97
		Mean	4.27	4.70	4.48
		SD, SE	1.679, 0.240	1.898, 0.274	1.794, 0.182
		Median	4.00	4.78	4.44
		Q1, Q3	2.89, 5.44	3.39, 6.00	3.11, 5.78
		Min, Max	0.7, 8.8	1.2, 8.1	0.7, 8.8
		Observed			
		n	49	48	97
		Mean	3.56	4.08	3.82
		SD, SE	1.962, 0.280	2.165, 0.312	2.070, 0.210
		Median	3.22	4.33	3.78
		Q1, Q3	2.22, 4.78	2.28, 5.67	2.22, 5.44
		Min, Max	0.0, 8.2	0.3, 9.4	0.0, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Change from Baseline			
		n	49	48	97
		Mean	-0.71	-0.62	-0.67
		SD, SE	1.723, 0.246	1.633, 0.236	1.671, 0.170
		Median	-0.67	-0.67	-0.67
		Q1, Q3	-1.56, 0.22	-1.78, 0.22	-1.67, 0.22
		Min, Max	-5.1, 3.3	-4.3, 4.0	-5.1, 4.0
		GEE Estimates			
		LS Mean (SE)	-0.28 (0.307)	-0.08 (0.277)	
		95% CI	(-0.88, 0.32)	(-0.62, 0.46)	
		LS Mean Difference (SE)		0.20 (0.313)	
		95% CI		(-0.42, 0.81)	
		p-value		0.5292	
		HedgesG (95% CI)		0.054 (-0.345, 0.452)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6		N_1	17	20	37
	Baseline	n	17	20	37
		Mean	6.55	7.00	6.79
		SD, SE	1.625, 0.394	1.374, 0.307	1.491, 0.245
		Median	6.56	7.17	7.00
		Q1, Q3	5.67, 7.67	6.17, 8.17	5.67, 7.89
		Min, Max	2.8, 9.0	4.1, 8.8	2.8, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Baseline			
		n	17	20	37
		Mean	6.55	7.00	6.79
		SD, SE	1.625, 0.394	1.374, 0.307	1.491, 0.245
		Median	6.56	7.17	7.00
		Q1, Q3	5.67, 7.67	6.17, 8.17	5.67, 7.89
		Min, Max	2.8, 9.0	4.1, 8.8	2.8, 9.0
		Observed			
		n	17	20	37
		Mean	5.92	6.03	5.98
		SD, SE	1.977, 0.480	1.991, 0.445	1.958, 0.322
		Median	6.44	6.50	6.44
		Q1, Q3	5.00, 7.44	5.17, 7.33	5.00, 7.44
		Min, Max	1.3, 8.2	0.9, 8.6	0.9, 8.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Change from Baseline			
		n	17	20	37
		Mean	-0.63	-0.97	-0.81
		SD, SE	1.424, 0.345	2.187, 0.489	1.860, 0.306
		Median	-0.56	-0.61	-0.56
		Q1, Q3	-1.33, 0.33	-1.39, 0.11	-1.33, 0.22
		Min, Max	-3.7, 1.1	-7.9, 2.8	-7.9, 2.8
		GEE Estimates			
		LS Mean (SE)	-0.36 (0.453)	-0.57 (0.191)	
		95% CI	(-1.25, 0.52)	(-0.95, -0.20)	
		LS Mean Difference (SE)		-0.21 (0.557)	
		95% CI		(-1.30, 0.88)	
		p-value		0.7054	
		HedgesG (95% CI)		-0.176 (-0.824, 0.472)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Baseline			
		n	16	19	35
		Mean	6.48	6.92	6.72
		SD, SE	1.652, 0.413	1.360, 0.312	1.494, 0.253
		Median	6.50	7.11	7.00
		Q1, Q3	5.67, 7.63	5.56, 8.00	5.67, 7.89
		Min, Max	2.8, 9.0	4.1, 8.8	2.8, 9.0
		Observed			
		n	16	19	35
		Mean	6.15	6.19	6.17
		SD, SE	2.382, 0.596	1.967, 0.451	2.134, 0.361
		Median	6.61	6.89	6.78
		Q1, Q3	4.89, 8.00	4.00, 7.78	4.67, 7.78
		Min, Max	1.0, 9.1	2.0, 8.7	1.0, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Change from Baseline			
		n	16	19	35
		Mean	-0.32	-0.73	-0.54
		SD, SE	1.777, 0.444	2.249, 0.516	2.028, 0.343
		Median	0.28	-0.44	-0.22
		Q1, Q3	-1.06, 1.00	-1.78, 0.44	-1.67, 0.89
		Min, Max	-4.0, 2.0	-6.8, 3.1	-6.8, 3.1
		GEE Estimates			
		LS Mean (SE)	-0.19 (0.543)	-0.39 (0.203)	
		95% CI	(-1.25, 0.87)	(-0.78, 0.01)	
		LS Mean Difference (SE)		-0.20 (0.635)	
		95% CI		(-1.44, 1.05)	
		p-value		0.7551	
		HedgesG (95% CI)		-0.187 (-0.853, 0.480)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU		N_1	58	58	116
	Baseline	n	58	58	116
		Mean	4.93	5.56	5.24
		SD, SE	2.016, 0.265	1.993, 0.262	2.020, 0.188
		Median	4.89	5.56	5.39
		Q1, Q3	3.00, 6.33	4.22, 7.11	3.56, 6.94
		Min, Max	0.7, 9.0	1.2, 8.8	0.7, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Baseline			
		n	58	58	116
		Mean	4.93	5.56	5.24
		SD, SE	2.016, 0.265	1.993, 0.262	2.020, 0.188
		Median	4.89	5.56	5.39
		Q1, Q3	3.00, 6.33	4.22, 7.11	3.56, 6.94
		Min, Max	0.7, 9.0	1.2, 8.8	0.7, 9.0
		Observed			
		n	58	58	116
		Mean	4.16	4.49	4.32
		SD, SE	2.317, 0.304	2.377, 0.312	2.343, 0.218
		Median	4.00	4.94	4.22
		Q1, Q3	2.11, 6.11	2.11, 6.56	2.11, 6.44
		Min, Max	0.3, 8.8	0.0, 8.8	0.0, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Change from Baseline			
		n	58	58	116
		Mean	-0.78	-1.07	-0.92
		SD, SE	1.631, 0.214	1.812, 0.238	1.723, 0.160
		Median	-0.44	-0.67	-0.56
		Q1, Q3	-1.78, 0.33	-1.89, 0.11	-1.78, 0.18
		Min, Max	-6.2, 2.1	-7.9, 2.8	-7.9, 2.8
		GEE Estimates			
		LS Mean (SE)	-0.70 (0.211)	-0.84 (0.245)	
		95% CI	(-1.11, -0.29)	(-1.32, -0.36)	
		LS Mean Difference (SE)		-0.14 (0.306)	
		95% CI		(-0.74, 0.46)	
		p-value		0.6553	
		HedgesG (95% CI)		-0.167 (-0.531, 0.198)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Baseline			
		n	57	57	114
		Mean	4.89	5.50	5.19
		SD, SE	2.000, 0.265	1.969, 0.261	2.000, 0.187
		Median	4.78	5.56	5.33
		Q1, Q3	3.00, 6.33	4.22, 7.00	3.56, 6.89
		Min, Max	0.7, 9.0	1.2, 8.8	0.7, 9.0
		Observed			
		n	57	57	114
		Mean	4.26	4.69	4.47
		SD, SE	2.399, 0.318	2.350, 0.311	2.374, 0.222
		Median	4.67	5.11	4.67
		Q1, Q3	2.56, 5.67	2.56, 6.33	2.56, 6.22
		Min, Max	0.0, 9.1	0.3, 9.4	0.0, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Change from Baseline			
		n	57	57	114
		Mean	-0.63	-0.81	-0.72
		SD, SE	1.773, 0.235	1.747, 0.231	1.755, 0.164
		Median	-0.56	-0.78	-0.61
		Q1, Q3	-1.78, 0.44	-1.89, 0.22	-1.89, 0.33
		Min, Max	-5.1, 3.3	-6.8, 3.1	-6.8, 3.3
		GEE Estimates			
		LS Mean (SE)	-0.58 (0.236)	-0.59 (0.243)	
		95% CI	(-1.04, -0.12)	(-1.07, -0.12)	
		LS Mean Difference (SE)		-0.01 (0.312)	
		95% CI		(-0.63, 0.60)	
		p-value		0.9627	
		HedgesG (95% CI)		-0.101 (-0.468, 0.266)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia		N_1	8	10	18
	Baseline	n	8	10	18
		Mean	4.32	4.32	4.32
		SD, SE	1.093, 0.386	2.127, 0.673	1.699, 0.401
		Median	4.00	4.00	4.00
		Q1, Q3	3.39, 5.33	2.33, 6.67	3.22, 5.33
		Min, Max	3.1, 6.0	1.4, 7.3	1.4, 7.3

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Baseline			
		n	8	10	18
		Mean	4.32	4.32	4.32
		SD, SE	1.093, 0.386	2.127, 0.673	1.699, 0.401
		Median	4.00	4.00	4.00
		Q1, Q3	3.39, 5.33	2.33, 6.67	3.22, 5.33
		Min, Max	3.1, 6.0	1.4, 7.3	1.4, 7.3
		Observed			
		n	8	10	18
		Mean	4.21	4.42	4.33
		SD, SE	2.451, 0.867	2.247, 0.710	2.271, 0.535
		Median	3.28	4.11	3.78
		Q1, Q3	2.44, 5.67	2.56, 6.11	2.44, 6.11
		Min, Max	1.9, 9.0	1.6, 8.6	1.6, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Change from Baseline			
		n	8	10	18
		Mean	-0.11	0.10	0.01
		SD, SE	1.721, 0.609	1.210, 0.383	1.417, 0.334
		Median	-0.56	0.00	-0.28
		Q1, Q3	-1.33, 0.44	-1.11, 1.44	-1.22, 1.11
		Min, Max	-1.7, 3.7	-1.4, 1.6	-1.7, 3.7
		GEE Estimates			
		LS Mean (SE)	0.66 (0.735)	0.62 (0.432)	
		95% CI	(-0.79, 2.10)	(-0.23, 1.46)	
		LS Mean Difference (SE)		-0.04 (0.717)	
		95% CI		(-1.45, 1.37)	
		p-value		0.9554	
		HedgesG (95% CI)		0.130 (-0.800, 1.061)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Baseline			
		n	8	10	18
		Mean	4.32	4.32	4.32
		SD, SE	1.093, 0.386	2.127, 0.673	1.699, 0.401
		Median	4.00	4.00	4.00
		Q1, Q3	3.39, 5.33	2.33, 6.67	3.22, 5.33
		Min, Max	3.1, 6.0	1.4, 7.3	1.4, 7.3
		Observed			
		n	8	10	18
		Mean	3.81	4.59	4.24
		SD, SE	1.966, 0.695	2.148, 0.679	2.048, 0.483
		Median	3.22	4.61	3.89
		Q1, Q3	2.50, 4.33	3.00, 5.67	2.56, 5.22
		Min, Max	2.1, 8.2	1.6, 8.2	1.6, 8.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Change from Baseline			
		n	8	10	18
		Mean	-0.51	0.27	-0.08
		SD, SE	1.488, 0.526	1.993, 0.630	1.781, 0.420
		Median	-1.06	0.39	-0.28
		Q1, Q3	-1.50, -0.17	-1.11, 1.22	-1.44, 1.11
		Min, Max	-1.6, 2.9	-3.3, 4.0	-3.3, 4.0
		GEE Estimates			
		LS Mean (SE)	0.25 (0.709)	0.78 (0.481)	
		95% CI	(-1.14, 1.64)	(-0.16, 1.73)	
		LS Mean Difference (SE)		0.53 (0.616)	
		95% CI		(-0.68, 1.74)	
		p-value		0.3904	
		HedgesG (95% CI)		0.392 (-0.547, 1.330)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male		N_1	23	24	47
	Baseline	n	23	24	47
		Mean	4.18	4.85	4.52
		SD, SE	1.946, 0.406	2.182, 0.445	2.075, 0.303
		Median	3.56	4.61	4.00
		Q1, Q3	2.89, 5.67	3.39, 6.72	2.89, 6.00
		Min, Max	0.7, 8.8	1.2, 8.6	0.7, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Baseline			
		n	23	24	47
		Mean	4.18	4.85	4.52
		SD, SE	1.946, 0.406	2.182, 0.445	2.075, 0.303
		Median	3.56	4.61	4.00
		Q1, Q3	2.89, 5.67	3.39, 6.72	2.89, 6.00
		Min, Max	0.7, 8.8	1.2, 8.6	0.7, 8.8
		Observed			
		n	23	24	47
		Mean	3.91	3.93	3.92
		SD, SE	2.560, 0.534	2.305, 0.471	2.406, 0.351
		Median	3.67	3.56	3.67
		Q1, Q3	1.33, 6.44	2.00, 6.22	2.00, 6.33
		Min, Max	0.3, 9.0	0.0, 7.7	0.0, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Change from Baseline			
		n	23	24	47
		Mean	-0.27	-0.92	-0.60
		SD, SE	1.401, 0.292	1.457, 0.297	1.451, 0.212
		Median	-0.33	-1.06	-0.56
		Q1, Q3	-1.56, 0.78	-1.72, 0.11	-1.56, 0.44
		Min, Max	-2.7, 3.7	-4.4, 1.6	-4.4, 3.7
		GEE Estimates			
		LS Mean (SE)	0.53 (0.483)	-0.05 (0.373)	
		95% CI	(-0.42, 1.48)	(-0.78, 0.68)	
		LS Mean Difference (SE)		-0.58 (0.395)	
		95% CI		(-1.36, 0.19)	
		p-value		0.1395	
		HedgesG (95% CI)		-0.435 (-1.013, 0.144)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Baseline			
		n	23	23	46
		Mean	4.18	4.69	4.43
		SD, SE	1.946, 0.406	2.079, 0.434	2.008, 0.296
		Median	3.56	4.33	4.00
		Q1, Q3	2.89, 5.67	3.33, 6.67	2.89, 5.89
		Min, Max	0.7, 8.8	1.2, 8.3	0.7, 8.8
		Observed			
		n	23	23	46
		Mean	3.62	3.78	3.70
		SD, SE	2.340, 0.488	2.016, 0.420	2.161, 0.319
		Median	3.22	3.78	3.44
		Q1, Q3	2.00, 5.11	2.44, 5.67	2.00, 5.22
		Min, Max	0.0, 8.4	0.3, 7.0	0.0, 8.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Change from Baseline			
		n	23	23	46
		Mean	-0.56	-0.90	-0.73
		SD, SE	1.920, 0.400	1.448, 0.302	1.690, 0.249
		Median	-0.78	-1.00	-0.89
		Q1, Q3	-1.44, 0.00	-1.78, 0.00	-1.44, 0.00
		Min, Max	-5.1, 3.3	-3.6, 1.7	-5.1, 3.3
		GEE Estimates			
		LS Mean (SE)	0.24 (0.520)	-0.07 (0.426)	
		95% CI	(-0.78, 1.26)	(-0.91, 0.76)	
		LS Mean Difference (SE)		-0.32 (0.449)	
		95% CI		(-1.20, 0.57)	
		p-value		0.4834	
		HedgesG (95% CI)		-0.194 (-0.773, 0.385)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female		N_1	43	44	87
	Baseline	n	43	44	87
		Mean	5.22	5.66	5.44
		SD, SE	1.845, 0.281	1.930, 0.291	1.890, 0.203
		Median	5.33	5.72	5.56
		Q1, Q3	3.56, 6.44	4.39, 7.11	4.11, 7.00
		Min, Max	2.0, 9.0	1.4, 8.8	1.4, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Baseline			
		n	43	44	87
		Mean	5.22	5.66	5.44
		SD, SE	1.845, 0.281	1.930, 0.291	1.890, 0.203
		Median	5.33	5.72	5.56
		Q1, Q3	3.56, 6.44	4.39, 7.11	4.11, 7.00
		Min, Max	2.0, 9.0	1.4, 8.8	1.4, 9.0
		Observed			
		n	43	44	87
		Mean	4.30	4.78	4.54
		SD, SE	2.192, 0.334	2.334, 0.352	2.264, 0.243
		Median	4.56	5.06	4.89
		Q1, Q3	2.33, 6.11	2.56, 6.67	2.44, 6.56
		Min, Max	0.9, 8.2	0.9, 8.8	0.9, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Change from Baseline			
		n	43	44	87
		Mean	-0.92	-0.89	-0.91
		SD, SE	1.732, 0.264	1.948, 0.294	1.834, 0.197
		Median	-0.67	-0.56	-0.56
		Q1, Q3	-1.78, 0.14	-1.72, 0.39	-1.78, 0.22
		Min, Max	-6.2, 2.1	-7.9, 2.8	-7.9, 2.8
		GEE Estimates			
		LS Mean (SE)	-0.49 (0.305)	-0.33 (0.294)	
		95% CI	(-1.09, 0.11)	(-0.91, 0.25)	
		LS Mean Difference (SE)		0.16 (0.365)	
		95% CI		(-0.56, 0.87)	
		p-value		0.6636	
		HedgesG (95% CI)		0.020 (-0.400, 0.440)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Baseline			
		n	42	44	86
		Mean	5.17	5.66	5.42
		SD, SE	1.827, 0.282	1.930, 0.291	1.886, 0.203
		Median	5.28	5.72	5.56
		Q1, Q3	3.56, 6.33	4.39, 7.11	4.11, 7.00
		Min, Max	2.0, 9.0	1.4, 8.8	1.4, 9.0
		Observed			
		n	42	44	86
		Mean	4.52	5.14	4.84
		SD, SE	2.308, 0.356	2.330, 0.351	2.327, 0.251
		Median	4.67	5.56	5.06
		Q1, Q3	2.56, 5.78	3.06, 6.83	2.56, 6.44
		Min, Max	0.0, 9.1	1.0, 9.4	0.0, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Change from Baseline			
		n	42	44	86
		Mean	-0.65	-0.52	-0.58
		SD, SE	1.642, 0.253	1.977, 0.298	1.812, 0.195
		Median	-0.50	-0.22	-0.33
		Q1, Q3	-1.78, 0.44	-1.78, 0.39	-1.78, 0.44
		Min, Max	-5.0, 2.0	-6.8, 4.0	-6.8, 4.0
		GEE Estimates			
		LS Mean (SE)	-0.25 (0.325)	0.04 (0.313)	
		95% CI	(-0.88, 0.39)	(-0.58, 0.65)	
		LS Mean Difference (SE)		0.29 (0.362)	
		95% CI		(-0.42, 0.99)	
		p-value		0.4306	
		HedgesG (95% CI)		0.069 (-0.354, 0.492)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White		N_1	53	55	108
	Baseline	n	53	55	108
		Mean	4.83	5.53	5.18
		SD, SE	2.013, 0.277	2.001, 0.270	2.028, 0.195
		Median	4.44	5.56	5.33
		Q1, Q3	3.00, 6.33	4.11, 7.11	3.50, 6.89
		Min, Max	0.7, 9.0	1.2, 8.8	0.7, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Baseline			
		n	53	55	108
		Mean	4.83	5.53	5.18
		SD, SE	2.013, 0.277	2.001, 0.270	2.028, 0.195
		Median	4.44	5.56	5.33
		Q1, Q3	3.00, 6.33	4.11, 7.11	3.50, 6.89
		Min, Max	0.7, 9.0	1.2, 8.8	0.7, 9.0
		Observed			
		n	53	55	108
		Mean	4.01	4.53	4.27
		SD, SE	2.326, 0.319	2.392, 0.323	2.363, 0.227
		Median	3.78	5.00	4.11
		Q1, Q3	2.11, 6.00	2.11, 6.56	2.11, 6.44
		Min, Max	0.3, 8.8	0.0, 8.8	0.0, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Change from Baseline			
		n	53	55	108
		Mean	-0.83	-1.00	-0.91
		SD, SE	1.638, 0.225	1.832, 0.247	1.733, 0.167
		Median	-0.56	-0.56	-0.56
		Q1, Q3	-1.78, 0.14	-1.78, 0.11	-1.78, 0.13
		Min, Max	-6.2, 2.1	-7.9, 2.8	-7.9, 2.8
		GEE Estimates			
		LS Mean (SE)	-0.75 (0.223)	-0.77 (0.255)	
		95% CI	(-1.19, -0.32)	(-1.27, -0.27)	
		LS Mean Difference (SE)		-0.01 (0.316)	
		95% CI		(-0.63, 0.61)	
		p-value		0.9658	
		HedgesG (95% CI)		-0.098 (-0.475, 0.280)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Baseline			
		n	53	55	108
		Mean	4.83	5.53	5.18
		SD, SE	2.013, 0.277	2.001, 0.270	2.028, 0.195
		Median	4.44	5.56	5.33
		Q1, Q3	3.00, 6.33	4.11, 7.11	3.50, 6.89
		Min, Max	0.7, 9.0	1.2, 8.8	0.7, 9.0
		Observed			
		n	53	55	108
		Mean	4.15	4.73	4.44
		SD, SE	2.299, 0.316	2.368, 0.319	2.342, 0.225
		Median	4.56	5.22	4.67
		Q1, Q3	2.56, 5.56	2.56, 6.44	2.56, 6.06
		Min, Max	0.0, 9.1	0.3, 9.4	0.0, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Change from Baseline			
		n	53	55	108
		Mean	-0.68	-0.80	-0.74
		SD, SE	1.784, 0.245	1.762, 0.238	1.765, 0.170
		Median	-0.56	-0.78	-0.67
		Q1, Q3	-1.78, 0.44	-1.89, 0.22	-1.83, 0.33
		Min, Max	-5.1, 3.3	-6.8, 3.1	-6.8, 3.3
		GEE Estimates			
		LS Mean (SE)	-0.61 (0.244)	-0.56 (0.250)	
		95% CI	(-1.09, -0.13)	(-1.06, -0.07)	
		LS Mean Difference (SE)		0.05 (0.319)	
		95% CI		(-0.58, 0.67)	
		p-value		0.8819	
		HedgesG (95% CI)		-0.062 (-0.439, 0.315)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White		N_1	13	13	26
	Baseline	n	13	13	26
		Mean	4.97	4.74	4.85
		SD, SE	1.625, 0.451	2.183, 0.605	1.889, 0.371
		Median	5.33	4.67	4.78
		Q1, Q3	3.56, 6.22	3.22, 6.67	3.22, 6.44
		Min, Max	2.8, 7.7	1.4, 8.6	1.4, 8.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Baseline			
		n	13	13	26
		Mean	4.97	4.74	4.85
		SD, SE	1.625, 0.451	2.183, 0.605	1.889, 0.371
		Median	5.33	4.67	4.78
		Q1, Q3	3.56, 6.22	3.22, 6.67	3.22, 6.44
		Min, Max	2.8, 7.7	1.4, 8.6	1.4, 8.6
		Observed			
		n	13	13	26
		Mean	4.80	4.26	4.53
		SD, SE	2.241, 0.622	2.195, 0.609	2.190, 0.430
		Median	4.56	3.89	4.11
		Q1, Q3	2.89, 6.44	2.56, 6.11	2.56, 6.33
		Min, Max	1.9, 9.0	1.6, 8.6	1.6, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Change from Baseline			
		n	13	13	26
		Mean	-0.17	-0.47	-0.32
		SD, SE	1.623, 0.450	1.525, 0.423	1.550, 0.304
		Median	-0.11	-0.78	-0.28
		Q1, Q3	-1.22, 0.44	-1.44, 1.11	-1.44, 0.78
		Min, Max	-3.1, 3.7	-3.0, 1.6	-3.1, 3.7
		GEE Estimates			
		LS Mean (SE)	0.55 (0.465)	0.01 (0.375)	
		95% CI	(-0.36, 1.46)	(-0.73, 0.74)	
		LS Mean Difference (SE)		-0.55 (0.528)	
		95% CI		(-1.58, 0.49)	
		p-value		0.3008	
		HedgesG (95% CI)		-0.177 (-0.947, 0.594)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Baseline			
		n	12	12	24
		Mean	4.75	4.42	4.58
		SD, SE	1.472, 0.425	1.939, 0.560	1.692, 0.345
		Median	4.72	4.33	4.39
		Q1, Q3	3.39, 6.11	2.78, 5.89	3.22, 6.11
		Min, Max	2.8, 7.0	1.4, 7.3	1.4, 7.3
		Observed			
		n	12	12	24
		Mean	4.44	4.44	4.44
		SD, SE	2.613, 0.754	2.070, 0.597	2.305, 0.471
		Median	3.72	4.56	4.11
		Q1, Q3	2.50, 6.94	2.61, 5.44	2.50, 6.11
		Min, Max	0.4, 8.4	1.6, 8.2	0.4, 8.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Change from Baseline			
		n	12	12	24
		Mean	-0.31	0.02	-0.15
		SD, SE	1.503, 0.434	1.964, 0.567	1.719, 0.351
		Median	-0.67	0.06	-0.11
		Q1, Q3	-1.50, 0.61	-1.28, 1.17	-1.44, 1.00
		Min, Max	-2.3, 2.9	-3.3, 4.0	-3.3, 4.0
		GEE Estimates			
		LS Mean (SE)	0.26 (0.553)	0.37 (0.446)	
		95% CI	(-0.82, 1.34)	(-0.51, 1.24)	
		LS Mean Difference (SE)		0.10 (0.590)	
		95% CI		(-1.05, 1.26)	
		p-value		0.8596	
		HedgesG (95% CI)		0.176 (-0.626, 0.978)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years		N_1	36	31	67
	Baseline	n	36	31	67
		Mean	5.00	5.71	5.33
		SD, SE	2.101, 0.350	1.896, 0.341	2.026, 0.247
		Median	4.61	5.89	5.33
		Q1, Q3	2.89, 6.50	4.22, 7.22	3.44, 7.00
		Min, Max	2.0, 9.0	1.2, 8.6	1.2, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Baseline			
		n	36	31	67
		Mean	5.00	5.71	5.33
		SD, SE	2.101, 0.350	1.896, 0.341	2.026, 0.247
		Median	4.61	5.89	5.33
		Q1, Q3	2.89, 6.50	4.22, 7.22	3.44, 7.00
		Min, Max	2.0, 9.0	1.2, 8.6	1.2, 9.0
		Observed			
		n	36	31	67
		Mean	4.40	5.18	4.76
		SD, SE	2.462, 0.410	2.263, 0.406	2.386, 0.292
		Median	3.89	6.11	5.00
		Q1, Q3	2.39, 6.50	3.11, 6.89	2.56, 6.78
		Min, Max	0.7, 9.0	0.8, 8.2	0.7, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Change from Baseline			
		n	36	31	67
		Mean	-0.60	-0.53	-0.57
		SD, SE	1.601, 0.267	1.448, 0.260	1.521, 0.186
		Median	-0.50	-0.44	-0.44
		Q1, Q3	-1.39, 0.28	-1.11, 0.11	-1.33, 0.22
		Min, Max	-6.2, 3.7	-4.4, 2.8	-6.2, 3.7
		GEE Estimates			
		LS Mean (SE)	-0.20 (0.402)	-0.07 (0.386)	
		95% CI	(-0.99, 0.59)	(-0.83, 0.69)	
		LS Mean Difference (SE)		0.13 (0.374)	
		95% CI		(-0.60, 0.86)	
		p-value		0.7293	
		HedgesG (95% CI)		0.043 (-0.437, 0.523)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Baseline			
		n	36	31	67
		Mean	5.00	5.71	5.33
		SD, SE	2.101, 0.350	1.896, 0.341	2.026, 0.247
		Median	4.61	5.89	5.33
		Q1, Q3	2.89, 6.50	4.22, 7.22	3.44, 7.00
		Min, Max	2.0, 9.0	1.2, 8.6	1.2, 9.0
		Observed			
		n	36	31	67
		Mean	4.31	5.30	4.77
		SD, SE	2.493, 0.415	2.080, 0.374	2.347, 0.287
		Median	4.33	5.67	5.11
		Q1, Q3	2.56, 6.50	3.56, 6.89	2.78, 6.78
		Min, Max	0.0, 8.9	1.2, 8.7	0.0, 8.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Change from Baseline			
		n	36	31	67
		Mean	-0.69	-0.41	-0.56
		SD, SE	1.529, 0.255	1.446, 0.260	1.486, 0.182
		Median	-0.67	-0.44	-0.56
		Q1, Q3	-1.78, 0.39	-1.44, 0.33	-1.56, 0.33
		Min, Max	-4.0, 2.9	-3.3, 3.1	-4.0, 3.1
		GEE Estimates			
		LS Mean (SE)	-0.28 (0.411)	0.05 (0.405)	
		95% CI	(-1.09, 0.52)	(-0.74, 0.85)	
		LS Mean Difference (SE)		0.34 (0.356)	
		95% CI		(-0.36, 1.03)	
		p-value		0.3424	
		HedgesG (95% CI)		0.180 (-0.301, 0.661)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years		N_1	30	37	67
	Baseline	n	30	37	67
		Mean	4.69	5.09	4.91
		SD, SE	1.726, 0.315	2.145, 0.353	1.964, 0.240
		Median	4.72	4.89	4.89
		Q1, Q3	3.33, 5.67	3.67, 7.00	3.44, 6.33
		Min, Max	0.7, 7.7	1.3, 8.8	0.7, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Baseline			
		n	30	37	67
		Mean	4.69	5.09	4.91
		SD, SE	1.726, 0.315	2.145, 0.353	1.964, 0.240
		Median	4.72	4.89	4.89
		Q1, Q3	3.33, 5.67	3.67, 7.00	3.44, 6.33
		Min, Max	0.7, 7.7	1.3, 8.8	0.7, 8.8
		Observed			
		n	30	37	67
		Mean	3.88	3.89	3.88
		SD, SE	2.130, 0.389	2.272, 0.373	2.193, 0.268
		Median	3.83	3.22	3.67
		Q1, Q3	2.11, 5.44	2.00, 5.44	2.00, 5.44
		Min, Max	0.3, 7.9	0.0, 8.8	0.0, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Change from Baseline			
		n	30	37	67
		Mean	-0.81	-1.20	-1.03
		SD, SE	1.713, 0.313	1.984, 0.326	1.864, 0.228
		Median	-0.44	-1.11	-1.00
		Q1, Q3	-2.33, 0.78	-2.22, 0.44	-2.22, 0.56
		Min, Max	-4.8, 2.1	-7.9, 1.4	-7.9, 2.1
		GEE Estimates			
		LS Mean (SE)	0.01 (0.428)	-0.29 (0.349)	
		95% CI	(-0.83, 0.85)	(-0.98, 0.39)	
		LS Mean Difference (SE)		-0.30 (0.406)	
		95% CI		(-1.10, 0.49)	
		p-value		0.4569	
		HedgesG (95% CI)		-0.204 (-0.687, 0.279)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Baseline			
		n	29	36	65
		Mean	4.58	4.99	4.81
		SD, SE	1.661, 0.308	2.092, 0.349	1.909, 0.237
		Median	4.44	4.89	4.89
		Q1, Q3	3.33, 5.67	3.56, 6.89	3.44, 6.11
		Min, Max	0.7, 7.7	1.3, 8.8	0.7, 8.8
		Observed			
		n	29	36	65
		Mean	4.06	4.14	4.10
		SD, SE	2.174, 0.404	2.381, 0.397	2.274, 0.282
		Median	4.56	3.83	4.22
		Q1, Q3	2.44, 5.33	2.00, 5.89	2.22, 5.56
		Min, Max	0.0, 9.1	0.3, 9.4	0.0, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Change from Baseline			
		n	29	36	65
		Mean	-0.53	-0.85	-0.71
		SD, SE	1.977, 0.367	2.074, 0.346	2.022, 0.251
		Median	-0.56	-0.83	-0.56
		Q1, Q3	-1.44, 0.56	-2.11, 0.17	-1.78, 0.44
		Min, Max	-5.1, 3.3	-6.8, 4.0	-6.8, 4.0
		GEE Estimates			
		LS Mean (SE)	0.24 (0.474)	0.03 (0.355)	
		95% CI	(-0.69, 1.16)	(-0.67, 0.72)	
		LS Mean Difference (SE)		-0.21 (0.453)	
		95% CI		(-1.10, 0.68)	
		p-value		0.6429	
		HedgesG (95% CI)		-0.157 (-0.647, 0.333)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5		N_1	41	39	80
	Baseline	n	41	39	80
		Mean	4.68	4.64	4.66
		SD, SE	1.870, 0.292	1.964, 0.315	1.904, 0.213
		Median	4.44	4.44	4.44
		Q1, Q3	3.00, 6.00	3.33, 6.44	3.17, 6.00
		Min, Max	2.1, 9.0	1.2, 8.1	1.2, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline			
		n	41	39	80
		Mean	4.68	4.64	4.66
		SD, SE	1.870, 0.292	1.964, 0.315	1.904, 0.213
		Median	4.44	4.44	4.44
		Q1, Q3	3.00, 6.00	3.33, 6.44	3.17, 6.00
		Min, Max	2.1, 9.0	1.2, 8.1	1.2, 9.0
		Observed			
		n	41	39	80
		Mean	3.92	4.02	3.96
		SD, SE	2.100, 0.328	2.059, 0.330	2.068, 0.231
		Median	3.67	4.00	3.72
		Q1, Q3	2.44, 5.44	2.11, 5.89	2.11, 5.61
		Min, Max	0.7, 8.8	0.0, 7.4	0.0, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline			
		n	41	39	80
		Mean	-0.77	-0.62	-0.70
		SD, SE	1.453, 0.227	1.569, 0.251	1.503, 0.168
		Median	-0.67	-0.44	-0.56
		Q1, Q3	-1.67, 0.14	-1.67, 0.56	-1.67, 0.39
		Min, Max	-4.8, 2.1	-4.4, 2.8	-4.8, 2.8
		GEE Estimates			
		LS Mean (SE)	-0.12 (0.269)	0.02 (0.268)	
		95% CI	(-0.65, 0.41)	(-0.50, 0.55)	
		LS Mean Difference (SE)		0.14 (0.305)	
		95% CI		(-0.45, 0.74)	
		p-value		0.6349	
		HedgesG (95% CI)		0.092 (-0.347, 0.531)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline			
		n	41	39	80
		Mean	4.68	4.64	4.66
		SD, SE	1.870, 0.292	1.964, 0.315	1.904, 0.213
		Median	4.44	4.44	4.44
		Q1, Q3	3.00, 6.00	3.33, 6.44	3.17, 6.00
		Min, Max	2.1, 9.0	1.2, 8.1	1.2, 9.0
		Observed			
		n	41	39	80
		Mean	3.97	4.43	4.19
		SD, SE	2.102, 0.328	2.194, 0.351	2.146, 0.240
		Median	4.22	5.00	4.44
		Q1, Q3	2.56, 5.11	2.44, 6.11	2.56, 5.78
		Min, Max	0.0, 9.1	0.3, 8.7	0.0, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline			
		n	41	39	80
		Mean	-0.71	-0.21	-0.47
		SD, SE	1.763, 0.275	1.658, 0.266	1.720, 0.192
		Median	-0.67	-0.11	-0.39
		Q1, Q3	-1.78, 0.33	-1.11, 0.67	-1.50, 0.39
		Min, Max	-5.0, 3.3	-3.6, 4.0	-5.0, 4.0
		GEE Estimates			
		LS Mean (SE)	-0.07 (0.317)	0.43 (0.308)	
		95% CI	(-0.69, 0.55)	(-0.17, 1.04)	
		LS Mean Difference (SE)		0.50 (0.340)	
		95% CI		(-0.16, 1.17)	
		p-value		0.1396	
		HedgesG (95% CI)		0.286 (-0.155, 0.726)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5		N_1	25	29	54
	Baseline	n	25	29	54
		Mean	5.15	6.36	5.80
		SD, SE	2.034, 0.407	1.735, 0.322	1.958, 0.266
		Median	5.22	6.89	5.83
		Q1, Q3	3.89, 7.00	5.44, 7.67	4.22, 7.33
		Min, Max	0.7, 8.4	2.8, 8.8	0.7, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline			
		n	25	29	54
		Mean	5.15	6.36	5.80
		SD, SE	2.034, 0.407	1.735, 0.322	1.958, 0.266
		Median	5.22	6.89	5.83
		Q1, Q3	3.89, 7.00	5.44, 7.67	4.22, 7.33
		Min, Max	0.7, 8.4	2.8, 8.8	0.7, 8.8
		Observed			
		n	25	29	54
		Mean	4.57	5.10	4.85
		SD, SE	2.624, 0.525	2.585, 0.480	2.592, 0.353
		Median	4.56	6.33	5.39
		Q1, Q3	2.11, 6.89	2.56, 6.89	2.44, 6.89
		Min, Max	0.3, 9.0	0.8, 8.8	0.3, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline			
		n	25	29	54
		Mean	-0.58	-1.26	-0.95
		SD, SE	1.943, 0.389	1.997, 0.371	1.983, 0.270
		Median	-0.33	-1.11	-0.61
		Q1, Q3	-1.44, 0.78	-2.00, -0.11	-1.56, 0.33
		Min, Max	-6.2, 3.7	-7.9, 1.4	-7.9, 3.7
		GEE Estimates			
		LS Mean (SE)	0.44 (0.410)	-0.14 (0.343)	
		95% CI	(-0.36, 1.25)	(-0.81, 0.53)	
		LS Mean Difference (SE)		-0.58 (0.499)	
		95% CI		(-1.56, 0.40)	
		p-value		0.2439	
		HedgesG (95% CI)		-0.335 (-0.873, 0.204)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline			
		n	24	28	52
		Mean	5.05	6.28	5.71
		SD, SE	2.008, 0.410	1.713, 0.324	1.939, 0.269
		Median	5.11	6.83	5.72
		Q1, Q3	3.61, 6.94	5.28, 7.61	4.22, 7.22
		Min, Max	0.7, 8.4	2.8, 8.8	0.7, 8.8
		Observed			
		n	24	28	52
		Mean	4.60	5.02	4.83
		SD, SE	2.704, 0.552	2.450, 0.463	2.553, 0.354
		Median	5.06	5.44	5.33
		Q1, Q3	2.00, 7.11	3.11, 6.89	2.50, 6.89
		Min, Max	0.0, 8.9	0.8, 9.4	0.0, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline			
		n	24	28	52
		Mean	-0.45	-1.26	-0.88
		SD, SE	1.698, 0.347	1.869, 0.353	1.821, 0.252
		Median	-0.44	-1.22	-0.89
		Q1, Q3	-1.28, 0.50	-2.11, 0.17	-2.00, 0.39
		Min, Max	-5.1, 2.9	-6.8, 1.9	-6.8, 2.9
		GEE Estimates			
		LS Mean (SE)	0.51 (0.387)	-0.16 (0.348)	
		95% CI	(-0.25, 1.26)	(-0.84, 0.52)	
		LS Mean Difference (SE)		-0.66 (0.460)	
		95% CI		(-1.56, 0.24)	
		p-value		0.1489	
		HedgesG (95% CI)		-0.436 (-0.987, 0.116)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	3.92	4.14	4.02
		SD, SE	1.431, 0.235	1.819, 0.332	1.607, 0.196
		Median	3.44	4.11	3.78
		Q1, Q3	2.78, 4.44	2.78, 5.11	2.78, 5.11
		Min, Max	2.0, 7.1	1.2, 8.1	1.2, 8.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline			
		n	37	30	67
		Mean	3.92	4.14	4.02
		SD, SE	1.431, 0.235	1.819, 0.332	1.607, 0.196
		Median	3.44	4.11	3.78
		Q1, Q3	2.78, 4.44	2.78, 5.11	2.78, 5.11
		Min, Max	2.0, 7.1	1.2, 8.1	1.2, 8.1
		Observed			
		n	37	30	67
		Mean	3.35	3.37	3.36
		SD, SE	1.706, 0.281	1.861, 0.340	1.763, 0.215
		Median	3.22	3.00	3.11
		Q1, Q3	2.11, 4.11	1.89, 5.00	1.89, 4.56
		Min, Max	0.7, 6.9	0.8, 6.8	0.7, 6.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-0.56	-0.77	-0.66
		SD, SE	1.179, 0.194	1.227, 0.224	1.196, 0.146
		Median	-0.44	-0.67	-0.67
		Q1, Q3	-1.44, 0.00	-1.67, 0.11	-1.56, 0.11
		Min, Max	-2.8, 2.1	-3.7, 1.6	-3.7, 2.1
		GEE Estimates			
		LS Mean (SE)	-0.01 (0.327)	-0.16 (0.334)	
		95% CI	(-0.65, 0.64)	(-0.82, 0.49)	
		LS Mean Difference (SE)		-0.15 (0.281)	
		95% CI		(-0.71, 0.40)	
		p-value		0.5812	
		HedgesG (95% CI)		-0.167 (-0.649, 0.315)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline			
		n	37	30	67
		Mean	3.92	4.14	4.02
		SD, SE	1.431, 0.235	1.819, 0.332	1.607, 0.196
		Median	3.44	4.11	3.78
		Q1, Q3	2.78, 4.44	2.78, 5.11	2.78, 5.11
		Min, Max	2.0, 7.1	1.2, 8.1	1.2, 8.1
		Observed			
		n	37	30	67
		Mean	2.97	3.70	3.30
		SD, SE	1.714, 0.282	1.987, 0.363	1.863, 0.228
		Median	2.78	3.17	3.00
		Q1, Q3	2.00, 4.22	2.22, 5.22	2.00, 4.78
		Min, Max	0.0, 6.9	0.8, 7.6	0.0, 7.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-0.95	-0.44	-0.72
		SD, SE	1.759, 0.289	1.690, 0.309	1.734, 0.212
		Median	-1.00	-0.44	-0.78
		Q1, Q3	-1.56, -0.11	-1.78, 0.11	-1.78, 0.00
		Min, Max	-5.1, 3.3	-3.6, 4.0	-5.1, 4.0
		GEE Estimates			
		LS Mean (SE)	-0.39 (0.368)	0.17 (0.410)	
		95% CI	(-1.11, 0.33)	(-0.64, 0.97)	
		LS Mean Difference (SE)		0.56 (0.365)	
		95% CI		(-0.16, 1.27)	
		p-value		0.1284	
		HedgesG (95% CI)		0.284 (-0.200, 0.768)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	6.06	6.35	6.22
		SD, SE	1.837, 0.341	1.667, 0.270	1.735, 0.212
		Median	6.00	6.78	6.44
		Q1, Q3	5.33, 7.56	5.44, 7.67	5.33, 7.56
		Min, Max	0.7, 9.0	1.7, 8.8	0.7, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline			
		n	29	38	67
		Mean	6.06	6.35	6.22
		SD, SE	1.837, 0.341	1.667, 0.270	1.735, 0.212
		Median	6.00	6.78	6.44
		Q1, Q3	5.33, 7.56	5.44, 7.67	5.33, 7.56
		Min, Max	0.7, 9.0	1.7, 8.8	0.7, 9.0
		Observed			
		n	29	38	67
		Mean	5.19	5.35	5.28
		SD, SE	2.594, 0.482	2.335, 0.379	2.432, 0.297
		Median	5.78	6.22	6.00
		Q1, Q3	2.67, 7.11	3.22, 6.89	3.11, 7.00
		Min, Max	0.3, 9.0	0.0, 8.8	0.0, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-0.86	-1.00	-0.94
		SD, SE	2.105, 0.391	2.128, 0.345	2.103, 0.257
		Median	-0.44	-0.56	-0.56
		Q1, Q3	-2.33, 0.78	-2.22, 0.56	-2.22, 0.56
		Min, Max	-6.2, 3.7	-7.9, 2.8	-7.9, 3.7
		GEE Estimates			
		LS Mean (SE)	-0.23 (0.518)	-0.28 (0.382)	
		95% CI	(-1.25, 0.78)	(-1.03, 0.47)	
		LS Mean Difference (SE)		-0.04 (0.498)	
		95% CI		(-1.02, 0.93)	
		p-value		0.9281	
		HedgesG (95% CI)		-0.061 (-0.544, 0.423)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline			
		n	28	37	65
		Mean	6.00	6.29	6.16
		SD, SE	1.844, 0.348	1.648, 0.271	1.727, 0.214
		Median	5.89	6.78	6.33
		Q1, Q3	5.28, 7.28	5.44, 7.56	5.33, 7.56
		Min, Max	0.7, 9.0	1.7, 8.8	0.7, 9.0
		Observed			
		n	28	37	65
		Mean	5.83	5.47	5.62
		SD, SE	2.066, 0.390	2.264, 0.372	2.171, 0.269
		Median	5.61	5.89	5.67
		Q1, Q3	4.67, 7.33	4.00, 6.89	4.56, 7.22
		Min, Max	0.3, 9.1	0.3, 9.4	0.3, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline			
		n	28	37	65
		Mean	-0.18	-0.82	-0.54
		SD, SE	1.619, 0.306	1.910, 0.314	1.806, 0.224
		Median	0.17	-0.89	-0.22
		Q1, Q3	-0.89, 1.00	-1.67, 0.33	-1.67, 0.44
		Min, Max	-4.0, 2.9	-6.8, 2.3	-6.8, 2.9
		GEE Estimates			
		LS Mean (SE)	0.40 (0.448)	-0.12 (0.394)	
		95% CI	(-0.48, 1.28)	(-0.90, 0.65)	
		LS Mean Difference (SE)		-0.53 (0.413)	
		95% CI		(-1.34, 0.28)	
		p-value		0.2030	
		HedgesG (95% CI)		-0.348 (-0.842, 0.147)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50		N_1	42	32	74
	Baseline	n	42	32	74
		Mean	4.22	4.11	4.17
		SD, SE	1.748, 0.270	1.764, 0.312	1.744, 0.203
		Median	3.94	3.89	3.94
		Q1, Q3	2.89, 5.67	2.94, 5.22	2.89, 5.44
		Min, Max	0.7, 8.8	1.3, 8.6	0.7, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Baseline			
		n	42	32	74
		Mean	4.22	4.11	4.17
		SD, SE	1.748, 0.270	1.764, 0.312	1.744, 0.203
		Median	3.94	3.89	3.94
		Q1, Q3	2.89, 5.67	2.94, 5.22	2.89, 5.44
		Min, Max	0.7, 8.8	1.3, 8.6	0.7, 8.8
		Observed			
		n	42	32	74
		Mean	3.53	3.36	3.45
		SD, SE	2.044, 0.315	1.962, 0.347	1.997, 0.232
		Median	3.39	3.00	3.17
		Q1, Q3	1.89, 5.00	1.94, 4.83	1.89, 5.00
		Min, Max	0.3, 8.8	0.0, 8.0	0.0, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Change from Baseline			
		n	42	32	74
		Mean	-0.70	-0.75	-0.72
		SD, SE	1.348, 0.208	1.357, 0.240	1.343, 0.156
		Median	-0.50	-0.56	-0.56
		Q1, Q3	-1.56, 0.00	-1.67, 0.11	-1.56, 0.11
		Min, Max	-4.8, 2.1	-4.0, 1.6	-4.8, 2.1
		GEE Estimates			
		LS Mean (SE)	0.21 (0.331)	0.03 (0.300)	
		95% CI	(-0.44, 0.85)	(-0.56, 0.62)	
		LS Mean Difference (SE)		-0.17 (0.301)	
		95% CI		(-0.76, 0.42)	
		p-value		0.5679	
		HedgesG (95% CI)		-0.039 (-0.499, 0.421)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Baseline			
		n	42	32	74
		Mean	4.22	4.11	4.17
		SD, SE	1.748, 0.270	1.764, 0.312	1.744, 0.203
		Median	3.94	3.89	3.94
		Q1, Q3	2.89, 5.67	2.94, 5.22	2.89, 5.44
		Min, Max	0.7, 8.8	1.3, 8.6	0.7, 8.8
		Observed			
		n	42	32	74
		Mean	3.39	3.59	3.48
		SD, SE	2.042, 0.315	2.101, 0.371	2.056, 0.239
		Median	3.11	3.17	3.11
		Q1, Q3	2.00, 4.78	1.89, 5.06	2.00, 5.00
		Min, Max	0.0, 8.3	0.3, 7.8	0.0, 8.3

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Change from Baseline			
		n	42	32	74
		Mean	-0.83	-0.52	-0.70
		SD, SE	1.768, 0.273	1.692, 0.299	1.730, 0.201
		Median	-0.83	-0.61	-0.78
		Q1, Q3	-1.56, 0.00	-1.72, 0.17	-1.67, 0.11
		Min, Max	-5.1, 3.3	-3.6, 4.0	-5.1, 4.0
		GEE Estimates			
		LS Mean (SE)	0.07 (0.385)	0.26 (0.371)	
		95% CI	(-0.69, 0.83)	(-0.46, 0.99)	
		LS Mean Difference (SE)		0.19 (0.355)	
		95% CI		(-0.50, 0.89)	
		p-value		0.5882	
		HedgesG (95% CI)		0.174 (-0.286, 0.635)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50		N_1	24	35	59
	Baseline	n	24	35	59
		Mean	5.97	6.49	6.28
		SD, SE	1.755, 0.358	1.595, 0.270	1.667, 0.217
		Median	5.72	7.00	6.78
		Q1, Q3	4.72, 7.56	5.44, 7.67	5.33, 7.56
		Min, Max	2.8, 9.0	1.2, 8.8	1.2, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Baseline			
		n	24	35	59
		Mean	5.97	6.49	6.28
		SD, SE	1.755, 0.358	1.595, 0.270	1.667, 0.217
		Median	5.72	7.00	6.78
		Q1, Q3	4.72, 7.56	5.44, 7.67	5.33, 7.56
		Min, Max	2.8, 9.0	1.2, 8.8	1.2, 9.0
		Observed			
		n	24	35	59
		Mean	5.27	5.43	5.37
		SD, SE	2.382, 0.486	2.239, 0.378	2.279, 0.297
		Median	5.39	6.33	6.11
		Q1, Q3	3.39, 7.28	3.44, 6.89	3.44, 6.89
		Min, Max	1.1, 9.0	0.8, 8.8	0.8, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Change from Baseline			
		n	24	35	59
		Mean	-0.70	-1.06	-0.91
		SD, SE	2.096, 0.428	2.117, 0.358	2.098, 0.273
		Median	-0.44	-0.78	-0.67
		Q1, Q3	-2.06, 0.83	-2.22, 0.56	-2.22, 0.78
		Min, Max	-6.2, 3.7	-7.9, 2.8	-7.9, 3.7
		GEE Estimates			
		LS Mean (SE)	-0.34 (0.533)	-0.36 (0.410)	
		95% CI	(-1.38, 0.71)	(-1.16, 0.44)	
		LS Mean Difference (SE)		-0.02 (0.520)	
		95% CI		(-1.04, 1.00)	
		p-value		0.9649	
		HedgesG (95% CI)		-0.167 (-0.687, 0.354)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Baseline			
		n	23	34	57
		Mean	5.90	6.43	6.22
		SD, SE	1.756, 0.366	1.577, 0.270	1.658, 0.220
		Median	5.67	6.94	6.56
		Q1, Q3	4.44, 7.56	5.44, 7.56	5.33, 7.56
		Min, Max	2.8, 9.0	1.2, 8.8	1.2, 9.0
		Observed			
		n	23	34	57
		Mean	5.67	5.66	5.66
		SD, SE	2.162, 0.451	2.067, 0.354	2.087, 0.276
		Median	5.56	5.89	5.67
		Q1, Q3	4.56, 7.33	4.00, 6.89	4.56, 7.00
		Min, Max	0.4, 9.1	1.2, 9.4	0.4, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Change from Baseline			
		n	23	34	57
		Mean	-0.22	-0.77	-0.55
		SD, SE	1.625, 0.339	1.960, 0.336	1.837, 0.243
		Median	0.11	-0.56	-0.11
		Q1, Q3	-1.44, 1.11	-2.00, 0.33	-1.67, 0.44
		Min, Max	-4.0, 2.9	-6.8, 2.3	-6.8, 2.9
		GEE Estimates			
		LS Mean (SE)	0.06 (0.503)	-0.10 (0.402)	
		95% CI	(-0.92, 1.05)	(-0.89, 0.69)	
		LS Mean Difference (SE)		-0.16 (0.454)	
		95% CI		(-1.05, 0.73)	
		p-value		0.7228	
		HedgesG (95% CI)		-0.289 (-0.821, 0.243)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	3.92	4.11	4.01
		SD, SE	1.431, 0.235	1.743, 0.318	1.568, 0.192
		Median	3.44	4.11	3.78
		Q1, Q3	2.78, 4.44	2.78, 5.33	2.78, 5.11
		Min, Max	2.0, 7.1	1.2, 7.2	1.2, 7.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Baseline			
		n	37	30	67
		Mean	3.92	4.11	4.01
		SD, SE	1.431, 0.235	1.743, 0.318	1.568, 0.192
		Median	3.44	4.11	3.78
		Q1, Q3	2.78, 4.44	2.78, 5.33	2.78, 5.11
		Min, Max	2.0, 7.1	1.2, 7.2	1.2, 7.2
		Observed			
		n	37	30	67
		Mean	3.35	3.57	3.45
		SD, SE	1.706, 0.281	1.943, 0.355	1.805, 0.221
		Median	3.22	3.17	3.22
		Q1, Q3	2.11, 4.11	2.00, 5.44	2.00, 4.89
		Min, Max	0.7, 6.9	0.8, 6.9	0.7, 6.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-0.56	-0.54	-0.56
		SD, SE	1.179, 0.194	1.103, 0.201	1.137, 0.139
		Median	-0.44	-0.44	-0.44
		Q1, Q3	-1.44, 0.00	-1.44, 0.11	-1.44, 0.11
		Min, Max	-2.8, 2.1	-3.0, 1.6	-3.0, 2.1
		GEE Estimates			
		LS Mean (SE)	-0.11 (0.313)	-0.06 (0.321)	
		95% CI	(-0.73, 0.50)	(-0.69, 0.57)	
		LS Mean Difference (SE)		0.05 (0.277)	
		95% CI		(-0.49, 0.60)	
		p-value		0.8472	
		HedgesG (95% CI)		0.017 (-0.464, 0.499)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Baseline			
		n	37	30	67
		Mean	3.92	4.11	4.01
		SD, SE	1.431, 0.235	1.743, 0.318	1.568, 0.192
		Median	3.44	4.11	3.78
		Q1, Q3	2.78, 4.44	2.78, 5.33	2.78, 5.11
		Min, Max	2.0, 7.1	1.2, 7.2	1.2, 7.2
		Observed			
		n	37	30	67
		Mean	2.97	3.79	3.34
		SD, SE	1.714, 0.282	2.019, 0.369	1.887, 0.231
		Median	2.78	3.44	3.00
		Q1, Q3	2.00, 4.22	2.22, 5.67	2.00, 4.78
		Min, Max	0.0, 6.9	0.8, 7.6	0.0, 7.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-0.95	-0.32	-0.67
		SD, SE	1.759, 0.289	1.599, 0.292	1.706, 0.208
		Median	-1.00	-0.44	-0.67
		Q1, Q3	-1.56, -0.11	-1.22, 0.22	-1.56, 0.11
		Min, Max	-5.1, 3.3	-3.6, 4.0	-5.1, 4.0
		GEE Estimates			
		LS Mean (SE)	-0.50 (0.355)	0.16 (0.404)	
		95% CI	(-1.20, 0.20)	(-0.63, 0.95)	
		LS Mean Difference (SE)		0.66 (0.366)	
		95% CI		(-0.06, 1.38)	
		p-value		0.0710	
		HedgesG (95% CI)		0.361 (-0.124, 0.847)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	6.06	6.37	6.23
		SD, SE	1.837, 0.341	1.699, 0.276	1.753, 0.214
		Median	6.00	6.83	6.44
		Q1, Q3	5.33, 7.56	5.33, 7.67	5.33, 7.67
		Min, Max	0.7, 9.0	1.7, 8.8	0.7, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Baseline			
		n	29	38	67
		Mean	6.06	6.37	6.23
		SD, SE	1.837, 0.341	1.699, 0.276	1.753, 0.214
		Median	6.00	6.83	6.44
		Q1, Q3	5.33, 7.56	5.33, 7.67	5.33, 7.67
		Min, Max	0.7, 9.0	1.7, 8.8	0.7, 9.0
		Observed			
		n	29	38	67
		Mean	5.19	5.19	5.19
		SD, SE	2.594, 0.482	2.404, 0.390	2.469, 0.302
		Median	5.78	6.00	5.89
		Q1, Q3	2.67, 7.11	3.11, 6.89	2.67, 7.00
		Min, Max	0.3, 9.0	0.0, 8.8	0.0, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-0.86	-1.18	-1.04
		SD, SE	2.105, 0.391	2.144, 0.348	2.117, 0.259
		Median	-0.44	-0.89	-0.78
		Q1, Q3	-2.33, 0.78	-2.22, 0.44	-2.33, 0.56
		Min, Max	-6.2, 3.7	-7.9, 2.8	-7.9, 3.7
		GEE Estimates			
		LS Mean (SE)	-0.15 (0.515)	-0.37 (0.379)	
		95% CI	(-1.16, 0.86)	(-1.11, 0.37)	
		LS Mean Difference (SE)		-0.22 (0.496)	
		95% CI		(-1.20, 0.75)	
		p-value		0.6543	
		HedgesG (95% CI)		-0.142 (-0.626, 0.342)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Baseline			
		n	28	37	65
		Mean	6.00	6.31	6.18
		SD, SE	1.844, 0.348	1.682, 0.277	1.746, 0.217
		Median	5.89	6.78	6.33
		Q1, Q3	5.28, 7.28	5.33, 7.67	5.33, 7.56
		Min, Max	0.7, 9.0	1.7, 8.8	0.7, 9.0
		Observed			
		n	28	37	65
		Mean	5.83	5.39	5.58
		SD, SE	2.066, 0.390	2.299, 0.378	2.195, 0.272
		Median	5.61	5.67	5.67
		Q1, Q3	4.67, 7.33	3.89, 6.89	4.56, 7.22
		Min, Max	0.3, 9.1	0.3, 9.4	0.3, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Change from Baseline			
		n	28	37	65
		Mean	-0.18	-0.92	-0.60
		SD, SE	1.619, 0.306	1.948, 0.320	1.837, 0.228
		Median	0.17	-1.00	-0.22
		Q1, Q3	-0.89, 1.00	-2.11, 0.33	-2.00, 0.44
		Min, Max	-4.0, 2.9	-6.8, 2.3	-6.8, 2.9
		GEE Estimates			
		LS Mean (SE)	0.49 (0.447)	-0.13 (0.395)	
		95% CI	(-0.39, 1.36)	(-0.91, 0.64)	
		LS Mean Difference (SE)		-0.62 (0.415)	
		95% CI		(-1.43, 0.19)	
		p-value		0.1337	
		HedgesG (95% CI)		-0.397 (-0.892, 0.099)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes		N_1	44	47	91
	Baseline	n	44	47	91
		Mean	4.95	5.79	5.38
		SD, SE	2.014, 0.304	2.013, 0.294	2.047, 0.215
		Median	5.11	5.78	5.56
		Q1, Q3	3.00, 6.33	4.33, 7.56	3.78, 7.00
		Min, Max	0.7, 9.0	1.2, 8.8	0.7, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	44	47	91
		Mean	4.95	5.79	5.38
		SD, SE	2.014, 0.304	2.013, 0.294	2.047, 0.215
		Median	5.11	5.78	5.56
		Q1, Q3	3.00, 6.33	4.33, 7.56	3.78, 7.00
		Min, Max	0.7, 9.0	1.2, 8.8	0.7, 9.0
		Observed			
		n	44	47	91
		Mean	3.94	4.70	4.33
		SD, SE	2.324, 0.350	2.401, 0.350	2.382, 0.250
		Median	3.89	5.22	4.56
		Q1, Q3	1.61, 6.06	2.56, 6.78	2.11, 6.44
		Min, Max	0.3, 8.2	0.0, 8.8	0.0, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	44	47	91
		Mean	-1.01	-1.09	-1.05
		SD, SE	1.730, 0.261	1.766, 0.258	1.740, 0.182
		Median	-0.67	-0.67	-0.67
		Q1, Q3	-2.11, -0.06	-1.78, 0.11	-1.78, 0.00
		Min, Max	-6.2, 2.1	-7.9, 1.2	-7.9, 2.1
		GEE Estimates			
		LS Mean (SE)	-1.18 (0.400)	-1.02 (0.306)	
		95% CI	(-1.96, -0.39)	(-1.61, -0.42)	
		LS Mean Difference (SE)		0.16 (0.368)	
		95% CI		(-0.56, 0.88)	
		p-value		0.6591	
		HedgesG (95% CI)		-0.046 (-0.457, 0.365)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	43	46	89
		Mean	4.88	5.73	5.32
		SD, SE	1.994, 0.304	1.993, 0.294	2.026, 0.215
		Median	5.00	5.78	5.44
		Q1, Q3	3.00, 6.33	4.33, 7.33	3.78, 7.00
		Min, Max	0.7, 9.0	1.2, 8.8	0.7, 9.0
		Observed			
		n	43	46	89
		Mean	4.19	4.74	4.47
		SD, SE	2.194, 0.335	2.328, 0.343	2.268, 0.240
		Median	4.67	5.22	4.67
		Q1, Q3	2.56, 5.56	2.78, 6.11	2.56, 5.89
		Min, Max	0.0, 8.9	0.3, 9.4	0.0, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	43	46	89
		Mean	-0.69	-0.99	-0.85
		SD, SE	1.777, 0.271	1.767, 0.261	1.768, 0.187
		Median	-0.44	-0.89	-0.67
		Q1, Q3	-1.78, 0.44	-2.00, 0.22	-1.89, 0.22
		Min, Max	-5.1, 3.3	-6.8, 1.9	-6.8, 3.3
		GEE Estimates			
		LS Mean (SE)	-0.89 (0.403)	-0.93 (0.367)	
		95% CI	(-1.68, -0.10)	(-1.65, -0.21)	
		LS Mean Difference (SE)		-0.04 (0.362)	
		95% CI		(-0.75, 0.67)	
		p-value		0.9201	
		HedgesG (95% CI)		-0.163 (-0.580, 0.253)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No		N_1	22	21	43
	Baseline	n	22	21	43
		Mean	4.68	4.45	4.57
		SD, SE	1.788, 0.381	1.838, 0.401	1.794, 0.274
		Median	4.44	4.44	4.44
		Q1, Q3	3.22, 6.00	3.22, 5.56	3.22, 6.00
		Min, Max	2.2, 8.8	1.4, 7.3	1.4, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Baseline			
		n	22	21	43
		Mean	4.68	4.45	4.57
		SD, SE	1.788, 0.381	1.838, 0.401	1.794, 0.274
		Median	4.44	4.44	4.44
		Q1, Q3	3.22, 6.00	3.22, 5.56	3.22, 6.00
		Min, Max	2.2, 8.8	1.4, 7.3	1.4, 8.8
		Observed			
		n	22	21	43
		Mean	4.61	3.99	4.31
		SD, SE	2.282, 0.486	2.180, 0.476	2.228, 0.340
		Median	3.89	3.89	3.89
		Q1, Q3	2.89, 6.44	2.11, 5.89	2.44, 6.33
		Min, Max	0.7, 9.0	0.8, 8.6	0.7, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Change from Baseline			
		n	22	21	43
		Mean	-0.07	-0.46	-0.26
		SD, SE	1.269, 0.271	1.772, 0.387	1.529, 0.233
		Median	-0.17	-0.11	-0.11
		Q1, Q3	-1.22, 0.44	-1.67, 0.67	-1.33, 0.44
		Min, Max	-1.7, 3.7	-4.4, 2.8	-4.4, 3.7
		GEE Estimates			
		LS Mean (SE)	0.87 (0.342)	0.05 (0.342)	
		95% CI	(0.20, 1.54)	(-0.62, 0.72)	
		LS Mean Difference (SE)		-0.82 (0.415)	
		95% CI		(-1.63, -0.00)	
		p-value		0.0487	
		HedgesG (95% CI)		-0.244 (-0.844, 0.356)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Baseline			
		n	22	21	43
		Mean	4.68	4.45	4.57
		SD, SE	1.788, 0.381	1.838, 0.401	1.794, 0.274
		Median	4.44	4.44	4.44
		Q1, Q3	3.22, 6.00	3.22, 5.56	3.22, 6.00
		Min, Max	2.2, 8.8	1.4, 7.3	1.4, 8.8
		Observed			
		n	22	21	43
		Mean	4.22	4.54	4.37
		SD, SE	2.661, 0.567	2.305, 0.503	2.469, 0.377
		Median	3.78	4.44	4.22
		Q1, Q3	2.44, 6.22	2.44, 6.44	2.44, 6.44
		Min, Max	0.0, 9.1	0.8, 8.2	0.0, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Change from Baseline			
		n	22	21	43
		Mean	-0.47	0.09	-0.19
		SD, SE	1.666, 0.355	1.722, 0.376	1.696, 0.259
		Median	-0.94	0.00	-0.33
		Q1, Q3	-1.56, 0.89	-1.11, 1.11	-1.44, 1.00
		Min, Max	-3.3, 2.9	-2.4, 4.0	-3.3, 4.0
		GEE Estimates			
		LS Mean (SE)	0.47 (0.405)	0.60 (0.349)	
		95% CI	(-0.32, 1.27)	(-0.08, 1.29)	
		LS Mean Difference (SE)		0.13 (0.448)	
		95% CI		(-0.75, 1.01)	
		p-value		0.7736	
		HedgesG (95% CI)		0.315 (-0.286, 0.917)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes		N_1	13	17	30
	Baseline	n	13	17	30
		Mean	4.40	5.80	5.19
		SD, SE	1.790, 0.496	2.499, 0.606	2.295, 0.419
		Median	4.00	6.89	5.44
		Q1, Q3	2.78, 5.67	3.78, 8.11	2.89, 7.00
		Min, Max	2.7, 7.6	1.2, 8.8	1.2, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	13	17	30
		Mean	4.40	5.80	5.19
		SD, SE	1.790, 0.496	2.499, 0.606	2.295, 0.419
		Median	4.00	6.89	5.44
		Q1, Q3	2.78, 5.67	3.78, 8.11	2.89, 7.00
		Min, Max	2.7, 7.6	1.2, 8.8	1.2, 8.8
		Observed			
		n	13	17	30
		Mean	3.24	4.42	3.91
		SD, SE	2.259, 0.627	2.685, 0.651	2.539, 0.464
		Median	2.44	4.89	3.67
		Q1, Q3	1.33, 4.56	1.56, 6.33	1.44, 6.33
		Min, Max	0.9, 7.9	0.8, 8.2	0.8, 8.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	13	17	30
		Mean	-1.16	-1.37	-1.28
		SD, SE	2.046, 0.567	2.097, 0.509	2.042, 0.373
		Median	-1.11	-0.56	-0.83
		Q1, Q3	-1.89, 0.78	-2.22, -0.44	-2.22, -0.11
		Min, Max	-6.2, 1.1	-7.9, 1.2	-7.9, 1.2
		GEE Estimates			
		LS Mean (SE)	-1.23 (0.485)	-0.97 (0.442)	
		95% CI	(-2.19, -0.28)	(-1.83, -0.10)	
		LS Mean Difference (SE)		0.27 (0.586)	
		95% CI		(-0.88, 1.42)	
		p-value		0.6464	
		HedgesG (95% CI)		-0.095 (-0.818, 0.627)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	13	16	29
		Mean	4.40	5.63	5.08
		SD, SE	1.790, 0.496	2.474, 0.619	2.244, 0.417
		Median	4.00	6.17	5.44
		Q1, Q3	2.78, 5.67	3.72, 7.56	2.89, 7.00
		Min, Max	2.7, 7.6	1.2, 8.8	1.2, 8.8
		Observed			
		n	13	16	29
		Mean	3.21	4.94	4.17
		SD, SE	2.046, 0.567	2.534, 0.634	2.450, 0.455
		Median	2.56	5.39	3.67
		Q1, Q3	2.00, 5.11	2.67, 6.61	2.00, 5.67
		Min, Max	0.0, 7.3	1.2, 8.7	0.0, 8.7

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	13	16	29
		Mean	-1.19	-0.68	-0.91
		SD, SE	1.607, 0.446	2.064, 0.516	1.858, 0.345
		Median	-1.00	-0.22	-0.56
		Q1, Q3	-2.00, -0.22	-1.22, 0.22	-1.67, 0.11
		Min, Max	-5.0, 1.1	-6.8, 1.9	-6.8, 1.9
		GEE Estimates			
		LS Mean (SE)	-1.26 (0.395)	-0.32 (0.438)	
		95% CI	(-2.03, -0.49)	(-1.18, 0.54)	
		LS Mean Difference (SE)		0.94 (0.504)	
		95% CI		(-0.05, 1.93)	
		p-value		0.0625	
		HedgesG (95% CI)		0.254 (-0.481, 0.989)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No		N_1	53	51	104
	Baseline	n	53	51	104
		Mean	4.97	5.23	5.10
		SD, SE	1.965, 0.270	1.876, 0.263	1.917, 0.188
		Median	5.00	5.33	5.17
		Q1, Q3	3.33, 6.33	4.00, 6.89	3.56, 6.61
		Min, Max	0.7, 9.0	1.3, 8.3	0.7, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Baseline			
		n	53	51	104
		Mean	4.97	5.23	5.10
		SD, SE	1.965, 0.270	1.876, 0.263	1.917, 0.188
		Median	5.00	5.33	5.17
		Q1, Q3	3.33, 6.33	4.00, 6.89	3.56, 6.61
		Min, Max	0.7, 9.0	1.3, 8.3	0.7, 9.0
		Observed			
		n	53	51	104
		Mean	4.39	4.49	4.44
		SD, SE	2.292, 0.315	2.245, 0.314	2.259, 0.221
		Median	4.11	4.56	4.22
		Q1, Q3	2.56, 6.44	2.56, 6.44	2.56, 6.44
		Min, Max	0.3, 9.0	0.0, 8.8	0.0, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Change from Baseline			
		n	53	51	104
		Mean	-0.58	-0.74	-0.66
		SD, SE	1.530, 0.210	1.653, 0.231	1.586, 0.155
		Median	-0.44	-0.67	-0.44
		Q1, Q3	-1.44, 0.33	-1.67, 0.56	-1.50, 0.39
		Min, Max	-4.8, 3.7	-4.4, 2.8	-4.8, 3.7
		GEE Estimates			
		LS Mean (SE)	-0.03 (0.293)	-0.16 (0.265)	
		95% CI	(-0.61, 0.54)	(-0.68, 0.36)	
		LS Mean Difference (SE)		-0.13 (0.300)	
		95% CI		(-0.72, 0.46)	
		p-value		0.6697	
		HedgesG (95% CI)		-0.097 (-0.481, 0.288)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Baseline			
		n	52	51	103
		Mean	4.92	5.23	5.07
		SD, SE	1.947, 0.270	1.876, 0.263	1.910, 0.188
		Median	4.89	5.33	5.11
		Q1, Q3	3.33, 6.28	4.00, 6.89	3.56, 6.56
		Min, Max	0.7, 9.0	1.3, 8.3	0.7, 9.0
		Observed			
		n	52	51	103
		Mean	4.45	4.59	4.52
		SD, SE	2.363, 0.328	2.249, 0.315	2.297, 0.226
		Median	4.61	5.00	4.67
		Q1, Q3	2.67, 6.00	2.56, 6.33	2.56, 6.22
		Min, Max	0.0, 9.1	0.3, 9.4	0.0, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Change from Baseline			
		n	52	51	103
		Mean	-0.47	-0.64	-0.56
		SD, SE	1.745, 0.242	1.747, 0.245	1.740, 0.171
		Median	-0.50	-0.67	-0.56
		Q1, Q3	-1.44, 0.61	-2.00, 0.33	-1.67, 0.44
		Min, Max	-5.1, 3.3	-4.3, 4.0	-5.1, 4.0
		GEE Estimates			
		LS Mean (SE)	0.05 (0.323)	-0.06 (0.286)	
		95% CI	(-0.58, 0.68)	(-0.62, 0.50)	
		LS Mean Difference (SE)		-0.11 (0.323)	
		95% CI		(-0.75, 0.52)	
		p-value		0.7251	
		HedgesG (95% CI)		-0.094 (-0.481, 0.292)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes		N_1	38	32	70
	Baseline	n	38	32	70
		Mean	5.27	5.19	5.23
		SD, SE	1.940, 0.315	1.885, 0.333	1.902, 0.227
		Median	5.33	5.11	5.33
		Q1, Q3	3.33, 6.56	3.72, 6.78	3.67, 6.56
		Min, Max	2.1, 9.0	1.4, 8.6	1.4, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Baseline			
		n	38	32	70
		Mean	5.27	5.19	5.23
		SD, SE	1.940, 0.315	1.885, 0.333	1.902, 0.227
		Median	5.33	5.11	5.33
		Q1, Q3	3.33, 6.56	3.72, 6.78	3.67, 6.56
		Min, Max	2.1, 9.0	1.4, 8.6	1.4, 9.0
		Observed			
		n	38	32	70
		Mean	4.46	4.12	4.31
		SD, SE	2.349, 0.381	2.363, 0.418	2.345, 0.280
		Median	4.22	4.17	4.22
		Q1, Q3	2.44, 6.44	1.94, 6.33	2.11, 6.33
		Min, Max	1.1, 9.0	0.0, 8.6	0.0, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Change from Baseline			
		n	38	32	70
		Mean	-0.81	-1.07	-0.93
		SD, SE	1.800, 0.292	1.803, 0.319	1.793, 0.214
		Median	-0.67	-1.17	-0.78
		Q1, Q3	-1.56, 0.33	-2.11, 0.39	-1.78, 0.33
		Min, Max	-6.2, 3.7	-4.4, 2.8	-6.2, 3.7
		GEE Estimates			
		LS Mean (SE)	0.13 (0.378)	-0.15 (0.321)	
		95% CI	(-0.61, 0.87)	(-0.78, 0.48)	
		LS Mean Difference (SE)		-0.28 (0.394)	
		95% CI		(-1.06, 0.49)	
		p-value		0.4693	
		HedgesG (95% CI)		-0.140 (-0.611, 0.331)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Baseline			
		n	37	31	68
		Mean	5.21	5.08	5.15
		SD, SE	1.924, 0.316	1.812, 0.325	1.861, 0.226
		Median	5.33	5.11	5.22
		Q1, Q3	3.33, 6.33	3.67, 6.44	3.61, 6.39
		Min, Max	2.1, 9.0	1.4, 8.3	1.4, 9.0
		Observed			
		n	37	31	68
		Mean	4.52	4.35	4.45
		SD, SE	2.152, 0.354	2.162, 0.388	2.142, 0.260
		Median	4.67	5.00	4.67
		Q1, Q3	2.78, 6.22	2.44, 5.89	2.67, 6.06
		Min, Max	0.0, 8.9	0.3, 8.2	0.0, 8.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Change from Baseline			
		n	37	31	68
		Mean	-0.68	-0.72	-0.70
		SD, SE	1.595, 0.262	1.777, 0.319	1.668, 0.202
		Median	-0.67	-0.44	-0.61
		Q1, Q3	-1.44, 0.22	-2.11, 0.22	-1.72, 0.22
		Min, Max	-4.0, 3.3	-4.3, 4.0	-4.3, 4.0
		GEE Estimates			
		LS Mean (SE)	0.22 (0.381)	0.16 (0.335)	
		95% CI	(-0.53, 0.97)	(-0.49, 0.82)	
		LS Mean Difference (SE)		-0.06 (0.360)	
		95% CI		(-0.76, 0.65)	
		p-value		0.8693	
		HedgesG (95% CI)		-0.023 (-0.500, 0.454)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No		N_1	28	36	64
	Baseline	n	28	36	64
		Mean	4.30	5.54	5.00
		SD, SE	1.807, 0.341	2.189, 0.365	2.109, 0.264
		Median	4.06	5.83	5.11
		Q1, Q3	2.83, 5.83	4.28, 7.06	3.39, 6.89
		Min, Max	0.7, 7.7	1.2, 8.8	0.7, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Baseline			
		n	28	36	64
		Mean	4.30	5.54	5.00
		SD, SE	1.807, 0.341	2.189, 0.365	2.109, 0.264
		Median	4.06	5.83	5.11
		Q1, Q3	2.83, 5.83	4.28, 7.06	3.39, 6.89
		Min, Max	0.7, 7.7	1.2, 8.8	0.7, 8.8
		Observed			
		n	28	36	64
		Mean	3.75	4.79	4.34
		SD, SE	2.243, 0.424	2.310, 0.385	2.322, 0.290
		Median	3.39	5.17	4.00
		Q1, Q3	2.00, 5.61	2.72, 6.78	2.50, 6.50
		Min, Max	0.3, 7.9	0.8, 8.8	0.3, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Change from Baseline			
		n	28	36	64
		Mean	-0.55	-0.75	-0.66
		SD, SE	1.421, 0.269	1.769, 0.295	1.617, 0.202
		Median	-0.33	-0.44	-0.33
		Q1, Q3	-1.61, 0.33	-1.11, 0.22	-1.33, 0.28
		Min, Max	-3.1, 2.1	-7.9, 1.6	-7.9, 2.1
		GEE Estimates			
		LS Mean (SE)	-0.38 (0.317)	-0.37 (0.335)	
		95% CI	(-1.00, 0.24)	(-1.03, 0.29)	
		LS Mean Difference (SE)		0.01 (0.341)	
		95% CI		(-0.66, 0.68)	
		p-value		0.9735	
		HedgesG (95% CI)		-0.120 (-0.614, 0.375)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Baseline			
		n	28	36	64
		Mean	4.30	5.54	5.00
		SD, SE	1.807, 0.341	2.189, 0.365	2.109, 0.264
		Median	4.06	5.83	5.11
		Q1, Q3	2.83, 5.83	4.28, 7.06	3.39, 6.89
		Min, Max	0.7, 7.7	1.2, 8.8	0.7, 8.8
		Observed			
		n	28	36	64
		Mean	3.77	4.95	4.44
		SD, SE	2.547, 0.481	2.418, 0.403	2.525, 0.316
		Median	3.28	5.44	4.50
		Q1, Q3	2.00, 5.44	2.78, 6.67	2.28, 6.06
		Min, Max	0.0, 9.1	0.8, 9.4	0.0, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-0.53	-0.59	-0.56
		SD, SE	1.921, 0.363	1.863, 0.310	1.873, 0.234
		Median	-0.39	-0.67	-0.50
		Q1, Q3	-1.67, 1.17	-1.67, 0.39	-1.67, 0.78
		Min, Max	-5.1, 2.3	-6.8, 3.1	-6.8, 3.1
		GEE Estimates			
		LS Mean (SE)	-0.36 (0.375)	-0.21 (0.346)	
		95% CI	(-1.10, 0.38)	(-0.89, 0.47)	
		LS Mean Difference (SE)		0.15 (0.434)	
		95% CI		(-0.70, 1.00)	
		p-value		0.7285	
		HedgesG (95% CI)		-0.031 (-0.525, 0.463)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High		N_1	29	37	66
	Baseline	n	29	37	66
		Mean	5.36	5.81	5.61
		SD, SE	2.168, 0.403	1.830, 0.301	1.982, 0.244
		Median	5.33	5.78	5.56
		Q1, Q3	3.33, 7.00	4.44, 7.00	4.00, 7.00
		Min, Max	0.7, 9.0	1.2, 8.8	0.7, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Baseline			
		n	29	37	66
		Mean	5.36	5.81	5.61
		SD, SE	2.168, 0.403	1.830, 0.301	1.982, 0.244
		Median	5.33	5.78	5.56
		Q1, Q3	3.33, 7.00	4.44, 7.00	4.00, 7.00
		Min, Max	0.7, 9.0	1.2, 8.8	0.7, 9.0
		Observed			
		n	29	37	66
		Mean	4.82	4.73	4.77
		SD, SE	2.541, 0.472	2.405, 0.395	2.447, 0.301
		Median	4.89	5.11	5.00
		Q1, Q3	2.44, 6.89	2.67, 6.33	2.56, 6.44
		Min, Max	0.3, 9.0	0.0, 8.8	0.0, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Change from Baseline			
		n	29	37	66
		Mean	-0.54	-1.08	-0.84
		SD, SE	1.643, 0.305	2.009, 0.330	1.863, 0.229
		Median	-0.44	-0.67	-0.56
		Q1, Q3	-1.44, 0.44	-1.89, 0.56	-1.78, 0.56
		Min, Max	-3.7, 3.7	-7.9, 1.4	-7.9, 3.7
		GEE Estimates			
		LS Mean (SE)	0.10 (0.369)	-0.45 (0.330)	
		95% CI	(-0.62, 0.82)	(-1.09, 0.20)	
		LS Mean Difference (SE)		-0.55 (0.421)	
		95% CI		(-1.37, 0.28)	
		p-value		0.1947	
		HedgesG (95% CI)		-0.284 (-0.772, 0.205)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Baseline			
		n	28	36	64
		Mean	5.28	5.73	5.53
		SD, SE	2.161, 0.408	1.795, 0.299	1.961, 0.245
		Median	5.33	5.72	5.50
		Q1, Q3	3.28, 6.94	4.39, 7.00	4.00, 7.00
		Min, Max	0.7, 9.0	1.2, 8.8	0.7, 9.0
		Observed			
		n	28	36	64
		Mean	4.80	5.20	5.02
		SD, SE	2.312, 0.437	2.285, 0.381	2.287, 0.286
		Median	4.72	5.22	5.17
		Q1, Q3	2.83, 6.50	3.72, 6.61	3.50, 6.50
		Min, Max	0.3, 8.9	0.3, 9.4	0.3, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-0.48	-0.53	-0.51
		SD, SE	1.541, 0.291	2.048, 0.341	1.830, 0.229
		Median	-0.17	-0.06	-0.11
		Q1, Q3	-1.11, 0.39	-1.44, 0.89	-1.39, 0.44
		Min, Max	-4.0, 2.9	-6.8, 4.0	-6.8, 4.0
		GEE Estimates			
		LS Mean (SE)	0.09 (0.377)	0.07 (0.321)	
		95% CI	(-0.65, 0.83)	(-0.56, 0.70)	
		LS Mean Difference (SE)		-0.02 (0.408)	
		95% CI		(-0.82, 0.78)	
		p-value		0.9628	
		HedgesG (95% CI)		-0.028 (-0.522, 0.466)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low		N_1	36	30	66
	Baseline	n	36	30	66
		Mean	4.38	4.79	4.57
		SD, SE	1.578, 0.263	2.200, 0.402	1.883, 0.232
		Median	4.28	4.56	4.44
		Q1, Q3	2.94, 5.72	3.11, 7.11	3.00, 6.00
		Min, Max	2.0, 7.6	1.3, 8.6	1.3, 8.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Baseline			
		n	36	30	66
		Mean	4.38	4.79	4.57
		SD, SE	1.578, 0.263	2.200, 0.402	1.883, 0.232
		Median	4.28	4.56	4.44
		Q1, Q3	2.94, 5.72	3.11, 7.11	3.00, 6.00
		Min, Max	2.0, 7.6	1.3, 8.6	1.3, 8.6
		Observed			
		n	36	30	66
		Mean	3.53	4.09	3.78
		SD, SE	1.902, 0.317	2.248, 0.410	2.069, 0.255
		Median	3.17	3.67	3.33
		Q1, Q3	2.00, 4.78	2.00, 6.44	2.00, 6.11
		Min, Max	0.7, 6.9	0.8, 8.0	0.7, 8.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Change from Baseline			
		n	36	30	66
		Mean	-0.85	-0.71	-0.78
		SD, SE	1.670, 0.278	1.479, 0.270	1.576, 0.194
		Median	-0.61	-0.61	-0.61
		Q1, Q3	-1.61, 0.28	-1.44, 0.11	-1.56, 0.11
		Min, Max	-6.2, 1.7	-4.2, 2.8	-6.2, 2.8
		GEE Estimates			
		LS Mean (SE)	0.04 (0.246)	0.12 (0.281)	
		95% CI	(-0.45, 0.52)	(-0.43, 0.67)	
		LS Mean Difference (SE)		0.09 (0.343)	
		95% CI		(-0.59, 0.76)	
		p-value		0.8019	
		HedgesG (95% CI)		0.087 (-0.398, 0.571)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Baseline			
		n	36	30	66
		Mean	4.38	4.79	4.57
		SD, SE	1.578, 0.263	2.200, 0.402	1.883, 0.232
		Median	4.28	4.56	4.44
		Q1, Q3	2.94, 5.72	3.11, 7.11	3.00, 6.00
		Min, Max	2.0, 7.6	1.3, 8.6	1.3, 8.6
		Observed			
		n	36	30	66
		Mean	3.60	4.00	3.78
		SD, SE	2.134, 0.356	2.218, 0.405	2.165, 0.267
		Median	3.28	3.44	3.33
		Q1, Q3	2.06, 5.11	2.22, 6.00	2.11, 5.56
		Min, Max	0.0, 8.3	0.8, 7.8	0.0, 8.3

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.2.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Global Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Change from Baseline			
		n	36	30	66
		Mean	-0.78	-0.79	-0.78
		SD, SE	1.867, 0.311	1.539, 0.281	1.713, 0.211
		Median	-0.94	-0.89	-0.89
		Q1, Q3	-1.78, 0.61	-1.89, 0.11	-1.89, 0.11
		Min, Max	-5.1, 3.3	-3.6, 3.1	-5.1, 3.3
		GEE Estimates			
		LS Mean (SE)	0.11 (0.294)	0.04 (0.324)	
		95% CI	(-0.47, 0.68)	(-0.59, 0.68)	
		LS Mean Difference (SE)		-0.07 (0.362)	
		95% CI		(-0.78, 0.64)	
		p-value		0.8544	
		HedgesG (95% CI)		-0.006 (-0.491, 0.478)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Global Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Global Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_gf_SUB.sas

Table 2.2.3.3.1.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6		N_1	27	17	44
	Baseline	n	27	17	44
		Mean	5.67	5.35	5.55
		SD, SE	1.209, 0.233	1.220, 0.296	1.209, 0.182
		Median	5.63	5.13	5.56
		Q1, Q3	5.00, 6.63	4.38, 6.25	4.87, 6.39
		Min, Max	3.6, 7.8	3.4, 7.5	3.4, 7.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Baseline			
		n	27	17	44
		Mean	5.67	5.35	5.55
		SD, SE	1.209, 0.233	1.220, 0.296	1.209, 0.182
		Median	5.63	5.13	5.56
		Q1, Q3	5.00, 6.63	4.38, 6.25	4.87, 6.39
		Min, Max	3.6, 7.8	3.4, 7.5	3.4, 7.8
		Observed			
		n	27	17	44
		Mean	5.33	4.52	5.02
		SD, SE	1.798, 0.346	1.520, 0.369	1.726, 0.260
		Median	5.38	4.25	4.81
		Q1, Q3	3.88, 6.38	3.63, 5.75	3.75, 5.94
		Min, Max	2.3, 9.1	2.3, 8.0	2.3, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Change from Baseline			
		n	27	17	44
		Mean	-0.34	-0.84	-0.53
		SD, SE	1.954, 0.376	1.731, 0.420	1.867, 0.281
		Median	-0.13	-0.38	-0.13
		Q1, Q3	-1.75, 1.00	-2.00, 0.38	-2.00, 0.75
		Min, Max	-3.9, 4.8	-4.0, 2.8	-4.0, 4.8
		GEE Estimates			
		LS Mean (SE)	0.90 (0.608)	0.20 (0.659)	
		95% CI	(-0.29, 2.10)	(-1.09, 1.49)	
		LS Mean Difference (SE)		-0.71 (0.505)	
		95% CI		(-1.70, 0.28)	
		p-value		0.1616	
		HedgesG (95% CI)		-0.257 (-0.866, 0.352)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Baseline			
		n	27	17	44
		Mean	5.67	5.35	5.55
		SD, SE	1.209, 0.233	1.220, 0.296	1.209, 0.182
		Median	5.63	5.13	5.56
		Q1, Q3	5.00, 6.63	4.38, 6.25	4.87, 6.39
		Min, Max	3.6, 7.8	3.4, 7.5	3.4, 7.8
		Observed			
		n	27	17	44
		Mean	5.23	4.42	4.92
		SD, SE	1.946, 0.375	1.710, 0.415	1.880, 0.283
		Median	5.50	4.13	4.63
		Q1, Q3	4.25, 6.25	3.25, 5.50	3.63, 6.13
		Min, Max	1.0, 8.6	1.2, 8.1	1.0, 8.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Change from Baseline			
		n	27	17	44
		Mean	-0.44	-0.93	-0.63
		SD, SE	2.229, 0.429	1.881, 0.456	2.093, 0.315
		Median	-0.63	-0.88	-0.69
		Q1, Q3	-1.50, 0.25	-1.75, 0.13	-1.69, 0.19
		Min, Max	-6.4, 4.5	-4.8, 3.0	-6.4, 4.5
		GEE Estimates			
		LS Mean (SE)	0.80 (0.549)	0.10 (0.636)	
		95% CI	(-0.28, 1.87)	(-1.14, 1.35)	
		LS Mean Difference (SE)		-0.69 (0.538)	
		95% CI		(-1.75, 0.36)	
		p-value		0.1961	
		HedgesG (95% CI)		-0.223 (-0.832, 0.385)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6		N_1	39	51	90
	Baseline	n	39	51	90
		Mean	7.48	7.46	7.47
		SD, SE	1.267, 0.203	1.438, 0.201	1.359, 0.143
		Median	7.50	7.88	7.60
		Q1, Q3	6.88, 8.13	6.86, 8.50	6.88, 8.50
		Min, Max	4.6, 9.9	2.8, 9.8	2.8, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Baseline			
		n	39	51	90
		Mean	7.48	7.46	7.47
		SD, SE	1.267, 0.203	1.438, 0.201	1.359, 0.143
		Median	7.50	7.88	7.60
		Q1, Q3	6.88, 8.13	6.86, 8.50	6.88, 8.50
		Min, Max	4.6, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	39	51	90
		Mean	6.44	6.78	6.63
		SD, SE	1.790, 0.287	1.829, 0.256	1.810, 0.191
		Median	6.50	7.25	7.25
		Q1, Q3	5.25, 7.75	6.13, 8.00	5.75, 7.88
		Min, Max	2.3, 9.5	0.9, 9.5	0.9, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Change from Baseline			
		n	39	51	90
		Mean	-1.04	-0.68	-0.84
		SD, SE	1.494, 0.239	1.569, 0.220	1.539, 0.162
		Median	-1.13	-0.38	-0.38
		Q1, Q3	-1.82, 0.13	-1.00, 0.00	-1.50, 0.00
		Min, Max	-4.0, 1.9	-7.5, 1.1	-7.5, 1.9
		GEE Estimates			
		LS Mean (SE)	-0.60 (0.302)	-0.27 (0.239)	
		95% CI	(-1.19, -0.01)	(-0.74, 0.19)	
		LS Mean Difference (SE)		0.33 (0.312)	
		95% CI		(-0.28, 0.94)	
		p-value		0.2907	
		HedgesG (95% CI)		0.231 (-0.188, 0.649)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Baseline			
		n	38	50	88
		Mean	7.47	7.45	7.46
		SD, SE	1.283, 0.208	1.450, 0.205	1.373, 0.146
		Median	7.50	7.75	7.54
		Q1, Q3	6.88, 8.13	6.86, 8.50	6.87, 8.50
		Min, Max	4.6, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	38	50	88
		Mean	6.67	6.52	6.59
		SD, SE	1.838, 0.298	2.091, 0.296	1.976, 0.211
		Median	7.13	7.00	7.06
		Q1, Q3	5.00, 7.83	5.50, 8.00	5.50, 7.94
		Min, Max	1.8, 10.0	0.0, 9.4	0.0, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.1
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Change from Baseline			
		n	38	50	88
		Mean	-0.81	-0.93	-0.88
		SD, SE	1.694, 0.275	1.841, 0.260	1.770, 0.189
		Median	-0.63	-0.50	-0.50
		Q1, Q3	-2.04, 0.25	-1.63, 0.25	-1.88, 0.25
		Min, Max	-4.5, 2.8	-7.0, 2.5	-7.0, 2.8
		GEE Estimates			
		LS Mean (SE)	-0.40 (0.324)	-0.52 (0.278)	
		95% CI	(-1.03, 0.24)	(-1.06, 0.03)	
		LS Mean Difference (SE)		-0.12 (0.355)	
		95% CI		(-0.81, 0.58)	
		p-value		0.7420	
		HedgesG (95% CI)		-0.070 (-0.491, 0.352)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6		N_1	49	48	97
	Baseline	n	49	48	97
		Mean	6.27	6.36	6.31
		SD, SE	1.300, 0.186	1.608, 0.232	1.453, 0.148
		Median	6.38	6.63	6.63
		Q1, Q3	5.38, 7.38	5.06, 7.50	5.13, 7.38
		Min, Max	3.6, 8.1	2.8, 9.0	2.8, 9.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Baseline			
		n	49	48	97
		Mean	6.27	6.36	6.31
		SD, SE	1.300, 0.186	1.608, 0.232	1.453, 0.148
		Median	6.38	6.63	6.63
		Q1, Q3	5.38, 7.38	5.06, 7.50	5.13, 7.38
		Min, Max	3.6, 8.1	2.8, 9.0	2.8, 9.0
		Observed			
		n	49	48	97
		Mean	5.62	5.72	5.67
		SD, SE	1.704, 0.243	1.934, 0.279	1.813, 0.184
		Median	5.75	5.94	5.75
		Q1, Q3	4.25, 7.13	4.13, 7.50	4.25, 7.25
		Min, Max	2.3, 9.1	0.9, 8.5	0.9, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Change from Baseline			
		n	49	48	97
		Mean	-0.65	-0.63	-0.64
		SD, SE	1.739, 0.248	1.545, 0.223	1.637, 0.166
		Median	-0.38	-0.25	-0.25
		Q1, Q3	-1.75, 0.50	-1.50, 0.31	-1.75, 0.38
		Min, Max	-3.9, 4.8	-6.1, 2.8	-6.1, 4.8
		GEE Estimates			
		LS Mean (SE)	-0.51 (0.272)	-0.46 (0.292)	
		95% CI	(-1.04, 0.02)	(-1.03, 0.11)	
		LS Mean Difference (SE)		0.05 (0.309)	
		95% CI		(-0.56, 0.65)	
		p-value		0.8758	
		HedgesG (95% CI)		0.010 (-0.388, 0.408)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Baseline			
		n	49	48	97
		Mean	6.27	6.36	6.31
		SD, SE	1.300, 0.186	1.608, 0.232	1.453, 0.148
		Median	6.38	6.63	6.63
		Q1, Q3	5.38, 7.38	5.06, 7.50	5.13, 7.38
		Min, Max	3.6, 8.1	2.8, 9.0	2.8, 9.0
		Observed			
		n	49	48	97
		Mean	5.70	5.54	5.62
		SD, SE	1.829, 0.261	2.145, 0.310	1.983, 0.201
		Median	5.63	5.94	5.75
		Q1, Q3	4.25, 7.25	3.63, 7.44	4.25, 7.25
		Min, Max	1.0, 9.1	0.0, 9.0	0.0, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Change from Baseline			
		n	49	48	97
		Mean	-0.57	-0.82	-0.69
		SD, SE	1.880, 0.269	1.779, 0.257	1.826, 0.185
		Median	-0.63	-0.50	-0.50
		Q1, Q3	-1.25, 0.25	-1.69, 0.19	-1.38, 0.25
		Min, Max	-6.4, 4.5	-7.0, 3.0	-7.0, 4.5
		GEE Estimates			
		LS Mean (SE)	-0.42 (0.285)	-0.64 (0.317)	
		95% CI	(-0.98, 0.13)	(-1.26, -0.02)	
		LS Mean Difference (SE)		-0.22 (0.351)	
		95% CI		(-0.91, 0.47)	
		p-value		0.5346	
		HedgesG (95% CI)		-0.134 (-0.532, 0.264)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6		N_1	17	20	37
	Baseline	n	17	20	37
		Mean	8.10	8.33	8.23
		SD, SE	1.322, 0.321	0.625, 0.140	0.998, 0.164
		Median	8.50	8.44	8.50
		Q1, Q3	7.13, 9.13	7.94, 8.63	7.63, 8.75
		Min, Max	5.4, 9.9	7.0, 9.8	5.4, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Baseline			
		n	17	20	37
		Mean	8.10	8.33	8.23
		SD, SE	1.322, 0.321	0.625, 0.140	0.998, 0.164
		Median	8.50	8.44	8.50
		Q1, Q3	7.13, 9.13	7.94, 8.63	7.63, 8.75
		Min, Max	5.4, 9.9	7.0, 9.8	5.4, 9.9
		Observed			
		n	17	20	37
		Mean	7.05	7.41	7.24
		SD, SE	1.938, 0.470	1.685, 0.377	1.789, 0.294
		Median	7.63	7.93	7.63
		Q1, Q3	5.75, 8.63	7.19, 8.19	6.88, 8.25
		Min, Max	2.3, 9.5	1.1, 9.5	1.1, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Change from Baseline			
		n	17	20	37
		Mean	-1.05	-0.93	-0.98
		SD, SE	1.673, 0.406	1.746, 0.391	1.690, 0.278
		Median	-1.13	-0.38	-0.63
		Q1, Q3	-2.00, -0.13	-1.19, -0.25	-1.50, -0.25
		Min, Max	-4.0, 1.9	-7.5, 1.0	-7.5, 1.9
		GEE Estimates			
		LS Mean (SE)	-1.11 (0.427)	-0.90 (0.190)	
		95% CI	(-1.95, -0.27)	(-1.27, -0.52)	
		LS Mean Difference (SE)		0.21 (0.527)	
		95% CI		(-0.82, 1.25)	
		p-value		0.6838	
		HedgesG (95% CI)		0.069 (-0.578, 0.716)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Baseline			
		n	16	19	35
		Mean	8.12	8.35	8.25
		SD, SE	1.363, 0.341	0.637, 0.146	1.023, 0.173
		Median	8.56	8.50	8.50
		Q1, Q3	7.06, 9.15	7.88, 8.63	7.50, 8.88
		Min, Max	5.4, 9.9	7.0, 9.8	5.4, 9.9
		Observed			
		n	16	19	35
		Mean	7.20	7.12	7.16
		SD, SE	2.141, 0.535	1.924, 0.441	1.996, 0.337
		Median	7.44	7.75	7.75
		Q1, Q3	6.19, 8.75	5.88, 8.13	6.00, 8.75
		Min, Max	1.8, 10.0	1.9, 9.4	1.8, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.2
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Change from Baseline			
		n	16	19	35
		Mean	-0.93	-1.23	-1.09
		SD, SE	2.101, 0.525	1.994, 0.457	2.018, 0.341
		Median	-1.31	-0.50	-0.75
		Q1, Q3	-2.25, 0.69	-2.50, 0.25	-2.25, 0.25
		Min, Max	-4.5, 2.8	-6.8, 0.6	-6.8, 2.8
		GEE Estimates			
		LS Mean (SE)	-1.07 (0.466)	-1.15 (0.232)	
		95% CI	(-1.99, -0.16)	(-1.60, -0.69)	
		LS Mean Difference (SE)		-0.08 (0.611)	
		95% CI		(-1.27, 1.12)	
		p-value		0.9021	
		HedgesG (95% CI)		-0.138 (-0.804, 0.527)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU		N_1	58	58	116
	Baseline	n	58	58	116
		Mean	6.79	7.11	6.95
		SD, SE	1.536, 0.202	1.587, 0.208	1.563, 0.145
		Median	7.06	7.44	7.13
		Q1, Q3	5.63, 7.75	6.38, 8.38	5.81, 8.13
		Min, Max	3.6, 9.9	2.8, 9.8	2.8, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Baseline			
		n	58	58	116
		Mean	6.79	7.11	6.95
		SD, SE	1.536, 0.202	1.587, 0.208	1.563, 0.145
		Median	7.06	7.44	7.13
		Q1, Q3	5.63, 7.75	6.38, 8.38	5.81, 8.13
		Min, Max	3.6, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	58	58	116
		Mean	5.99	6.30	6.14
		SD, SE	1.848, 0.243	2.018, 0.265	1.932, 0.179
		Median	6.00	6.94	6.31
		Q1, Q3	4.88, 7.40	4.75, 8.00	4.75, 7.69
		Min, Max	2.3, 9.5	0.9, 9.5	0.9, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Change from Baseline			
		n	58	58	116
		Mean	-0.80	-0.81	-0.81
		SD, SE	1.767, 0.232	1.641, 0.215	1.698, 0.158
		Median	-0.81	-0.38	-0.38
		Q1, Q3	-1.75, 0.38	-1.38, 0.00	-1.75, 0.13
		Min, Max	-4.0, 4.8	-7.5, 2.8	-7.5, 4.8
		GEE Estimates			
		LS Mean (SE)	-0.76 (0.235)	-0.65 (0.229)	
		95% CI	(-1.22, -0.30)	(-1.10, -0.20)	
		LS Mean Difference (SE)		0.11 (0.292)	
		95% CI		(-0.46, 0.69)	
		p-value		0.6975	
		HedgesG (95% CI)		-0.008 (-0.372, 0.356)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Baseline			
		n	57	57	114
		Mean	6.77	7.09	6.93
		SD, SE	1.545, 0.205	1.596, 0.211	1.572, 0.147
		Median	7.00	7.38	7.13
		Q1, Q3	5.63, 7.75	6.38, 8.38	5.75, 8.13
		Min, Max	3.6, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	57	57	114
		Mean	6.15	6.04	6.10
		SD, SE	1.992, 0.264	2.195, 0.291	2.087, 0.195
		Median	6.25	6.38	6.31
		Q1, Q3	4.63, 7.63	4.50, 7.88	4.63, 7.83
		Min, Max	1.0, 10.0	0.0, 9.4	0.0, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Change from Baseline			
		n	57	57	114
		Mean	-0.62	-1.05	-0.83
		SD, SE	2.018, 0.267	1.868, 0.247	1.947, 0.182
		Median	-0.63	-0.50	-0.56
		Q1, Q3	-1.88, 0.25	-1.75, 0.13	-1.88, 0.25
		Min, Max	-6.4, 4.5	-7.0, 3.0	-7.0, 4.5
		GEE Estimates			
		LS Mean (SE)	-0.61 (0.266)	-0.88 (0.257)	
		95% CI	(-1.13, -0.09)	(-1.38, -0.37)	
		LS Mean Difference (SE)		-0.27 (0.334)	
		95% CI		(-0.92, 0.39)	
		p-value		0.4242	
		HedgesG (95% CI)		-0.217 (-0.585, 0.152)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia		N_1	8	10	18
	Baseline	n	8	10	18
		Mean	6.37	5.94	6.13
		SD, SE	1.494, 0.528	1.794, 0.567	1.634, 0.385
		Median	6.94	5.69	6.63
		Q1, Q3	5.19, 7.47	4.38, 7.88	4.86, 7.57
		Min, Max	3.8, 8.0	3.8, 8.4	3.8, 8.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Baseline			
		n	8	10	18
		Mean	6.37	5.94	6.13
		SD, SE	1.494, 0.528	1.794, 0.567	1.634, 0.385
		Median	6.94	5.69	6.63
		Q1, Q3	5.19, 7.47	4.38, 7.88	4.86, 7.57
		Min, Max	3.8, 8.0	3.8, 8.4	3.8, 8.4
		Observed			
		n	8	10	18
		Mean	5.94	5.76	5.84
		SD, SE	2.096, 0.741	1.980, 0.626	1.973, 0.465
		Median	5.75	6.00	5.75
		Q1, Q3	4.50, 7.50	3.75, 7.63	4.25, 7.63
		Min, Max	2.9, 9.1	2.3, 7.9	2.3, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Change from Baseline			
		n	8	10	18
		Mean	-0.43	-0.18	-0.29
		SD, SE	1.370, 0.484	1.267, 0.401	1.280, 0.302
		Median	-0.31	-0.10	-0.13
		Q1, Q3	-1.35, 0.38	-0.25, 0.86	-0.88, 0.75
		Min, Max	-2.6, 1.8	-2.6, 1.1	-2.6, 1.8
		GEE Estimates			
		LS Mean (SE)	-0.71 (0.586)	-0.35 (0.536)	
		95% CI	(-1.85, 0.44)	(-1.40, 0.70)	
		LS Mean Difference (SE)		0.36 (0.498)	
		95% CI		(-0.62, 1.33)	
		p-value		0.4738	
		HedgesG (95% CI)		0.169 (-0.762, 1.101)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Baseline			
		n	8	10	18
		Mean	6.37	5.94	6.13
		SD, SE	1.494, 0.528	1.794, 0.567	1.634, 0.385
		Median	6.94	5.69	6.63
		Q1, Q3	5.19, 7.47	4.38, 7.88	4.86, 7.57
		Min, Max	3.8, 8.0	3.8, 8.4	3.8, 8.4
		Observed			
		n	8	10	18
		Mean	5.47	5.68	5.58
		SD, SE	2.100, 0.742	2.263, 0.716	2.130, 0.502
		Median	5.38	6.38	6.00
		Q1, Q3	3.63, 6.75	3.38, 7.50	3.38, 7.25
		Min, Max	3.1, 9.1	2.6, 9.0	2.6, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.3
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Region
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Change from Baseline			
		n	8	10	18
		Mean	-0.90	-0.27	-0.55
		SD, SE	1.133, 0.401	1.567, 0.495	1.390, 0.328
		Median	-0.88	-0.25	-0.54
		Q1, Q3	-1.38, -0.47	-1.75, 0.63	-1.63, 0.50
		Min, Max	-2.9, 1.1	-2.5, 2.5	-2.9, 2.5
		GEE Estimates			
		LS Mean (SE)	-1.17 (0.552)	-0.43 (0.555)	
		95% CI	(-2.26, -0.09)	(-1.52, 0.65)	
		LS Mean Difference (SE)		0.74 (0.565)	
		95% CI		(-0.37, 1.85)	
		p-value		0.1899	
		HedgesG (95% CI)		0.406 (-0.533, 1.345)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male		N_1	23	24	47
	Baseline	n	23	24	47
		Mean	6.59	6.17	6.38
		SD, SE	1.375, 0.287	1.846, 0.377	1.629, 0.238
		Median	7.13	6.33	6.63
		Q1, Q3	5.50, 7.57	4.62, 8.00	5.00, 7.75
		Min, Max	3.6, 9.2	2.8, 8.9	2.8, 9.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Baseline			
		n	23	24	47
		Mean	6.59	6.17	6.38
		SD, SE	1.375, 0.287	1.846, 0.377	1.629, 0.238
		Median	7.13	6.33	6.63
		Q1, Q3	5.50, 7.57	4.62, 8.00	5.00, 7.75
		Min, Max	3.6, 9.2	2.8, 8.9	2.8, 9.2
		Observed			
		n	23	24	47
		Mean	5.96	5.54	5.74
		SD, SE	1.889, 0.394	2.175, 0.444	2.029, 0.296
		Median	6.00	6.00	6.00
		Q1, Q3	3.88, 7.75	3.75, 7.56	3.75, 7.63
		Min, Max	2.3, 9.1	0.9, 8.4	0.9, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Change from Baseline			
		n	23	24	47
		Mean	-0.64	-0.63	-0.64
		SD, SE	1.669, 0.348	1.078, 0.220	1.383, 0.202
		Median	-0.13	-0.25	-0.25
		Q1, Q3	-1.75, 0.63	-1.65, 0.13	-1.75, 0.25
		Min, Max	-3.9, 1.9	-2.9, 0.6	-3.9, 1.9
		GEE Estimates			
		LS Mean (SE)	-0.17 (0.568)	-0.34 (0.471)	
		95% CI	(-1.29, 0.94)	(-1.26, 0.58)	
		LS Mean Difference (SE)		-0.17 (0.407)	
		95% CI		(-0.96, 0.63)	
		p-value		0.6844	
		HedgesG (95% CI)		0.002 (-0.570, 0.574)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Baseline			
		n	23	23	46
		Mean	6.59	6.09	6.34
		SD, SE	1.375, 0.287	1.845, 0.385	1.629, 0.240
		Median	7.13	6.25	6.56
		Q1, Q3	5.50, 7.57	4.38, 8.00	5.00, 7.75
		Min, Max	3.6, 9.2	2.8, 8.9	2.8, 9.2
		Observed			
		n	23	23	46
		Mean	5.93	5.37	5.65
		SD, SE	2.176, 0.454	2.450, 0.511	2.309, 0.340
		Median	6.25	5.50	6.00
		Q1, Q3	4.25, 7.63	3.38, 7.75	4.25, 7.63
		Min, Max	1.0, 9.1	0.0, 9.0	0.0, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Change from Baseline			
		n	23	23	46
		Mean	-0.66	-0.72	-0.69
		SD, SE	2.067, 0.431	1.714, 0.357	1.878, 0.277
		Median	-0.63	-0.46	-0.48
		Q1, Q3	-1.25, 0.33	-1.88, 0.38	-1.75, 0.33
		Min, Max	-6.4, 2.8	-4.8, 3.0	-6.4, 3.0
		GEE Estimates			
		LS Mean (SE)	-0.20 (0.595)	-0.40 (0.511)	
		95% CI	(-1.36, 0.97)	(-1.41, 0.60)	
		LS Mean Difference (SE)		-0.21 (0.548)	
		95% CI		(-1.28, 0.87)	
		p-value		0.7063	
		HedgesG (95% CI)		-0.031 (-0.609, 0.547)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female		N_1	43	44	87
	Baseline	n	43	44	87
		Mean	6.82	7.35	7.09
		SD, SE	1.612, 0.246	1.397, 0.211	1.522, 0.163
		Median	6.88	7.50	7.33
		Q1, Q3	5.63, 7.88	6.81, 8.50	6.25, 8.13
		Min, Max	3.8, 9.9	3.8, 9.8	3.8, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Baseline			
		n	43	44	87
		Mean	6.82	7.35	7.09
		SD, SE	1.612, 0.246	1.397, 0.211	1.522, 0.163
		Median	6.88	7.50	7.33
		Q1, Q3	5.63, 7.88	6.81, 8.50	6.25, 8.13
		Min, Max	3.8, 9.9	3.8, 9.8	3.8, 9.9
		Observed			
		n	43	44	87
		Mean	6.00	6.59	6.30
		SD, SE	1.870, 0.285	1.829, 0.276	1.862, 0.200
		Median	5.75	7.25	6.75
		Q1, Q3	4.75, 7.40	5.75, 8.00	4.88, 7.75
		Min, Max	2.3, 9.5	1.1, 9.5	1.1, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Change from Baseline			
		n	43	44	87
		Mean	-0.82	-0.77	-0.79
		SD, SE	1.761, 0.269	1.832, 0.276	1.787, 0.192
		Median	-0.75	-0.38	-0.38
		Q1, Q3	-2.00, 0.13	-1.19, 0.06	-1.75, 0.13
		Min, Max	-4.0, 4.8	-7.5, 2.8	-7.5, 4.8
		GEE Estimates			
		LS Mean (SE)	-0.90 (0.274)	-0.55 (0.258)	
		95% CI	(-1.44, -0.36)	(-1.06, -0.05)	
		LS Mean Difference (SE)		0.35 (0.333)	
		95% CI		(-0.30, 1.00)	
		p-value		0.2952	
		HedgesG (95% CI)		0.027 (-0.393, 0.447)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Baseline			
		n	42	44	86
		Mean	6.80	7.35	7.08
		SD, SE	1.625, 0.251	1.397, 0.211	1.529, 0.165
		Median	6.88	7.50	7.29
		Q1, Q3	5.63, 7.88	6.81, 8.50	6.25, 8.13
		Min, Max	3.8, 9.9	3.8, 9.8	3.8, 9.9
		Observed			
		n	42	44	86
		Mean	6.14	6.31	6.23
		SD, SE	1.922, 0.297	1.998, 0.301	1.951, 0.210
		Median	6.06	6.75	6.38
		Q1, Q3	4.63, 7.63	5.00, 7.88	4.88, 7.75
		Min, Max	1.8, 10.0	1.9, 9.4	1.8, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.4
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Gender
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Change from Baseline			
		n	42	44	86
		Mean	-0.65	-1.04	-0.85
		SD, SE	1.871, 0.289	1.907, 0.288	1.889, 0.204
		Median	-0.69	-0.50	-0.63
		Q1, Q3	-1.88, 0.25	-1.69, 0.13	-1.75, 0.25
		Min, Max	-4.5, 4.5	-7.0, 2.5	-7.0, 4.5
		GEE Estimates			
		LS Mean (SE)	-0.77 (0.285)	-0.83 (0.288)	
		95% CI	(-1.33, -0.21)	(-1.39, -0.26)	
		LS Mean Difference (SE)		-0.06 (0.349)	
		95% CI		(-0.74, 0.62)	
		p-value		0.8622	
		HedgesG (95% CI)		-0.202 (-0.626, 0.221)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White		N_1	53	55	108
	Baseline	n	53	55	108
		Mean	6.76	7.13	6.95
		SD, SE	1.600, 0.220	1.612, 0.217	1.609, 0.155
		Median	7.13	7.50	7.19
		Q1, Q3	5.50, 7.75	6.40, 8.50	5.69, 8.13
		Min, Max	3.6, 9.9	2.8, 9.8	2.8, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Baseline			
		n	53	55	108
		Mean	6.76	7.13	6.95
		SD, SE	1.600, 0.220	1.612, 0.217	1.609, 0.155
		Median	7.13	7.50	7.19
		Q1, Q3	5.50, 7.75	6.40, 8.50	5.69, 8.13
		Min, Max	3.6, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	53	55	108
		Mean	5.93	6.36	6.15
		SD, SE	1.877, 0.258	1.991, 0.268	1.939, 0.187
		Median	6.00	7.00	6.38
		Q1, Q3	4.75, 7.38	4.75, 8.00	4.75, 7.63
		Min, Max	2.3, 9.5	0.9, 9.5	0.9, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Change from Baseline			
		n	53	55	108
		Mean	-0.83	-0.77	-0.80
		SD, SE	1.776, 0.244	1.647, 0.222	1.704, 0.164
		Median	-0.75	-0.38	-0.38
		Q1, Q3	-1.75, 0.13	-1.38, 0.13	-1.56, 0.13
		Min, Max	-4.0, 4.8	-7.5, 2.8	-7.5, 4.8
		GEE Estimates			
		LS Mean (SE)	-0.85 (0.248)	-0.65 (0.237)	
		95% CI	(-1.33, -0.36)	(-1.11, -0.18)	
		LS Mean Difference (SE)		0.20 (0.303)	
		95% CI		(-0.39, 0.80)	
		p-value		0.5078	
		HedgesG (95% CI)		0.036 (-0.341, 0.414)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Baseline			
		n	53	55	108
		Mean	6.76	7.13	6.95
		SD, SE	1.600, 0.220	1.612, 0.217	1.609, 0.155
		Median	7.13	7.50	7.19
		Q1, Q3	5.50, 7.75	6.40, 8.50	5.69, 8.13
		Min, Max	3.6, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	53	55	108
		Mean	6.07	6.12	6.09
		SD, SE	1.970, 0.271	2.198, 0.296	2.080, 0.200
		Median	6.13	6.50	6.31
		Q1, Q3	4.63, 7.63	4.50, 7.88	4.63, 7.79
		Min, Max	1.0, 10.0	0.0, 9.4	0.0, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Change from Baseline			
		n	53	55	108
		Mean	-0.69	-1.01	-0.85
		SD, SE	1.989, 0.273	1.885, 0.254	1.935, 0.186
		Median	-0.63	-0.50	-0.56
		Q1, Q3	-1.88, 0.25	-1.75, 0.13	-1.81, 0.19
		Min, Max	-6.4, 4.5	-7.0, 3.0	-7.0, 4.5
		GEE Estimates			
		LS Mean (SE)	-0.70 (0.275)	-0.89 (0.268)	
		95% CI	(-1.24, -0.16)	(-1.42, -0.37)	
		LS Mean Difference (SE)		-0.19 (0.344)	
		95% CI		(-0.86, 0.49)	
		p-value		0.5829	
		HedgesG (95% CI)		-0.166 (-0.544, 0.212)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White		N_1	13	13	26
	Baseline	n	13	13	26
		Mean	6.67	6.12	6.39
		SD, SE	1.230, 0.341	1.659, 0.460	1.458, 0.286
		Median	7.00	6.38	6.88
		Q1, Q3	6.71, 7.38	4.86, 7.88	5.00, 7.57
		Min, Max	3.8, 8.0	3.8, 8.4	3.8, 8.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Baseline			
		n	13	13	26
		Mean	6.67	6.12	6.39
		SD, SE	1.230, 0.341	1.659, 0.460	1.458, 0.286
		Median	7.00	6.38	6.88
		Q1, Q3	6.71, 7.38	4.86, 7.88	5.00, 7.57
		Min, Max	3.8, 8.0	3.8, 8.4	3.8, 8.4
		Observed			
		n	13	13	26
		Mean	6.22	5.59	5.91
		SD, SE	1.854, 0.514	2.035, 0.564	1.934, 0.379
		Median	5.75	5.75	5.75
		Q1, Q3	5.25, 7.88	3.75, 7.63	4.25, 7.75
		Min, Max	2.9, 9.1	2.3, 8.0	2.3, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Change from Baseline			
		n	13	13	26
		Mean	-0.45	-0.53	-0.49
		SD, SE	1.487, 0.412	1.420, 0.394	1.425, 0.279
		Median	-0.50	-0.13	-0.19
		Q1, Q3	-1.75, 0.50	-2.00, 0.75	-1.82, 0.75
		Min, Max	-2.6, 1.9	-3.0, 1.1	-3.0, 1.9
		GEE Estimates			
		LS Mean (SE)	0.05 (0.490)	-0.28 (0.407)	
		95% CI	(-0.91, 1.01)	(-1.08, 0.52)	
		LS Mean Difference (SE)		-0.33 (0.498)	
		95% CI		(-1.31, 0.65)	
		p-value		0.5089	
		HedgesG (95% CI)		-0.052 (-0.820, 0.717)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Baseline			
		n	12	12	24
		Mean	6.58	5.96	6.27
		SD, SE	1.239, 0.358	1.629, 0.470	1.450, 0.296
		Median	6.94	6.06	6.79
		Q1, Q3	6.11, 7.38	4.62, 7.44	4.94, 7.38
		Min, Max	3.8, 8.0	3.8, 8.4	3.8, 8.4
		Observed			
		n	12	12	24
		Mean	6.06	5.41	5.73
		SD, SE	2.226, 0.643	2.155, 0.622	2.169, 0.443
		Median	6.19	5.25	6.00
		Q1, Q3	4.06, 7.94	3.44, 7.25	3.56, 7.38
		Min, Max	3.1, 9.1	2.6, 9.0	2.6, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.5
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Race
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Change from Baseline			
		n	12	12	24
		Mean	-0.51	-0.56	-0.54
		SD, SE	1.689, 0.488	1.613, 0.466	1.615, 0.330
		Median	-0.75	-0.42	-0.54
		Q1, Q3	-1.38, 0.69	-1.99, 0.56	-1.69, 0.56
		Min, Max	-3.3, 2.4	-2.9, 2.5	-3.3, 2.5
		GEE Estimates			
		LS Mean (SE)	-0.16 (0.562)	-0.28 (0.469)	
		95% CI	(-1.26, 0.94)	(-1.20, 0.64)	
		LS Mean Difference (SE)		-0.12 (0.616)	
		95% CI		(-1.33, 1.09)	
		p-value		0.8479	
		HedgesG (95% CI)		-0.025 (-0.825, 0.775)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years		N_1	36	31	67
	Baseline	n	36	31	67
		Mean	6.93	7.24	7.07
		SD, SE	1.610, 0.268	1.694, 0.304	1.644, 0.201
		Median	7.13	7.88	7.38
		Q1, Q3	6.25, 7.81	6.25, 8.50	6.25, 8.25
		Min, Max	3.6, 9.9	3.4, 9.8	3.4, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Baseline			
		n	36	31	67
		Mean	6.93	7.24	7.07
		SD, SE	1.610, 0.268	1.694, 0.304	1.644, 0.201
		Median	7.13	7.88	7.38
		Q1, Q3	6.25, 7.81	6.25, 8.50	6.25, 8.25
		Min, Max	3.6, 9.9	3.4, 9.8	3.4, 9.9
		Observed			
		n	36	31	67
		Mean	6.27	6.48	6.37
		SD, SE	1.961, 0.327	1.967, 0.353	1.951, 0.238
		Median	6.00	7.13	6.88
		Q1, Q3	4.94, 7.81	4.75, 8.13	4.88, 7.88
		Min, Max	2.3, 9.5	2.3, 9.5	2.3, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Change from Baseline			
		n	36	31	67
		Mean	-0.66	-0.76	-0.71
		SD, SE	1.743, 0.290	1.064, 0.191	1.459, 0.178
		Median	-0.88	-0.38	-0.63
		Q1, Q3	-1.75, 0.38	-1.38, -0.08	-1.75, 0.13
		Min, Max	-4.0, 4.8	-3.0, 1.0	-4.0, 4.8
		GEE Estimates			
		LS Mean (SE)	-0.82 (0.375)	-0.89 (0.349)	
		95% CI	(-1.56, -0.09)	(-1.58, -0.21)	
		LS Mean Difference (SE)		-0.07 (0.336)	
		95% CI		(-0.73, 0.59)	
		p-value		0.8310	
		HedgesG (95% CI)		-0.071 (-0.552, 0.409)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Baseline			
		n	36	31	67
		Mean	6.93	7.24	7.07
		SD, SE	1.610, 0.268	1.694, 0.304	1.644, 0.201
		Median	7.13	7.88	7.38
		Q1, Q3	6.25, 7.81	6.25, 8.50	6.25, 8.25
		Min, Max	3.6, 9.9	3.4, 9.8	3.4, 9.9
		Observed			
		n	36	31	67
		Mean	6.25	6.45	6.34
		SD, SE	2.018, 0.336	2.007, 0.361	2.000, 0.244
		Median	6.31	6.88	6.50
		Q1, Q3	4.63, 7.56	4.63, 8.13	4.63, 7.83
		Min, Max	1.6, 10.0	2.6, 9.4	1.6, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Change from Baseline			
		n	36	31	67
		Mean	-0.68	-0.79	-0.73
		SD, SE	1.760, 0.293	1.509, 0.271	1.637, 0.200
		Median	-0.63	-0.46	-0.63
		Q1, Q3	-1.91, 0.25	-1.75, 0.13	-1.88, 0.25
		Min, Max	-4.5, 4.5	-5.1, 3.0	-5.1, 4.5
		GEE Estimates			
		LS Mean (SE)	-0.85 (0.382)	-0.92 (0.375)	
		95% CI	(-1.59, -0.10)	(-1.66, -0.19)	
		LS Mean Difference (SE)		-0.08 (0.378)	
		95% CI		(-0.82, 0.66)	
		p-value		0.8400	
		HedgesG (95% CI)		-0.066 (-0.546, 0.414)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years		N_1	30	37	67
	Baseline	n	30	37	67
		Mean	6.51	6.68	6.61
		SD, SE	1.412, 0.258	1.604, 0.264	1.512, 0.185
		Median	6.13	7.00	6.88
		Q1, Q3	5.38, 7.50	6.00, 7.88	5.38, 7.75
		Min, Max	4.3, 9.8	2.8, 9.0	2.8, 9.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Baseline			
		n	30	37	67
		Mean	6.51	6.68	6.61
		SD, SE	1.412, 0.258	1.604, 0.264	1.512, 0.185
		Median	6.13	7.00	6.88
		Q1, Q3	5.38, 7.50	6.00, 7.88	5.38, 7.75
		Min, Max	4.3, 9.8	2.8, 9.0	2.8, 9.8
		Observed			
		n	30	37	67
		Mean	5.64	6.00	5.84
		SD, SE	1.705, 0.311	2.041, 0.336	1.892, 0.231
		Median	5.44	6.25	6.00
		Q1, Q3	4.13, 6.50	4.75, 7.63	4.25, 7.50
		Min, Max	3.0, 9.5	0.9, 8.5	0.9, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Change from Baseline			
		n	30	37	67
		Mean	-0.87	-0.68	-0.77
		SD, SE	1.711, 0.312	1.952, 0.321	1.837, 0.224
		Median	-0.42	-0.38	-0.38
		Q1, Q3	-2.00, 0.38	-1.15, 0.50	-1.63, 0.50
		Min, Max	-3.9, 1.5	-7.5, 2.8	-7.5, 2.8
		GEE Estimates			
		LS Mean (SE)	-0.22 (0.370)	-0.02 (0.320)	
		95% CI	(-0.95, 0.50)	(-0.64, 0.61)	
		LS Mean Difference (SE)		0.21 (0.408)	
		95% CI		(-0.59, 1.01)	
		p-value		0.6113	
		HedgesG (95% CI)		0.098 (-0.383, 0.580)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Baseline			
		n	29	36	65
		Mean	6.47	6.65	6.57
		SD, SE	1.417, 0.263	1.611, 0.269	1.519, 0.188
		Median	6.00	7.00	6.86
		Q1, Q3	5.38, 7.38	5.63, 7.75	5.38, 7.63
		Min, Max	4.3, 9.8	2.8, 9.0	2.8, 9.8
		Observed			
		n	29	36	65
		Mean	5.84	5.59	5.71
		SD, SE	1.992, 0.370	2.293, 0.382	2.151, 0.267
		Median	5.63	6.00	5.71
		Q1, Q3	4.25, 7.63	3.69, 7.56	4.25, 7.63
		Min, Max	1.0, 9.4	0.0, 9.0	0.0, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.6
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Age
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Change from Baseline			
		n	29	36	65
		Mean	-0.63	-1.05	-0.86
		SD, SE	2.147, 0.399	2.092, 0.349	2.111, 0.262
		Median	-0.63	-0.50	-0.50
		Q1, Q3	-1.25, 0.00	-1.81, 0.31	-1.63, 0.25
		Min, Max	-6.4, 3.9	-7.0, 2.5	-7.0, 3.9
		GEE Estimates			
		LS Mean (SE)	-0.02 (0.432)	-0.37 (0.354)	
		95% CI	(-0.87, 0.83)	(-1.07, 0.32)	
		LS Mean Difference (SE)		-0.35 (0.482)	
		95% CI		(-1.30, 0.59)	
		p-value		0.4643	
		HedgesG (95% CI)		-0.197 (-0.687, 0.293)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5		N_1	41	39	80
	Baseline	n	41	39	80
		Mean	6.72	6.45	6.59
		SD, SE	1.629, 0.254	1.706, 0.273	1.662, 0.186
		Median	7.00	6.63	6.88
		Q1, Q3	5.63, 7.75	5.00, 8.00	5.44, 7.81
		Min, Max	3.6, 9.8	2.8, 9.1	2.8, 9.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline			
		n	41	39	80
		Mean	6.72	6.45	6.59
		SD, SE	1.629, 0.254	1.706, 0.273	1.662, 0.186
		Median	7.00	6.63	6.88
		Q1, Q3	5.63, 7.75	5.00, 8.00	5.44, 7.81
		Min, Max	3.6, 9.8	2.8, 9.1	2.8, 9.8
		Observed			
		n	41	39	80
		Mean	6.03	5.95	5.99
		SD, SE	1.765, 0.276	1.945, 0.311	1.844, 0.206
		Median	6.00	6.38	6.06
		Q1, Q3	4.88, 7.38	4.25, 7.50	4.75, 7.45
		Min, Max	2.3, 9.5	0.9, 8.6	0.9, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Change from Baseline			
		n	41	39	80
		Mean	-0.69	-0.50	-0.60
		SD, SE	1.682, 0.263	1.220, 0.195	1.469, 0.164
		Median	-0.88	-0.25	-0.44
		Q1, Q3	-1.75, 0.25	-1.38, 0.25	-1.52, 0.25
		Min, Max	-3.9, 4.8	-3.0, 2.8	-3.9, 4.8
		GEE Estimates			
		LS Mean (SE)	-0.75 (0.336)	-0.67 (0.339)	
		95% CI	(-1.41, -0.09)	(-1.33, -0.00)	
		LS Mean Difference (SE)		0.08 (0.308)	
		95% CI		(-0.53, 0.68)	
		p-value		0.8039	
		HedgesG (95% CI)		0.124 (-0.315, 0.562)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline			
		n	41	39	80
		Mean	6.72	6.45	6.59
		SD, SE	1.629, 0.254	1.706, 0.273	1.662, 0.186
		Median	7.00	6.63	6.88
		Q1, Q3	5.63, 7.75	5.00, 8.00	5.44, 7.81
		Min, Max	3.6, 9.8	2.8, 9.1	2.8, 9.8
		Observed			
		n	41	39	80
		Mean	6.05	5.75	5.90
		SD, SE	1.772, 0.277	2.001, 0.320	1.881, 0.210
		Median	6.13	6.00	6.13
		Q1, Q3	4.63, 7.25	4.00, 7.63	4.44, 7.63
		Min, Max	1.6, 9.4	0.0, 8.1	0.0, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Change from Baseline			
		n	41	39	80
		Mean	-0.67	-0.70	-0.69
		SD, SE	1.813, 0.283	1.396, 0.224	1.613, 0.180
		Median	-0.75	-0.50	-0.63
		Q1, Q3	-1.88, -0.13	-1.13, 0.00	-1.56, -0.06
		Min, Max	-3.6, 4.5	-5.1, 3.0	-5.1, 4.5
		GEE Estimates			
		LS Mean (SE)	-0.73 (0.340)	-0.87 (0.350)	
		95% CI	(-1.40, -0.06)	(-1.56, -0.18)	
		LS Mean Difference (SE)		-0.14 (0.335)	
		95% CI		(-0.80, 0.51)	
		p-value		0.6711	
		HedgesG (95% CI)		-0.020 (-0.458, 0.419)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5		N_1	25	29	54
	Baseline	n	25	29	54
		Mean	6.77	7.59	7.21
		SD, SE	1.373, 0.275	1.361, 0.253	1.414, 0.192
		Median	6.75	7.88	7.44
		Q1, Q3	5.50, 7.50	7.13, 8.63	6.25, 8.13
		Min, Max	4.9, 9.9	3.9, 9.8	3.9, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline			
		n	25	29	54
		Mean	6.77	7.59	7.21
		SD, SE	1.373, 0.275	1.361, 0.253	1.414, 0.192
		Median	6.75	7.88	7.44
		Q1, Q3	5.50, 7.50	7.13, 8.63	6.25, 8.13
		Min, Max	4.9, 9.9	3.9, 9.8	3.9, 9.9
		Observed			
		n	25	29	54
		Mean	5.91	6.57	6.27
		SD, SE	2.047, 0.409	2.068, 0.384	2.066, 0.281
		Median	5.50	7.50	6.81
		Q1, Q3	4.75, 7.63	5.50, 8.00	4.75, 8.00
		Min, Max	2.3, 9.5	1.1, 9.5	1.1, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Change from Baseline			
		n	25	29	54
		Mean	-0.86	-1.02	-0.95
		SD, SE	1.806, 0.361	1.985, 0.369	1.888, 0.257
		Median	-0.13	-0.38	-0.38
		Q1, Q3	-1.88, 0.38	-1.00, -0.08	-1.75, 0.13
		Min, Max	-4.0, 1.9	-7.5, 1.1	-7.5, 1.9
		GEE Estimates			
		LS Mean (SE)	-0.19 (0.412)	-0.13 (0.332)	
		95% CI	(-1.00, 0.61)	(-0.78, 0.52)	
		LS Mean Difference (SE)		0.06 (0.471)	
		95% CI		(-0.86, 0.99)	
		p-value		0.8931	
		HedgesG (95% CI)		-0.077 (-0.612, 0.458)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline			
		n	24	28	52
		Mean	6.73	7.57	7.19
		SD, SE	1.387, 0.283	1.383, 0.261	1.435, 0.199
		Median	6.73	7.75	7.38
		Q1, Q3	5.44, 7.50	7.06, 8.63	6.25, 8.25
		Min, Max	4.9, 9.9	3.9, 9.8	3.9, 9.9
		Observed			
		n	24	28	52
		Mean	6.10	6.32	6.22
		SD, SE	2.384, 0.487	2.431, 0.459	2.388, 0.331
		Median	6.19	6.88	6.63
		Q1, Q3	4.44, 7.98	4.63, 8.38	4.44, 8.19
		Min, Max	1.0, 10.0	1.2, 9.4	1.0, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.7
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Change from Baseline			
		n	24	28	52
		Mean	-0.63	-1.25	-0.97
		SD, SE	2.146, 0.438	2.306, 0.436	2.234, 0.310
		Median	-0.38	-0.48	-0.42
		Q1, Q3	-1.56, 1.06	-2.50, 0.31	-2.19, 0.56
		Min, Max	-6.4, 2.8	-7.0, 2.5	-7.0, 2.8
		GEE Estimates			
		LS Mean (SE)	-0.02 (0.484)	-0.34 (0.402)	
		95% CI	(-0.97, 0.93)	(-1.13, 0.45)	
		LS Mean Difference (SE)		-0.32 (0.575)	
		95% CI		(-1.45, 0.81)	
		p-value		0.5785	
		HedgesG (95% CI)		-0.269 (-0.817, 0.279)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	6.38	6.34	6.36
		SD, SE	1.418, 0.233	1.641, 0.300	1.510, 0.184
		Median	6.88	6.45	6.63
		Q1, Q3	5.38, 7.50	5.00, 7.50	5.13, 7.50
		Min, Max	3.6, 9.1	3.4, 9.0	3.4, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline			
		n	37	30	67
		Mean	6.38	6.34	6.36
		SD, SE	1.418, 0.233	1.641, 0.300	1.510, 0.184
		Median	6.88	6.45	6.63
		Q1, Q3	5.38, 7.50	5.00, 7.50	5.13, 7.50
		Min, Max	3.6, 9.1	3.4, 9.0	3.4, 9.1
		Observed			
		n	37	30	67
		Mean	5.59	5.71	5.65
		SD, SE	1.706, 0.280	1.816, 0.332	1.744, 0.213
		Median	5.75	5.75	5.75
		Q1, Q3	4.25, 6.50	4.00, 7.25	4.13, 7.25
		Min, Max	2.3, 9.1	2.3, 8.5	2.3, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.3.1.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-0.78	-0.62	-0.71
		SD, SE	1.796, 0.295	1.354, 0.247	1.603, 0.196
		Median	-0.88	-0.44	-0.63
		Q1, Q3	-1.75, 0.25	-1.38, 0.25	-1.75, 0.25
		Min, Max	-4.0, 4.8	-3.0, 2.8	-4.0, 4.8
		GEE Estimates			
		LS Mean (SE)	-1.03 (0.468)	-0.90 (0.463)	
		95% CI	(-1.95, -0.11)	(-1.81, 0.01)	
		LS Mean Difference (SE)		0.13 (0.357)	
		95% CI		(-0.57, 0.83)	
		p-value		0.7114	
		HedgesG (95% CI)		0.097 (-0.385, 0.579)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.3.1.24.8
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Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline			
		n	37	30	67
		Mean	6.38	6.34	6.36
		SD, SE	1.418, 0.233	1.641, 0.300	1.510, 0.184
		Median	6.88	6.45	6.63
		Q1, Q3	5.38, 7.50	5.00, 7.50	5.13, 7.50
		Min, Max	3.6, 9.1	3.4, 9.0	3.4, 9.1
		Observed			
		n	37	30	67
		Mean	5.39	5.42	5.40
		SD, SE	1.946, 0.320	2.033, 0.371	1.970, 0.241
		Median	5.00	5.50	5.50
		Q1, Q3	4.25, 7.25	3.63, 7.38	4.13, 7.25
		Min, Max	1.0, 8.3	1.2, 8.6	1.0, 8.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-0.99	-0.92	-0.96
		SD, SE	2.046, 0.336	1.539, 0.281	1.823, 0.223
		Median	-0.75	-0.81	-0.75
		Q1, Q3	-1.95, 0.00	-1.75, -0.13	-1.88, -0.13
		Min, Max	-6.4, 4.5	-4.8, 3.0	-6.4, 4.5
		GEE Estimates			
		LS Mean (SE)	-1.23 (0.469)	-1.20 (0.471)	
		95% CI	(-2.15, -0.32)	(-2.12, -0.27)	
		LS Mean Difference (SE)		0.04 (0.414)	
		95% CI		(-0.77, 0.85)	
		p-value		0.9247	
		HedgesG (95% CI)		0.036 (-0.446, 0.517)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	7.21	7.41	7.32
		SD, SE	1.557, 0.289	1.530, 0.248	1.533, 0.187
		Median	7.13	7.88	7.50
		Q1, Q3	5.88, 8.50	7.00, 8.38	6.25, 8.50
		Min, Max	4.3, 9.9	2.8, 9.8	2.8, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline			
		n	29	38	67
		Mean	7.21	7.41	7.32
		SD, SE	1.557, 0.289	1.530, 0.248	1.533, 0.187
		Median	7.13	7.88	7.50
		Q1, Q3	5.88, 8.50	7.00, 8.38	6.25, 8.50
		Min, Max	4.3, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	29	38	67
		Mean	6.49	6.61	6.56
		SD, SE	1.959, 0.364	2.083, 0.338	2.016, 0.246
		Median	7.13	7.38	7.25
		Q1, Q3	5.25, 7.88	6.00, 8.00	5.50, 8.00
		Min, Max	3.0, 9.5	0.9, 9.5	0.9, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-0.71	-0.80	-0.76
		SD, SE	1.646, 0.306	1.783, 0.289	1.713, 0.209
		Median	-0.33	-0.31	-0.33
		Q1, Q3	-1.75, 0.50	-1.38, 0.00	-1.75, 0.13
		Min, Max	-3.8, 1.9	-7.5, 1.1	-7.5, 1.9
		GEE Estimates			
		LS Mean (SE)	-0.05 (0.420)	-0.12 (0.304)	
		95% CI	(-0.88, 0.77)	(-0.72, 0.48)	
		LS Mean Difference (SE)		-0.07 (0.405)	
		95% CI		(-0.86, 0.73)	
		p-value		0.8671	
		HedgesG (95% CI)		-0.046 (-0.530, 0.437)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline			
		n	28	37	65
		Mean	7.19	7.40	7.31
		SD, SE	1.582, 0.299	1.547, 0.254	1.554, 0.193
		Median	7.13	7.88	7.50
		Q1, Q3	5.81, 8.56	7.00, 8.38	6.25, 8.50
		Min, Max	4.3, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	28	37	65
		Mean	6.97	6.45	6.67
		SD, SE	1.724, 0.326	2.232, 0.367	2.031, 0.252
		Median	7.00	6.88	6.88
		Q1, Q3	5.63, 8.50	5.71, 8.00	5.71, 8.13
		Min, Max	3.3, 10.0	0.0, 9.4	0.0, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.8
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Change from Baseline			
		n	28	37	65
		Mean	-0.22	-0.94	-0.63
		SD, SE	1.693, 0.320	2.068, 0.340	1.935, 0.240
		Median	-0.42	-0.38	-0.38
		Q1, Q3	-1.19, 1.06	-1.63, 0.25	-1.25, 0.50
		Min, Max	-3.6, 3.9	-7.0, 2.5	-7.0, 3.9
		GEE Estimates			
		LS Mean (SE)	0.40 (0.419)	-0.25 (0.350)	
		95% CI	(-0.43, 1.22)	(-0.94, 0.43)	
		LS Mean Difference (SE)		-0.65 (0.417)	
		95% CI		(-1.47, 0.17)	
		p-value		0.1192	
		HedgesG (95% CI)		-0.368 (-0.863, 0.127)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50		N_1	42	32	74
	Baseline	n	42	32	74
		Mean	6.48	6.10	6.32
		SD, SE	1.429, 0.220	1.758, 0.311	1.579, 0.184
		Median	6.88	6.38	6.51
		Q1, Q3	5.50, 7.50	4.87, 7.31	5.13, 7.50
		Min, Max	3.6, 9.2	2.8, 9.1	2.8, 9.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.3.1.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Baseline			
		n	42	32	74
		Mean	6.48	6.10	6.32
		SD, SE	1.429, 0.220	1.758, 0.311	1.579, 0.184
		Median	6.88	6.38	6.51
		Q1, Q3	5.50, 7.50	4.87, 7.31	5.13, 7.50
		Min, Max	3.6, 9.2	2.8, 9.1	2.8, 9.2
		Observed			
		n	42	32	74
		Mean	5.67	5.35	5.53
		SD, SE	1.765, 0.272	1.905, 0.337	1.821, 0.212
		Median	5.80	5.50	5.75
		Q1, Q3	4.25, 7.25	3.75, 6.94	4.13, 7.25
		Min, Max	2.3, 9.1	0.9, 8.5	0.9, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.3.1.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 12	Change from Baseline			
		n	42	32	74
		Mean	-0.81	-0.75	-0.78
		SD, SE	1.780, 0.275	1.426, 0.252	1.626, 0.189
		Median	-0.88	-0.38	-0.63
		Q1, Q3	-1.82, 0.25	-1.78, 0.13	-1.82, 0.13
		Min, Max	-4.0, 4.8	-4.0, 2.8	-4.0, 4.8
		GEE Estimates			
		LS Mean (SE)	-0.59 (0.486)	-0.75 (0.431)	
		95% CI	(-1.54, 0.36)	(-1.59, 0.10)	
		LS Mean Difference (SE)		-0.16 (0.355)	
		95% CI		(-0.85, 0.54)	
		p-value		0.6593	
		HedgesG (95% CI)		0.032 (-0.428, 0.492)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.3.1.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Baseline			
		n	42	32	74
		Mean	6.48	6.10	6.32
		SD, SE	1.429, 0.220	1.758, 0.311	1.579, 0.184
		Median	6.88	6.38	6.51
		Q1, Q3	5.50, 7.50	4.87, 7.31	5.13, 7.50
		Min, Max	3.6, 9.2	2.8, 9.1	2.8, 9.2
		Observed			
		n	42	32	74
		Mean	5.61	4.91	5.31
		SD, SE	1.964, 0.303	2.145, 0.379	2.059, 0.239
		Median	5.63	4.38	5.25
		Q1, Q3	4.25, 7.25	3.44, 6.81	3.75, 7.13
		Min, Max	1.0, 8.6	0.0, 8.8	0.0, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.3.1.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat <= 50	Week 24	Change from Baseline			
		n	42	32	74
		Mean	-0.87	-1.19	-1.01
		SD, SE	1.953, 0.301	1.727, 0.305	1.853, 0.215
		Median	-0.75	-1.06	-0.88
		Q1, Q3	-1.88, 0.00	-2.05, -0.19	-1.88, -0.13
		Min, Max	-6.4, 4.5	-5.1, 3.0	-6.4, 4.5
		GEE Estimates			
		LS Mean (SE)	-0.65 (0.497)	-1.18 (0.455)	
		95% CI	(-1.63, 0.32)	(-2.07, -0.29)	
		LS Mean Difference (SE)		-0.53 (0.414)	
		95% CI		(-1.34, 0.28)	
		p-value		0.2019	
		HedgesG (95% CI)		-0.167 (-0.628, 0.294)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.3.1.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50		N_1	24	35	59
	Baseline	n	24	35	59
		Mean	7.19	7.72	7.51
		SD, SE	1.614, 0.330	1.137, 0.192	1.363, 0.178
		Median	7.44	7.88	7.63
		Q1, Q3	5.81, 8.31	7.33, 8.63	6.86, 8.50
		Min, Max	4.3, 9.9	4.4, 9.8	4.3, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.3.1.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Baseline			
		n	24	35	59
		Mean	7.19	7.72	7.51
		SD, SE	1.614, 0.330	1.137, 0.192	1.363, 0.178
		Median	7.44	7.88	7.63
		Q1, Q3	5.81, 8.31	7.33, 8.63	6.86, 8.50
		Min, Max	4.3, 9.9	4.4, 9.8	4.3, 9.9
		Observed			
		n	24	35	59
		Mean	6.54	7.01	6.82
		SD, SE	1.937, 0.395	1.810, 0.306	1.861, 0.242
		Median	6.38	7.50	7.38
		Q1, Q3	5.25, 8.19	6.25, 8.13	5.75, 8.13
		Min, Max	3.0, 9.5	1.1, 9.5	1.1, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 12	Change from Baseline			
		n	24	35	59
		Mean	-0.66	-0.71	-0.69
		SD, SE	1.639, 0.334	1.778, 0.301	1.709, 0.222
		Median	-0.35	-0.38	-0.38
		Q1, Q3	-1.75, 0.56	-0.88, 0.00	-1.50, 0.25
		Min, Max	-3.8, 1.9	-7.5, 1.1	-7.5, 1.9
		GEE Estimates			
		LS Mean (SE)	-0.47 (0.430)	-0.21 (0.327)	
		95% CI	(-1.32, 0.37)	(-0.85, 0.43)	
		LS Mean Difference (SE)		0.26 (0.431)	
		95% CI		(-0.58, 1.11)	
		p-value		0.5433	
		HedgesG (95% CI)		-0.031 (-0.550, 0.489)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Baseline			
		n	23	34	57
		Mean	7.17	7.71	7.49
		SD, SE	1.646, 0.343	1.153, 0.198	1.386, 0.184
		Median	7.38	7.88	7.63
		Q1, Q3	5.75, 8.50	7.33, 8.63	6.86, 8.50
		Min, Max	4.3, 9.9	4.4, 9.8	4.3, 9.9
		Observed			
		n	23	34	57
		Mean	6.91	6.99	6.96
		SD, SE	1.819, 0.379	1.766, 0.303	1.772, 0.235
		Median	6.88	7.50	7.25
		Q1, Q3	5.50, 8.75	6.00, 8.13	5.88, 8.13
		Min, Max	3.3, 10.0	1.9, 9.4	1.9, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.9
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=67)	Total (N=133)
WOMAC Pain Score at BL cat > 50	Week 24	Change from Baseline			
		n	23	34	57
		Mean	-0.26	-0.72	-0.53
		SD, SE	1.853, 0.386	1.949, 0.334	1.908, 0.253
		Median	-0.38	-0.38	-0.38
		Q1, Q3	-1.50, 1.00	-1.25, 0.38	-1.25, 0.50
		Min, Max	-3.6, 3.9	-7.0, 2.5	-7.0, 3.9
		GEE Estimates			
		LS Mean (SE)	-0.14 (0.443)	-0.20 (0.354)	
		95% CI	(-1.01, 0.73)	(-0.90, 0.49)	
		LS Mean Difference (SE)		-0.06 (0.424)	
		95% CI		(-0.89, 0.77)	
		p-value		0.8799	
		HedgesG (95% CI)		-0.234 (-0.765, 0.297)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5		N_1	37	30	67
	Baseline	n	37	30	67
		Mean	6.38	6.30	6.34
		SD, SE	1.418, 0.233	1.640, 0.299	1.510, 0.184
		Median	6.88	6.39	6.50
		Q1, Q3	5.38, 7.50	5.00, 7.50	5.13, 7.50
		Min, Max	3.6, 9.1	3.4, 9.0	3.4, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Baseline			
		n	37	30	67
		Mean	6.38	6.30	6.34
		SD, SE	1.418, 0.233	1.640, 0.299	1.510, 0.184
		Median	6.88	6.39	6.50
		Q1, Q3	5.38, 7.50	5.00, 7.50	5.13, 7.50
		Min, Max	3.6, 9.1	3.4, 9.0	3.4, 9.1
		Observed			
		n	37	30	67
		Mean	5.59	5.71	5.64
		SD, SE	1.706, 0.280	1.744, 0.318	1.711, 0.209
		Median	5.75	5.81	5.75
		Q1, Q3	4.25, 6.50	4.00, 7.13	4.13, 7.13
		Min, Max	2.3, 9.1	2.3, 8.5	2.3, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Change from Baseline			
		n	37	30	67
		Mean	-0.78	-0.59	-0.70
		SD, SE	1.796, 0.295	1.276, 0.233	1.576, 0.192
		Median	-0.88	-0.44	-0.63
		Q1, Q3	-1.75, 0.25	-1.38, 0.13	-1.63, 0.25
		Min, Max	-4.0, 4.8	-3.0, 2.8	-4.0, 4.8
		GEE Estimates			
		LS Mean (SE)	-1.03 (0.469)	-0.88 (0.463)	
		95% CI	(-1.95, -0.11)	(-1.79, 0.03)	
		LS Mean Difference (SE)		0.15 (0.347)	
		95% CI		(-0.53, 0.83)	
		p-value		0.6724	
		HedgesG (95% CI)		0.117 (-0.365, 0.599)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Baseline			
		n	37	30	67
		Mean	6.38	6.30	6.34
		SD, SE	1.418, 0.233	1.640, 0.299	1.510, 0.184
		Median	6.88	6.39	6.50
		Q1, Q3	5.38, 7.50	5.00, 7.50	5.13, 7.50
		Min, Max	3.6, 9.1	3.4, 9.0	3.4, 9.1
		Observed			
		n	37	30	67
		Mean	5.39	5.41	5.40
		SD, SE	1.946, 0.320	1.978, 0.361	1.945, 0.238
		Median	5.00	5.50	5.50
		Q1, Q3	4.25, 7.25	3.63, 7.00	4.13, 7.25
		Min, Max	1.0, 8.3	1.2, 8.6	1.0, 8.6

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Change from Baseline			
		n	37	30	67
		Mean	-0.99	-0.90	-0.95
		SD, SE	2.046, 0.336	1.509, 0.275	1.812, 0.221
		Median	-0.75	-0.81	-0.75
		Q1, Q3	-1.95, 0.00	-1.75, -0.13	-1.88, 0.00
		Min, Max	-6.4, 4.5	-4.8, 3.0	-6.4, 4.5
		GEE Estimates			
		LS Mean (SE)	-1.23 (0.469)	-1.18 (0.472)	
		95% CI	(-2.15, -0.31)	(-2.11, -0.26)	
		LS Mean Difference (SE)		0.05 (0.408)	
		95% CI		(-0.75, 0.85)	
		p-value		0.9114	
		HedgesG (95% CI)		0.047 (-0.434, 0.529)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5		N_1	29	38	67
	Baseline	n	29	38	67
		Mean	7.21	7.44	7.34
		SD, SE	1.557, 0.289	1.511, 0.245	1.524, 0.186
		Median	7.13	7.75	7.50
		Q1, Q3	5.88, 8.50	7.13, 8.38	6.63, 8.50
		Min, Max	4.3, 9.9	2.8, 9.8	2.8, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Baseline			
		n	29	38	67
		Mean	7.21	7.44	7.34
		SD, SE	1.557, 0.289	1.511, 0.245	1.524, 0.186
		Median	7.13	7.75	7.50
		Q1, Q3	5.88, 8.50	7.13, 8.38	6.63, 8.50
		Min, Max	4.3, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	29	38	67
		Mean	6.49	6.62	6.56
		SD, SE	1.959, 0.364	2.130, 0.345	2.043, 0.250
		Median	7.13	7.50	7.25
		Q1, Q3	5.25, 7.88	6.00, 8.00	5.25, 8.00
		Min, Max	3.0, 9.5	0.9, 9.5	0.9, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Change from Baseline			
		n	29	38	67
		Mean	-0.71	-0.82	-0.77
		SD, SE	1.646, 0.306	1.825, 0.296	1.738, 0.212
		Median	-0.33	-0.38	-0.38
		Q1, Q3	-1.75, 0.50	-1.50, 0.00	-1.75, 0.13
		Min, Max	-3.8, 1.9	-7.5, 1.1	-7.5, 1.9
		GEE Estimates			
		LS Mean (SE)	-0.05 (0.423)	-0.14 (0.306)	
		95% CI	(-0.88, 0.78)	(-0.74, 0.46)	
		LS Mean Difference (SE)		-0.08 (0.410)	
		95% CI		(-0.89, 0.72)	
		p-value		0.8362	
		HedgesG (95% CI)		-0.058 (-0.542, 0.425)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Baseline			
		n	28	37	65
		Mean	7.19	7.42	7.32
		SD, SE	1.582, 0.299	1.529, 0.251	1.544, 0.192
		Median	7.13	7.63	7.50
		Q1, Q3	5.81, 8.56	7.13, 8.38	6.63, 8.50
		Min, Max	4.3, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	28	37	65
		Mean	6.97	6.46	6.68
		SD, SE	1.724, 0.326	2.268, 0.373	2.052, 0.254
		Median	7.00	7.00	7.00
		Q1, Q3	5.63, 8.50	5.00, 8.13	5.50, 8.13
		Min, Max	3.3, 10.0	0.0, 9.4	0.0, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.10
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Change from Baseline			
		n	28	37	65
		Mean	-0.22	-0.96	-0.64
		SD, SE	1.693, 0.320	2.085, 0.343	1.948, 0.242
		Median	-0.42	-0.38	-0.38
		Q1, Q3	-1.19, 1.06	-1.88, 0.25	-1.25, 0.50
		Min, Max	-3.6, 3.9	-7.0, 2.5	-7.0, 3.9
		GEE Estimates			
		LS Mean (SE)	0.40 (0.422)	-0.26 (0.350)	
		95% CI	(-0.43, 1.22)	(-0.95, 0.42)	
		LS Mean Difference (SE)		-0.66 (0.420)	
		95% CI		(-1.48, 0.16)	
		p-value		0.1164	
		HedgesG (95% CI)		-0.375 (-0.870, 0.120)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes		N_1	44	47	91
	Baseline	n	44	47	91
		Mean	6.82	7.25	7.04
		SD, SE	1.477, 0.223	1.504, 0.219	1.498, 0.157
		Median	6.81	7.50	7.25
		Q1, Q3	5.63, 7.81	6.63, 8.38	6.00, 8.13
		Min, Max	4.0, 9.9	2.8, 9.8	2.8, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	44	47	91
		Mean	6.82	7.25	7.04
		SD, SE	1.477, 0.223	1.504, 0.219	1.498, 0.157
		Median	6.81	7.50	7.25
		Q1, Q3	5.63, 7.81	6.63, 8.38	6.00, 8.13
		Min, Max	4.0, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	44	47	91
		Mean	5.76	6.47	6.12
		SD, SE	1.840, 0.277	1.917, 0.280	1.904, 0.200
		Median	5.56	6.88	6.25
		Q1, Q3	4.19, 7.31	5.50, 8.00	4.75, 7.75
		Min, Max	2.3, 9.5	0.9, 9.5	0.9, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	44	47	91
		Mean	-1.07	-0.78	-0.92
		SD, SE	1.723, 0.260	1.729, 0.252	1.722, 0.181
		Median	-0.88	-0.38	-0.38
		Q1, Q3	-2.25, 0.13	-1.38, 0.00	-1.88, 0.13
		Min, Max	-4.0, 1.9	-7.5, 2.8	-7.5, 2.8
		GEE Estimates			
		LS Mean (SE)	-0.97 (0.546)	-0.51 (0.479)	
		95% CI	(-2.04, 0.10)	(-1.45, 0.42)	
		LS Mean Difference (SE)		0.46 (0.351)	
		95% CI		(-0.23, 1.15)	
		p-value		0.1920	
		HedgesG (95% CI)		0.164 (-0.248, 0.576)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	43	46	89
		Mean	6.80	7.23	7.02
		SD, SE	1.487, 0.227	1.516, 0.224	1.509, 0.160
		Median	6.75	7.44	7.13
		Q1, Q3	5.63, 7.88	6.63, 8.38	6.00, 8.13
		Min, Max	4.0, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	43	46	89
		Mean	6.00	6.14	6.07
		SD, SE	1.951, 0.298	2.159, 0.318	2.051, 0.217
		Median	5.75	6.44	6.25
		Q1, Q3	4.63, 7.25	5.00, 7.88	4.63, 7.75
		Min, Max	1.0, 10.0	0.0, 9.4	0.0, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	43	46	89
		Mean	-0.80	-1.09	-0.95
		SD, SE	2.027, 0.309	1.881, 0.277	1.947, 0.206
		Median	-0.63	-0.56	-0.63
		Q1, Q3	-2.13, 0.25	-1.75, 0.00	-1.88, 0.13
		Min, Max	-6.4, 3.9	-7.0, 2.5	-7.0, 3.9
		GEE Estimates			
		LS Mean (SE)	-0.73 (0.561)	-0.82 (0.511)	
		95% CI	(-1.83, 0.37)	(-1.82, 0.18)	
		LS Mean Difference (SE)		-0.08 (0.390)	
		95% CI		(-0.85, 0.68)	
		p-value		0.8300	
		HedgesG (95% CI)		-0.147 (-0.563, 0.270)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No		N_1	22	21	43
	Baseline	n	22	21	43
		Mean	6.58	6.25	6.42
		SD, SE	1.645, 0.351	1.810, 0.395	1.715, 0.261
		Median	7.06	6.38	7.00
		Q1, Q3	5.50, 7.50	4.86, 7.88	5.00, 7.75
		Min, Max	3.6, 9.8	3.4, 8.9	3.4, 9.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Baseline			
		n	22	21	43
		Mean	6.58	6.25	6.42
		SD, SE	1.645, 0.351	1.810, 0.395	1.715, 0.261
		Median	7.06	6.38	7.00
		Q1, Q3	5.50, 7.50	4.86, 7.88	5.00, 7.75
		Min, Max	3.6, 9.8	3.4, 8.9	3.4, 9.8
		Observed			
		n	22	21	43
		Mean	6.45	5.65	6.06
		SD, SE	1.861, 0.397	2.135, 0.466	2.016, 0.307
		Median	6.25	5.75	6.00
		Q1, Q3	5.75, 7.75	3.75, 7.50	4.25, 7.63
		Min, Max	2.3, 9.5	2.3, 8.6	2.3, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Change from Baseline			
		n	22	21	43
		Mean	-0.13	-0.59	-0.36
		SD, SE	1.566, 0.334	1.291, 0.282	1.440, 0.220
		Median	-0.13	-0.25	-0.25
		Q1, Q3	-1.32, 0.63	-1.38, 0.63	-1.38, 0.63
		Min, Max	-2.6, 4.8	-3.0, 1.0	-3.0, 4.8
		GEE Estimates			
		LS Mean (SE)	0.33 (0.429)	-0.46 (0.287)	
		95% CI	(-0.51, 1.17)	(-1.02, 0.11)	
		LS Mean Difference (SE)		-0.79 (0.490)	
		95% CI		(-1.75, 0.17)	
		p-value		0.1067	
		HedgesG (95% CI)		-0.308 (-0.910, 0.293)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Baseline			
		n	22	21	43
		Mean	6.58	6.25	6.42
		SD, SE	1.645, 0.351	1.810, 0.395	1.715, 0.261
		Median	7.06	6.38	7.00
		Q1, Q3	5.50, 7.50	4.86, 7.88	5.00, 7.75
		Min, Max	3.6, 9.8	3.4, 8.9	3.4, 9.8
		Observed			
		n	22	21	43
		Mean	6.21	5.67	5.94
		SD, SE	2.136, 0.455	2.281, 0.498	2.199, 0.335
		Median	6.25	5.71	6.25
		Q1, Q3	4.25, 7.83	3.63, 7.75	4.00, 7.75
		Min, Max	1.6, 9.4	1.2, 9.0	1.2, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.11
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Change from Baseline			
		n	22	21	43
		Mean	-0.37	-0.58	-0.47
		SD, SE	1.722, 0.367	1.727, 0.377	1.707, 0.260
		Median	-0.75	-0.25	-0.46
		Q1, Q3	-1.25, 0.33	-1.75, 0.50	-1.50, 0.50
		Min, Max	-3.3, 4.5	-4.8, 3.0	-4.8, 4.5
		GEE Estimates			
		LS Mean (SE)	0.09 (0.462)	-0.44 (0.328)	
		95% CI	(-0.81, 1.00)	(-1.09, 0.20)	
		LS Mean Difference (SE)		-0.54 (0.601)	
		95% CI		(-1.71, 0.64)	
		p-value		0.3713	
		HedgesG (95% CI)		-0.117 (-0.715, 0.482)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes		N_1	13	17	30
	Baseline	n	13	17	30
		Mean	6.46	7.60	7.10
		SD, SE	1.466, 0.406	1.232, 0.299	1.434, 0.262
		Median	6.25	7.63	7.31
		Q1, Q3	5.38, 7.63	6.63, 8.63	6.00, 8.13
		Min, Max	4.0, 9.2	4.9, 9.8	4.0, 9.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	13	17	30
		Mean	6.46	7.60	7.10
		SD, SE	1.466, 0.406	1.232, 0.299	1.434, 0.262
		Median	6.25	7.63	7.31
		Q1, Q3	5.38, 7.63	6.63, 8.63	6.00, 8.13
		Min, Max	4.0, 9.2	4.9, 9.8	4.0, 9.8
		Observed			
		n	13	17	30
		Mean	5.39	6.53	6.04
		SD, SE	2.110, 0.585	2.141, 0.519	2.167, 0.396
		Median	5.00	7.25	6.50
		Q1, Q3	4.13, 7.25	6.00, 8.00	4.25, 7.75
		Min, Max	2.3, 9.0	1.1, 9.5	1.1, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Change from Baseline			
		n	13	17	30
		Mean	-1.06	-1.07	-1.06
		SD, SE	1.816, 0.504	1.982, 0.481	1.879, 0.343
		Median	-0.75	-0.38	-0.38
		Q1, Q3	-1.75, 0.13	-0.50, -0.13	-1.42, 0.00
		Min, Max	-4.0, 1.5	-7.5, 0.3	-7.5, 1.5
		GEE Estimates			
		LS Mean (SE)	-1.19 (0.533)	-0.88 (0.493)	
		95% CI	(-2.23, -0.14)	(-1.85, 0.09)	
		LS Mean Difference (SE)		0.31 (0.645)	
		95% CI		(-0.96, 1.57)	
		p-value		0.6356	
		HedgesG (95% CI)		-0.003 (-0.725, 0.720)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	13	16	29
		Mean	6.46	7.57	7.07
		SD, SE	1.466, 0.406	1.268, 0.317	1.449, 0.269
		Median	6.25	7.63	7.13
		Q1, Q3	5.38, 7.63	6.63, 8.63	6.00, 8.13
		Min, Max	4.0, 9.2	4.9, 9.8	4.0, 9.8
		Observed			
		n	13	16	29
		Mean	5.57	6.38	6.01
		SD, SE	1.986, 0.551	2.175, 0.544	2.096, 0.389
		Median	5.63	6.19	6.00
		Q1, Q3	4.25, 7.13	5.50, 7.88	4.63, 7.50
		Min, Max	1.8, 8.8	1.9, 9.4	1.8, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Change from Baseline			
		n	13	16	29
		Mean	-0.89	-1.20	-1.06
		SD, SE	1.941, 0.538	1.761, 0.440	1.816, 0.337
		Median	-0.38	-0.81	-0.63
		Q1, Q3	-2.04, 0.00	-1.31, -0.25	-1.50, -0.13
		Min, Max	-4.5, 2.8	-6.8, 0.6	-6.8, 2.8
		GEE Estimates			
		LS Mean (SE)	-1.01 (0.545)	-0.95 (0.459)	
		95% CI	(-2.08, 0.05)	(-1.85, -0.05)	
		LS Mean Difference (SE)		0.06 (0.591)	
		95% CI		(-1.10, 1.22)	
		p-value		0.9163	
		HedgesG (95% CI)		-0.156 (-0.889, 0.576)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No		N_1	53	51	104
	Baseline	n	53	51	104
		Mean	6.81	6.72	6.76
		SD, SE	1.546, 0.212	1.731, 0.242	1.632, 0.160
		Median	7.13	7.25	7.13
		Q1, Q3	5.63, 7.75	5.13, 8.13	5.50, 8.00
		Min, Max	3.6, 9.9	2.8, 9.1	2.8, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.3.1.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Baseline			
		n	53	51	104
		Mean	6.81	6.72	6.76
		SD, SE	1.546, 0.212	1.731, 0.242	1.632, 0.160
		Median	7.13	7.25	7.13
		Q1, Q3	5.63, 7.75	5.13, 8.13	5.50, 8.00
		Min, Max	3.6, 9.9	2.8, 9.1	2.8, 9.9
		Observed			
		n	53	51	104
		Mean	6.13	6.11	6.12
		SD, SE	1.789, 0.246	1.971, 0.276	1.871, 0.183
		Median	6.00	6.75	6.13
		Q1, Q3	4.88, 7.40	4.63, 7.75	4.75, 7.63
		Min, Max	2.3, 9.5	0.9, 8.6	0.9, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
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Table 2.2.3.3.1.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Change from Baseline			
		n	53	51	104
		Mean	-0.68	-0.60	-0.64
		SD, SE	1.703, 0.234	1.454, 0.204	1.579, 0.155
		Median	-0.50	-0.25	-0.38
		Q1, Q3	-1.75, 0.38	-1.50, 0.50	-1.75, 0.44
		Min, Max	-3.9, 4.8	-6.1, 2.8	-6.1, 4.8
		GEE Estimates			
		LS Mean (SE)	-0.43 (0.291)	-0.40 (0.262)	
		95% CI	(-1.00, 0.14)	(-0.92, 0.11)	
		LS Mean Difference (SE)		0.02 (0.289)	
		95% CI		(-0.54, 0.59)	
		p-value		0.9369	
		HedgesG (95% CI)		0.046 (-0.339, 0.430)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Baseline			
		n	52	51	103
		Mean	6.79	6.72	6.76
		SD, SE	1.556, 0.216	1.731, 0.242	1.637, 0.161
		Median	7.06	7.25	7.13
		Q1, Q3	5.56, 7.66	5.13, 8.13	5.50, 8.00
		Min, Max	3.6, 9.9	2.8, 9.1	2.8, 9.9
		Observed			
		n	52	51	103
		Mean	6.20	5.87	6.03
		SD, SE	2.004, 0.278	2.204, 0.309	2.102, 0.207
		Median	6.25	6.50	6.38
		Q1, Q3	4.63, 7.73	4.00, 7.75	4.38, 7.75
		Min, Max	1.0, 10.0	0.0, 9.0	0.0, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.12
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Change from Baseline			
		n	52	51	103
		Mean	-0.60	-0.85	-0.72
		SD, SE	1.937, 0.269	1.869, 0.262	1.899, 0.187
		Median	-0.69	-0.46	-0.50
		Q1, Q3	-1.56, 0.29	-1.88, 0.38	-1.88, 0.33
		Min, Max	-6.4, 4.5	-7.0, 3.0	-7.0, 4.5
		GEE Estimates			
		LS Mean (SE)	-0.37 (0.313)	-0.65 (0.298)	
		95% CI	(-0.98, 0.24)	(-1.23, -0.07)	
		LS Mean Difference (SE)		-0.28 (0.354)	
		95% CI		(-0.97, 0.42)	
		p-value		0.4325	
		HedgesG (95% CI)		-0.130 (-0.517, 0.256)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes		N_1	38	32	70
	Baseline	n	38	32	70
		Mean	7.04	6.54	6.81
		SD, SE	1.493, 0.242	1.621, 0.287	1.562, 0.187
		Median	7.25	7.06	7.13
		Q1, Q3	5.88, 7.88	5.19, 7.63	5.63, 7.75
		Min, Max	3.8, 9.9	2.8, 9.0	2.8, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Baseline			
		n	38	32	70
		Mean	7.04	6.54	6.81
		SD, SE	1.493, 0.242	1.621, 0.287	1.562, 0.187
		Median	7.25	7.06	7.13
		Q1, Q3	5.88, 7.88	5.19, 7.63	5.63, 7.75
		Min, Max	3.8, 9.9	2.8, 9.0	2.8, 9.9
		Observed			
		n	38	32	70
		Mean	6.15	5.82	6.00
		SD, SE	1.797, 0.291	2.176, 0.385	1.971, 0.236
		Median	6.00	6.50	6.13
		Q1, Q3	4.88, 7.38	3.75, 7.74	4.63, 7.63
		Min, Max	2.3, 9.5	0.9, 8.6	0.9, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Change from Baseline			
		n	38	32	70
		Mean	-0.88	-0.72	-0.81
		SD, SE	1.788, 0.290	1.801, 0.318	1.783, 0.213
		Median	-0.88	-0.25	-0.38
		Q1, Q3	-1.82, 0.13	-2.00, 0.50	-2.00, 0.13
		Min, Max	-4.0, 4.8	-6.1, 2.8	-6.1, 4.8
		GEE Estimates			
		LS Mean (SE)	-0.22 (0.373)	-0.29 (0.275)	
		95% CI	(-0.95, 0.51)	(-0.83, 0.25)	
		LS Mean Difference (SE)		-0.07 (0.427)	
		95% CI		(-0.91, 0.76)	
		p-value		0.8625	
		HedgesG (95% CI)		0.086 (-0.384, 0.557)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Baseline			
		n	37	31	68
		Mean	7.02	6.49	6.78
		SD, SE	1.509, 0.248	1.626, 0.292	1.573, 0.191
		Median	7.13	7.00	7.13
		Q1, Q3	5.88, 7.88	5.13, 7.63	5.56, 7.75
		Min, Max	3.8, 9.9	2.8, 9.0	2.8, 9.9
		Observed			
		n	37	31	68
		Mean	6.29	5.65	6.00
		SD, SE	1.759, 0.289	2.288, 0.411	2.027, 0.246
		Median	6.25	6.00	6.25
		Q1, Q3	4.88, 7.25	3.63, 7.50	4.75, 7.50
		Min, Max	1.8, 10.0	0.0, 9.0	0.0, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Change from Baseline			
		n	37	31	68
		Mean	-0.73	-0.84	-0.78
		SD, SE	1.756, 0.289	2.048, 0.368	1.881, 0.228
		Median	-0.63	-0.50	-0.63
		Q1, Q3	-1.63, 0.13	-1.88, 0.50	-1.81, 0.25
		Min, Max	-4.5, 4.5	-7.0, 3.0	-7.0, 4.5
		GEE Estimates			
		LS Mean (SE)	-0.10 (0.392)	-0.39 (0.321)	
		95% CI	(-0.87, 0.67)	(-1.02, 0.24)	
		LS Mean Difference (SE)		-0.29 (0.450)	
		95% CI		(-1.17, 0.59)	
		p-value		0.5154	
		HedgesG (95% CI)		-0.057 (-0.534, 0.420)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No		N_1	28	36	64
	Baseline	n	28	36	64
		Mean	6.34	7.29	6.87
		SD, SE	1.505, 0.284	1.630, 0.272	1.635, 0.204
		Median	6.54	7.94	7.00
		Q1, Q3	5.44, 7.38	6.45, 8.56	5.63, 8.13
		Min, Max	3.6, 9.8	3.8, 9.8	3.6, 9.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Baseline			
		n	28	36	64
		Mean	6.34	7.29	6.87
		SD, SE	1.505, 0.284	1.630, 0.272	1.635, 0.204
		Median	6.54	7.94	7.00
		Q1, Q3	5.44, 7.38	6.45, 8.56	5.63, 8.13
		Min, Max	3.6, 9.8	3.8, 9.8	3.6, 9.8
		Observed			
		n	28	36	64
		Mean	5.76	6.57	6.22
		SD, SE	1.958, 0.370	1.800, 0.300	1.900, 0.237
		Median	5.63	6.94	6.25
		Q1, Q3	4.19, 7.51	5.81, 7.81	4.94, 7.75
		Min, Max	2.3, 9.5	1.1, 9.5	1.1, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Change from Baseline			
		n	28	36	64
		Mean	-0.58	-0.72	-0.66
		SD, SE	1.635, 0.309	1.422, 0.237	1.508, 0.189
		Median	-0.19	-0.38	-0.38
		Q1, Q3	-1.54, 0.75	-1.08, 0.00	-1.29, 0.19
		Min, Max	-3.8, 1.9	-7.5, 0.8	-7.5, 1.9
		GEE Estimates			
		LS Mean (SE)	-0.85 (0.455)	-0.74 (0.458)	
		95% CI	(-1.74, 0.04)	(-1.64, 0.15)	
		LS Mean Difference (SE)		0.11 (0.363)	
		95% CI		(-0.60, 0.82)	
		p-value		0.7696	
		HedgesG (95% CI)		-0.088 (-0.582, 0.406)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Baseline			
		n	28	36	64
		Mean	6.34	7.29	6.87
		SD, SE	1.505, 0.284	1.630, 0.272	1.635, 0.204
		Median	6.54	7.94	7.00
		Q1, Q3	5.44, 7.38	6.45, 8.56	5.63, 8.13
		Min, Max	3.6, 9.8	3.8, 9.8	3.6, 9.8
		Observed			
		n	28	36	64
		Mean	5.78	6.28	6.06
		SD, SE	2.284, 0.432	2.094, 0.349	2.175, 0.272
		Median	5.56	6.81	6.31
		Q1, Q3	4.25, 8.13	4.19, 7.94	4.25, 8.06
		Min, Max	1.0, 9.4	1.9, 9.4	1.0, 9.4

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.14
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: Active Fractures and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-0.56	-1.01	-0.81
		SD, SE	2.160, 0.408	1.659, 0.277	1.892, 0.237
		Median	-0.69	-0.50	-0.50
		Q1, Q3	-1.60, 0.91	-1.69, -0.06	-1.69, 0.19
		Min, Max	-6.4, 3.9	-6.8, 1.3	-6.8, 3.9
		GEE Estimates			
		LS Mean (SE)	-0.83 (0.456)	-1.04 (0.460)	
		95% CI	(-1.72, 0.07)	(-1.94, -0.14)	
		LS Mean Difference (SE)		-0.21 (0.442)	
		95% CI		(-1.08, 0.66)	
		p-value		0.6341	
		HedgesG (95% CI)		-0.233 (-0.729, 0.262)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High		N_1	29	37	66
	Baseline	n	29	37	66
		Mean	7.04	7.15	7.10
		SD, SE	1.379, 0.256	1.585, 0.261	1.488, 0.183
		Median	7.13	7.50	7.23
		Q1, Q3	5.88, 7.88	6.38, 8.25	6.00, 8.13
		Min, Max	4.6, 9.9	2.8, 9.8	2.8, 9.9

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Baseline			
		n	29	37	66
		Mean	7.04	7.15	7.10
		SD, SE	1.379, 0.256	1.585, 0.261	1.488, 0.183
		Median	7.13	7.50	7.23
		Q1, Q3	5.88, 7.88	6.38, 8.25	6.00, 8.13
		Min, Max	4.6, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	29	37	66
		Mean	6.22	6.33	6.28
		SD, SE	1.901, 0.353	2.205, 0.363	2.063, 0.254
		Median	6.00	7.25	6.81
		Q1, Q3	5.25, 7.63	5.75, 7.88	5.25, 7.88
		Min, Max	2.3, 9.5	0.9, 9.5	0.9, 9.5

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 12	Change from Baseline			
		n	29	37	66
		Mean	-0.82	-0.81	-0.82
		SD, SE	1.530, 0.284	1.889, 0.311	1.728, 0.213
		Median	-0.75	-0.25	-0.38
		Q1, Q3	-1.75, 0.13	-1.50, 0.00	-1.63, 0.13
		Min, Max	-4.0, 1.9	-7.5, 2.8	-7.5, 2.8
		GEE Estimates			
		LS Mean (SE)	-0.35 (0.421)	-0.38 (0.363)	
		95% CI	(-1.18, 0.48)	(-1.09, 0.33)	
		LS Mean Difference (SE)		-0.03 (0.402)	
		95% CI		(-0.82, 0.76)	
		p-value		0.9384	
		HedgesG (95% CI)		0.005 (-0.481, 0.492)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Baseline			
		n	28	36	64
		Mean	7.01	7.12	7.07
		SD, SE	1.397, 0.264	1.601, 0.267	1.504, 0.188
		Median	7.13	7.50	7.13
		Q1, Q3	5.75, 7.94	6.19, 8.31	5.94, 8.13
		Min, Max	4.6, 9.9	2.8, 9.8	2.8, 9.9
		Observed			
		n	28	36	64
		Mean	6.50	6.19	6.32
		SD, SE	1.838, 0.347	2.259, 0.377	2.075, 0.259
		Median	6.31	6.75	6.50
		Q1, Q3	5.25, 7.81	5.00, 7.81	5.00, 7.81
		Min, Max	1.8, 10.0	0.0, 9.4	0.0, 10.0

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = High	Week 24	Change from Baseline			
		n	28	36	64
		Mean	-0.52	-0.93	-0.75
		SD, SE	1.602, 0.303	2.152, 0.359	1.928, 0.241
		Median	-0.50	-0.50	-0.50
		Q1, Q3	-1.06, 0.25	-1.69, 0.38	-1.38, 0.25
		Min, Max	-4.5, 2.8	-7.0, 3.0	-7.0, 3.0
		GEE Estimates			
		LS Mean (SE)	-0.10 (0.428)	-0.49 (0.386)	
		95% CI	(-0.94, 0.74)	(-1.25, 0.27)	
		LS Mean Difference (SE)		-0.39 (0.414)	
		95% CI		(-1.20, 0.42)	
		p-value		0.3436	
		HedgesG (95% CI)		-0.209 (-0.704, 0.286)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low		N_1	36	30	66
	Baseline	n	36	30	66
		Mean	6.41	6.70	6.54
		SD, SE	1.532, 0.255	1.760, 0.321	1.633, 0.201
		Median	6.69	7.13	6.87
		Q1, Q3	5.31, 7.50	5.13, 8.13	5.13, 7.75
		Min, Max	3.6, 9.2	3.4, 9.0	3.4, 9.2

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Baseline			
		n	36	30	66
		Mean	6.41	6.70	6.54
		SD, SE	1.532, 0.255	1.760, 0.321	1.633, 0.201
		Median	6.69	7.13	6.87
		Q1, Q3	5.31, 7.50	5.13, 8.13	5.13, 7.75
		Min, Max	3.6, 9.2	3.4, 9.0	3.4, 9.2
		Observed			
		n	36	30	66
		Mean	5.70	6.07	5.87
		SD, SE	1.752, 0.292	1.796, 0.328	1.768, 0.218
		Median	5.81	6.19	5.94
		Q1, Q3	4.25, 7.19	4.50, 7.50	4.25, 7.50
		Min, Max	2.3, 9.1	3.1, 8.6	2.3, 9.1

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 12	Change from Baseline			
		n	36	30	66
		Mean	-0.71	-0.64	-0.68
		SD, SE	1.898, 0.316	1.198, 0.219	1.606, 0.198
		Median	-0.63	-0.44	-0.44
		Q1, Q3	-1.94, 0.75	-1.15, 0.38	-1.75, 0.63
		Min, Max	-3.9, 4.8	-3.0, 1.1	-3.9, 4.8
		GEE Estimates			
		LS Mean (SE)	0.08 (0.255)	0.18 (0.232)	
		95% CI	(-0.42, 0.58)	(-0.28, 0.63)	
		LS Mean Difference (SE)		0.10 (0.341)	
		95% CI		(-0.57, 0.77)	
		p-value		0.7643	
		HedgesG (95% CI)		0.045 (-0.439, 0.530)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Baseline			
		n	36	30	66
		Mean	6.41	6.70	6.54
		SD, SE	1.532, 0.255	1.760, 0.321	1.633, 0.201
		Median	6.69	7.13	6.87
		Q1, Q3	5.31, 7.50	5.13, 8.13	5.13, 7.75
		Min, Max	3.6, 9.2	3.4, 9.0	3.4, 9.2
		Observed			
		n	36	30	66
		Mean	5.65	5.74	5.69
		SD, SE	2.019, 0.336	2.157, 0.394	2.067, 0.254
		Median	5.81	5.94	5.94
		Q1, Q3	4.25, 7.44	3.63, 7.75	4.13, 7.63
		Min, Max	1.0, 8.6	1.2, 8.8	1.0, 8.8

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.3.3.1.24.15
Subgroup Analysis: Change from baseline to post-baseline visits in Brief Fatigue Inventory (BFI) Worst Fatigue score
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

Subgroup	Visit	Statistics	Placebo (N=65)	KRN23 (N=67)	Total (N=132)
6MWT score at BL = Low	Week 24	Change from Baseline			
		n	36	30	66
		Mean	-0.77	-0.96	-0.86
		SD, SE	2.185, 0.364	1.431, 0.261	1.869, 0.230
		Median	-0.88	-0.81	-0.88
		Q1, Q3	-1.99, 0.29	-1.88, 0.13	-1.88, 0.25
		Min, Max	-6.4, 4.5	-4.8, 1.3	-6.4, 4.5
		GEE Estimates			
		LS Mean (SE)	0.02 (0.279)	-0.15 (0.254)	
		95% CI	(-0.52, 0.57)	(-0.65, 0.35)	
		LS Mean Difference (SE)		-0.17 (0.410)	
		95% CI		(-0.97, 0.63)	
		p-value		0.6772	
		HedgesG (95% CI)		-0.102 (-0.587, 0.382)	

The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.The GEE Estimates are from the GEE model which includes the change from baseline for BFI Worst Fatigue as the dependent variable, region, visit, treatment, actual randomization stratification and visit by treatment as fixed factors, and baseline of BFI Worst Fatigue as a covariate, with compound symmetry covariance structure.
Data source: ADBFI.sas7bdat, ADSL.sas7bdat Program source: t_bfi_wf_SUB.sas

Table 2.2.8.24.1
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6		N1	27	17	44
	Baseline	n	27	17	44
		Mean	2.70	2.94	2.80
		SD, SE	0.823, 0.158	0.748, 0.181	0.795, 0.120
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	2.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.1
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Baseline			
		n	27	16	43
		Mean	2.70	2.88	2.77
		SD, SE	0.823, 0.158	0.719, 0.180	0.782, 0.119
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	2.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.1
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 12	Observed			
		n	27	16	43
		Mean	3.56	3.00	3.35
		SD, SE	1.251, 0.241	0.894, 0.224	1.152, 0.176
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	2.00, 3.50	3.00, 4.00
		Min, Max	1.0, 6.0	2.0, 5.0	1.0, 6.0
		GEE Estimates			
		LS Mean (SE)	3.75 (0.130)	3.20 (0.249)	
		95% CI	(3.49, 4.00)	(2.71, 3.68)	
		LS Mean Difference (SE)		-0.55 (0.325)	
		95% CI		(-1.19, 0.08)	
		p-value		0.0886	
		HedgesG (95% CI)		-0.470 (-1.096, 0.156)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.1
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Baseline			
		n	26	17	43
		Mean	2.73	2.94	2.81
		SD, SE	0.827, 0.162	0.748, 0.181	0.794, 0.121
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	2.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.1
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL <= 6	Week 24	Observed			
		n	26	17	43
		Mean	3.65	3.29	3.51
		SD, SE	1.441, 0.283	0.920, 0.223	1.261, 0.192
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 7.0	2.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.83 (0.163)	3.50 (0.250)	
		95% CI	(3.51, 4.15)	(3.01, 3.99)	
		LS Mean Difference (SE)		-0.33 (0.354)	
		95% CI		(-1.02, 0.37)	
		p-value		0.3549	
		HedgesG (95% CI)		-0.273 (-0.887, 0.341)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.1
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6		N1	39	51	90
	Baseline	n	39	51	90
		Mean	3.21	3.25	3.23
		SD, SE	0.767, 0.123	0.560, 0.078	0.654, 0.069
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.1
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Baseline			
		n	39	51	90
		Mean	3.21	3.25	3.23
		SD, SE	0.767, 0.123	0.560, 0.078	0.654, 0.069
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.1
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 12	Observed			
		n	39	51	90
		Mean	3.64	3.65	3.64
		SD, SE	1.038, 0.166	1.197, 0.168	1.125, 0.119
		Median	3.00	4.00	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.65 (0.163)	3.66 (0.170)	
		95% CI	(3.33, 3.97)	(3.33, 3.99)	
		LS Mean Difference (SE)		0.01 (0.234)	
		95% CI		(-0.45, 0.47)	
		p-value		0.9727	
		HedgesG (95% CI)		0.005 (-0.412, 0.422)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.1
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Baseline			
		n	38	50	88
		Mean	3.18	3.24	3.22
		SD, SE	0.766, 0.124	0.555, 0.079	0.651, 0.069
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.1
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Baseline BPI Worst Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Worst Pain at BL > 6	Week 24	Observed			
		n	38	50	88
		Mean	3.97	3.62	3.77
		SD, SE	1.365, 0.221	1.323, 0.187	1.345, 0.143
		Median	4.00	3.00	3.50
		Q1, Q3	3.00, 5.00	3.00, 5.00	3.00, 5.00
		Min, Max	2.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.97 (0.216)	3.65 (0.189)	
		95% CI	(3.55, 4.39)	(3.28, 4.02)	
		LS Mean Difference (SE)		-0.32 (0.285)	
		95% CI		(-0.88, 0.24)	
		p-value		0.2590	
		HedgesG (95% CI)		-0.258 (-0.682, 0.165)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.2
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6		N1	49	48	97
	Baseline	n	49	48	97
		Mean	2.82	3.10	2.96
		SD, SE	0.808, 0.115	0.555, 0.080	0.706, 0.072
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	3.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.2
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Baseline			
		n	49	47	96
		Mean	2.82	3.09	2.95
		SD, SE	0.808, 0.115	0.545, 0.079	0.701, 0.072
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	3.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.2
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 12	Observed			
		n	49	47	96
		Mean	3.57	3.43	3.50
		SD, SE	1.208, 0.173	1.118, 0.163	1.161, 0.118
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.57 (0.171)	3.42 (0.160)	
		95% CI	(3.24, 3.91)	(3.10, 3.73)	
		LS Mean Difference (SE)		-0.15 (0.234)	
		95% CI		(-0.61, 0.31)	
		p-value		0.5126	
		HedgesG (95% CI)		-0.123 (-0.524, 0.278)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.2
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Baseline			
		n	48	48	96
		Mean	2.83	3.10	2.97
		SD, SE	0.808, 0.117	0.555, 0.080	0.703, 0.072
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	3.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.2
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL <= 6	Week 24	Observed			
		n	48	48	96
		Mean	3.73	3.50	3.61
		SD, SE	1.425, 0.206	1.167, 0.168	1.301, 0.133
		Median	4.00	3.00	3.50
		Q1, Q3	3.00, 5.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.72 (0.202)	3.50 (0.167)	
		95% CI	(3.33, 4.12)	(3.17, 3.83)	
		LS Mean Difference (SE)		-0.22 (0.262)	
		95% CI		(-0.73, 0.29)	
		p-value		0.3987	
		HedgesG (95% CI)		-0.173 (-0.574, 0.228)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.2
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6		N1	17	20	37
	Baseline	n	17	20	37
		Mean	3.53	3.35	3.43
		SD, SE	0.624, 0.151	0.745, 0.167	0.689, 0.113
		Median	4.00	3.50	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.2
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Baseline			
		n	17	20	37
		Mean	3.53	3.35	3.43
		SD, SE	0.624, 0.151	0.745, 0.167	0.689, 0.113
		Median	4.00	3.50	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.2
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 12	Observed			
		n	17	20	37
		Mean	3.71	3.65	3.68
		SD, SE	0.849, 0.206	1.268, 0.284	1.082, 0.178
		Median	4.00	4.00	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 5.0	1.0, 6.0	1.0, 6.0
		GEE Estimates			
		LS Mean (SE)	3.71 (0.200)	3.65 (0.276)	
		95% CI	(3.31, 4.10)	(3.11, 4.19)	
		LS Mean Difference (SE)		-0.06 (0.341)	
		95% CI		(-0.72, 0.61)	
		p-value		0.8698	
		HedgesG (95% CI)		-0.048 (-0.695, 0.598)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.2
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Baseline			
		n	16	19	35
		Mean	3.50	3.32	3.40
		SD, SE	0.632, 0.158	0.749, 0.172	0.695, 0.117
		Median	4.00	3.00	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.2
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup:Baseline BPI Average Pain

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
BPI Average Pain at BL > 6	Week 24	Observed			
		n	16	19	35
		Mean	4.19	3.63	3.89
		SD, SE	1.276, 0.319	1.422, 0.326	1.367, 0.231
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 5.00	3.00, 5.00	3.00, 5.00
		Min, Max	3.0, 7.0	2.0, 6.0	2.0, 7.0
		GEE Estimates			
		LS Mean (SE)	4.15 (0.305)	3.69 (0.314)	
		95% CI	(3.56, 4.75)	(3.07, 4.30)	
		LS Mean Difference (SE)		-0.47 (0.437)	
		95% CI		(-1.33, 0.39)	
		p-value		0.2848	
		HedgesG (95% CI)		-0.388 (-1.060, 0.283)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.3
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU		N1	58	58	116
	Baseline	n	58	58	116
		Mean	3.02	3.17	3.09
		SD, SE	0.848, 0.111	0.625, 0.082	0.746, 0.069
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.3
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Baseline			
		n	58	57	115
		Mean	3.02	3.16	3.09
		SD, SE	0.848, 0.111	0.621, 0.082	0.744, 0.069
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.3
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 12	Observed			
		n	58	57	115
		Mean	3.53	3.53	3.53
		SD, SE	1.080, 0.142	1.226, 0.162	1.150, 0.107
		Median	3.00	4.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 6.0	1.0, 6.0	1.0, 6.0
		GEE Estimates			
		LS Mean (SE)	3.60 (0.140)	3.58 (0.169)	
		95% CI	(3.33, 3.88)	(3.25, 3.91)	
		LS Mean Difference (SE)		-0.02 (0.211)	
		95% CI		(-0.43, 0.39)	
		p-value		0.9201	
		HedgesG (95% CI)		-0.007 (-0.373, 0.359)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.3
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Baseline			
		n	56	57	113
		Mean	3.02	3.16	3.09
		SD, SE	0.842, 0.113	0.621, 0.082	0.739, 0.069
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.3
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
North America/EU	Week 24	Observed			
		n	56	57	113
		Mean	3.82	3.56	3.69
		SD, SE	1.390, 0.186	1.296, 0.172	1.344, 0.126
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 5.00	3.00, 4.00	3.00, 5.00
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.87 (0.181)	3.64 (0.181)	
		95% CI	(3.52, 4.23)	(3.29, 4.00)	
		LS Mean Difference (SE)		-0.23 (0.246)	
		95% CI		(-0.72, 0.25)	
		p-value		0.3416	
		HedgesG (95% CI)		-0.191 (-0.560, 0.179)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.3
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia		N1	8	10	18
	Baseline	n	8	10	18
		Mean	2.88	3.20	3.06
		SD, SE	0.641, 0.227	0.632, 0.200	0.639, 0.151
		Median	3.00	3.00	3.00
		Q1, Q3	2.50, 3.00	3.00, 4.00	3.00, 3.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.3
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Baseline			
		n	8	10	18
		Mean	2.88	3.20	3.06
		SD, SE	0.641, 0.227	0.632, 0.200	0.639, 0.151
		Median	3.00	3.00	3.00
		Q1, Q3	2.50, 3.00	3.00, 4.00	3.00, 3.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.3
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 12	Observed			
		n	8	10	18
		Mean	4.13	3.30	3.67
		SD, SE	1.356, 0.479	0.675, 0.213	1.085, 0.256
		Median	4.00	3.00	3.50
		Q1, Q3	3.00, 4.50	3.00, 4.00	3.00, 4.00
		Min, Max	3.0, 7.0	2.0, 4.0	2.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.91 (0.467)	3.17 (0.131)	
		95% CI	(2.99, 4.82)	(2.91, 3.42)	
		LS Mean Difference (SE)		-0.74 (0.511)	
		95% CI		(-1.74, 0.26)	
		p-value		0.1489	
		HedgesG (95% CI)		-0.719 (-1.678, 0.240)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.3
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Baseline			
		n	8	10	18
		Mean	2.88	3.20	3.06
		SD, SE	0.641, 0.227	0.632, 0.200	0.639, 0.151
		Median	3.00	3.00	3.00
		Q1, Q3	2.50, 3.00	3.00, 4.00	3.00, 3.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.3
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Region

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Asia	Week 24	Observed			
		n	8	10	18
		Mean	4.00	3.40	3.67
		SD, SE	1.512, 0.535	0.843, 0.267	1.188, 0.280
		Median	4.00	3.00	3.50
		Q1, Q3	3.00, 4.50	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	2.0, 5.0	2.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.78 (0.516)	3.27 (0.174)	
		95% CI	(2.77, 4.79)	(2.93, 3.61)	
		LS Mean Difference (SE)		-0.51 (0.580)	
		95% CI		(-1.65, 0.62)	
		p-value		0.3769	
		HedgesG (95% CI)		-0.455 (-1.397, 0.486)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.4
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male		N1	23	24	47
	Baseline	n	23	24	47
		Mean	3.00	3.13	3.06
		SD, SE	0.905, 0.189	0.680, 0.139	0.791, 0.115
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 3.50	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.4
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Baseline			
		n	23	23	46
		Mean	3.00	3.09	3.04
		SD, SE	0.905, 0.189	0.668, 0.139	0.788, 0.116
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 3.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.4
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 12	Observed			
		n	23	23	46
		Mean	3.83	3.70	3.76
		SD, SE	1.193, 0.249	1.020, 0.213	1.099, 0.162
		Median	4.00	4.00	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	2.0, 6.0	2.0, 7.0
		GEE Estimates			
		LS Mean (SE)	4.20 (0.257)	3.94 (0.245)	
		95% CI	(3.70, 4.70)	(3.46, 4.42)	
		LS Mean Difference (SE)		-0.26 (0.305)	
		95% CI		(-0.86, 0.34)	
		p-value		0.3919	
		HedgesG (95% CI)		-0.113 (-0.691, 0.465)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.4
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Baseline			
		n	22	23	45
		Mean	3.05	3.09	3.07
		SD, SE	0.899, 0.192	0.668, 0.139	0.780, 0.116
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 3.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.4
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Male	Week 24	Observed			
		n	22	23	45
		Mean	4.09	3.57	3.82
		SD, SE	1.571, 0.335	1.237, 0.258	1.419, 0.212
		Median	4.00	3.00	4.00
		Q1, Q3	3.00, 5.00	3.00, 4.00	3.00, 5.00
		Min, Max	2.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	4.44 (0.314)	3.88 (0.280)	
		95% CI	(3.82, 5.06)	(3.33, 4.43)	
		LS Mean Difference (SE)		-0.56 (0.382)	
		95% CI		(-1.31, 0.19)	
		p-value		0.1420	
		HedgesG (95% CI)		-0.358 (-0.947, 0.231)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.4
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female		N1	43	44	87
	Baseline	n	43	44	87
		Mean	3.00	3.20	3.10
		SD, SE	0.787, 0.120	0.594, 0.090	0.699, 0.075
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.4
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Baseline			
		n	43	44	87
		Mean	3.00	3.20	3.10
		SD, SE	0.787, 0.120	0.594, 0.090	0.699, 0.075
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.4
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 12	Observed			
		n	43	44	87
		Mean	3.49	3.39	3.44
		SD, SE	1.077, 0.164	1.224, 0.185	1.148, 0.123
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	2.50, 4.00	3.00, 4.00
		Min, Max	1.0, 6.0	1.0, 6.0	1.0, 6.0
		GEE Estimates			
		LS Mean (SE)	3.51 (0.160)	3.41 (0.188)	
		95% CI	(3.20, 3.83)	(3.04, 3.78)	
		LS Mean Difference (SE)		-0.10 (0.244)	
		95% CI		(-0.58, 0.38)	
		p-value		0.6790	
		HedgesG (95% CI)		-0.087 (-0.507, 0.334)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.4
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Baseline			
		n	42	44	86
		Mean	2.98	3.20	3.09
		SD, SE	0.780, 0.120	0.594, 0.090	0.697, 0.075
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 3.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.4
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Gender

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Sex = Female	Week 24	Observed			
		n	42	44	86
		Mean	3.71	3.52	3.62
		SD, SE	1.293, 0.200	1.248, 0.188	1.266, 0.137
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 5.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 7.0	2.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.73 (0.193)	3.55 (0.195)	
		95% CI	(3.35, 4.11)	(3.16, 3.93)	
		LS Mean Difference (SE)		-0.18 (0.270)	
		95% CI		(-0.71, 0.35)	
		p-value		0.4986	
		HedgesG (95% CI)		-0.148 (-0.571, 0.276)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.5
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White		N1	53	55	108
	Baseline	n	53	55	108
		Mean	2.96	3.16	3.06
		SD, SE	0.854, 0.117	0.631, 0.085	0.752, 0.072
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.5
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Baseline			
		n	53	54	107
		Mean	2.96	3.15	3.06
		SD, SE	0.854, 0.117	0.627, 0.085	0.750, 0.073
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.5
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 12	Observed			
		n	53	54	107
		Mean	3.55	3.54	3.54
		SD, SE	1.119, 0.154	1.224, 0.167	1.168, 0.113
		Median	3.00	4.00	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 6.0	1.0, 6.0	1.0, 6.0
		GEE Estimates			
		LS Mean (SE)	3.60 (0.155)	3.57 (0.175)	
		95% CI	(3.30, 3.90)	(3.23, 3.91)	
		LS Mean Difference (SE)		-0.03 (0.221)	
		95% CI		(-0.46, 0.41)	
		p-value		0.8994	
		HedgesG (95% CI)		-0.008 (-0.387, 0.370)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
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Table 2.2.8.24.5
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Baseline			
		n	52	55	107
		Mean	2.98	3.16	3.07
		SD, SE	0.852, 0.118	0.631, 0.085	0.749, 0.072
		Median	3.00	3.00	3.00
		Q1, Q3	2.50, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
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Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.5
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = White	Week 24	Observed			
		n	52	55	107
		Mean	3.83	3.60	3.71
		SD, SE	1.382, 0.192	1.300, 0.175	1.339, 0.129
		Median	4.00	3.00	4.00
		Q1, Q3	3.00, 5.00	3.00, 4.00	3.00, 5.00
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.87 (0.191)	3.64 (0.186)	
		95% CI	(3.50, 4.25)	(3.28, 4.01)	
		LS Mean Difference (SE)		-0.23 (0.254)	
		95% CI		(-0.73, 0.27)	
		p-value		0.3665	
		HedgesG (95% CI)		-0.167 (-0.546, 0.213)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.5
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White		N1	13	13	26
	Baseline	n	13	13	26
		Mean	3.15	3.23	3.19
		SD, SE	0.689, 0.191	0.599, 0.166	0.634, 0.124
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.5
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Baseline			
		n	13	13	26
		Mean	3.15	3.23	3.19
		SD, SE	0.689, 0.191	0.599, 0.166	0.634, 0.124
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.5
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 12	Observed			
		n	13	13	26
		Mean	3.85	3.31	3.58
		SD, SE	1.144, 0.317	0.855, 0.237	1.027, 0.201
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	3.0, 7.0	2.0, 5.0	2.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.93 (0.292)	3.39 (0.264)	
		95% CI	(3.36, 4.50)	(2.87, 3.91)	
		LS Mean Difference (SE)		-0.54 (0.381)	
		95% CI		(-1.29, 0.21)	
		p-value		0.1579	
		HedgesG (95% CI)		-0.496 (-1.277, 0.284)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.5
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Baseline			
		n	12	12	24
		Mean	3.08	3.17	3.13
		SD, SE	0.669, 0.193	0.577, 0.167	0.612, 0.125
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 3.50	3.00, 3.50	3.00, 3.50
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.5
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Race

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Race = Non-White	Week 24	Observed			
		n	12	12	24
		Mean	3.92	3.25	3.58
		SD, SE	1.505, 0.434	0.866, 0.250	1.248, 0.255
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.50	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	2.0, 5.0	2.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.94 (0.394)	3.46 (0.290)	
		95% CI	(3.17, 4.71)	(2.89, 4.03)	
		LS Mean Difference (SE)		-0.48 (0.472)	
		95% CI		(-1.40, 0.45)	
		p-value		0.3106	
		HedgesG (95% CI)		-0.502 (-1.315, 0.311)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.6
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years		N1	36	31	67
	Baseline	n	36	31	67
		Mean	2.97	3.13	3.04
		SD, SE	0.941, 0.157	0.499, 0.090	0.767, 0.094
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 3.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.6
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Baseline			
		n	36	30	66
		Mean	2.97	3.10	3.03
		SD, SE	0.941, 0.157	0.481, 0.088	0.764, 0.094
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 3.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
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Table 2.2.8.24.6
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 12	Observed			
		n	36	30	66
		Mean	3.61	3.57	3.59
		SD, SE	0.964, 0.161	1.006, 0.184	0.976, 0.120
		Median	3.00	4.00	3.50
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.66 (0.161)	3.58 (0.181)	
		95% CI	(3.34, 3.97)	(3.23, 3.93)	
		LS Mean Difference (SE)		-0.08 (0.235)	
		95% CI		(-0.54, 0.38)	
		p-value		0.7421	
		HedgesG (95% CI)		-0.044 (-0.529, 0.441)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
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Table 2.2.8.24.6
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Baseline			
		n	36	31	67
		Mean	2.97	3.13	3.04
		SD, SE	0.941, 0.157	0.499, 0.090	0.767, 0.094
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 3.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
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Table 2.2.8.24.6
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age <= 41 Years	Week 24	Observed			
		n	36	31	67
		Mean	3.81	3.65	3.73
		SD, SE	1.064, 0.177	1.226, 0.220	1.136, 0.139
		Median	4.00	3.00	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	2.0, 6.0	2.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.85 (0.177)	3.67 (0.219)	
		95% CI	(3.50, 4.20)	(3.24, 4.10)	
		LS Mean Difference (SE)		-0.18 (0.273)	
		95% CI		(-0.71, 0.36)	
		p-value		0.5104	
		HedgesG (95% CI)		-0.137 (-0.618, 0.344)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.6
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years		N1	30	37	67
	Baseline	n	30	37	67
		Mean	3.03	3.22	3.13
		SD, SE	0.669, 0.122	0.712, 0.117	0.694, 0.085
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 3.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.6
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Baseline			
		n	30	37	67
		Mean	3.03	3.22	3.13
		SD, SE	0.669, 0.122	0.712, 0.117	0.694, 0.085
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 3.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.6
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 12	Observed			
		n	30	37	67
		Mean	3.60	3.43	3.51
		SD, SE	1.303, 0.238	1.281, 0.211	1.284, 0.157
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	2.00, 4.00	3.00, 4.00
		Min, Max	1.0, 6.0	1.0, 6.0	1.0, 6.0
		GEE Estimates			
		LS Mean (SE)	3.67 (0.243)	3.50 (0.253)	
		95% CI	(3.19, 4.15)	(3.00, 3.99)	
		LS Mean Difference (SE)		-0.17 (0.310)	
		95% CI		(-0.78, 0.44)	
		p-value		0.5811	
		HedgesG (95% CI)		-0.126 (-0.608, 0.356)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.6
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Baseline			
		n	28	36	64
		Mean	3.04	3.19	3.13
		SD, SE	0.637, 0.120	0.710, 0.118	0.678, 0.085
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 3.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.6
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Age

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Age > 41 Years	Week 24	Observed			
		n	28	36	64
		Mean	3.89	3.44	3.64
		SD, SE	1.750, 0.331	1.252, 0.209	1.495, 0.187
		Median	4.00	3.00	3.00
		Q1, Q3	2.50, 5.00	3.00, 4.00	3.00, 5.00
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.93 (0.327)	3.55 (0.252)	
		95% CI	(3.29, 4.57)	(3.05, 4.04)	
		LS Mean Difference (SE)		-0.38 (0.373)	
		95% CI		(-1.12, 0.35)	
		p-value		0.3047	
		HedgesG (95% CI)		-0.293 (-0.789, 0.204)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.7
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5		N1	41	39	80
	Baseline	n	41	39	80
		Mean	2.88	3.10	2.99
		SD, SE	0.812, 0.127	0.680, 0.109	0.755, 0.084
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 4.00	3.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.7
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Baseline			
		n	41	38	79
		Mean	2.88	3.08	2.97
		SD, SE	0.812, 0.127	0.673, 0.109	0.751, 0.084
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	3.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.7
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 12	Observed			
		n	41	38	79
		Mean	3.46	3.42	3.44
		SD, SE	1.120, 0.175	1.056, 0.171	1.083, 0.122
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 6.0	2.0, 6.0	1.0, 6.0
		GEE Estimates			
		LS Mean (SE)	3.59 (0.182)	3.55 (0.205)	
		95% CI	(3.23, 3.95)	(3.15, 3.95)	
		LS Mean Difference (SE)		-0.03 (0.241)	
		95% CI		(-0.51, 0.44)	
		p-value		0.8866	
		HedgesG (95% CI)		-0.038 (-0.479, 0.403)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.7
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Baseline			
		n	40	39	79
		Mean	2.90	3.10	3.00
		SD, SE	0.810, 0.128	0.680, 0.109	0.751, 0.085
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 4.00	3.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.7
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat <= 62.5	Week 24	Observed			
		n	40	39	79
		Mean	3.68	3.51	3.59
		SD, SE	1.366, 0.216	1.254, 0.201	1.306, 0.147
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.79 (0.224)	3.66 (0.230)	
		95% CI	(3.35, 4.23)	(3.21, 4.11)	
		LS Mean Difference (SE)		-0.14 (0.288)	
		95% CI		(-0.70, 0.43)	
		p-value		0.6369	
		HedgesG (95% CI)		-0.121 (-0.562, 0.321)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.7
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5		N1	25	29	54
	Baseline	n	25	29	54
		Mean	3.20	3.28	3.24
		SD, SE	0.816, 0.163	0.528, 0.098	0.671, 0.091
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
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Table 2.2.8.24.7
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Baseline			
		n	25	29	54
		Mean	3.20	3.28	3.24
		SD, SE	0.816, 0.163	0.528, 0.098	0.671, 0.091
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.7
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 12	Observed			
		n	25	29	54
		Mean	3.84	3.59	3.70
		SD, SE	1.106, 0.221	1.296, 0.241	1.207, 0.164
		Median	4.00	4.00	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.83 (0.213)	3.58 (0.237)	
		95% CI	(3.42, 4.25)	(3.12, 4.05)	
		LS Mean Difference (SE)		-0.25 (0.318)	
		95% CI		(-0.87, 0.37)	
		p-value		0.4330	
		HedgesG (95% CI)		-0.202 (-0.739, 0.334)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.7
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Baseline			
		n	24	28	52
		Mean	3.17	3.25	3.21
		SD, SE	0.816, 0.167	0.518, 0.098	0.667, 0.092
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.7
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Stiffness at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Stiffness at BL cat > 62.5	Week 24	Observed			
		n	24	28	52
		Mean	4.13	3.57	3.83
		SD, SE	1.424, 0.291	1.230, 0.232	1.339, 0.186
		Median	4.00	3.00	4.00
		Q1, Q3	3.00, 5.00	3.00, 4.00	3.00, 5.00
		Min, Max	2.0, 7.0	2.0, 6.0	2.0, 7.0
		GEE Estimates			
		LS Mean (SE)	4.09 (0.276)	3.61 (0.230)	
		95% CI	(3.55, 4.63)	(3.16, 4.06)	
		LS Mean Difference (SE)		-0.48 (0.353)	
		95% CI		(-1.18, 0.21)	
		p-value		0.1706	
		HedgesG (95% CI)		-0.404 (-0.955, 0.147)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.8
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8		N1	37	30	67
	Baseline	n	37	30	67
		Mean	2.65	2.97	2.79
		SD, SE	0.789, 0.130	0.615, 0.112	0.729, 0.089
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	2.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.8
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Baseline			
		n	37	30	67
		Mean	2.65	2.97	2.79
		SD, SE	0.789, 0.130	0.615, 0.112	0.729, 0.089
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	2.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.8
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 12	Observed			
		n	37	30	67
		Mean	3.68	3.27	3.49
		SD, SE	1.002, 0.165	1.112, 0.203	1.064, 0.130
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 6.0	1.0, 6.0	1.0, 6.0
		GEE Estimates			
		LS Mean (SE)	3.98 (0.247)	3.55 (0.326)	
		95% CI	(3.49, 4.46)	(2.92, 4.19)	
		LS Mean Difference (SE)		-0.42 (0.252)	
		95% CI		(-0.92, 0.07)	
		p-value		0.0930	
		HedgesG (95% CI)		-0.378 (-0.864, 0.107)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.8
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Baseline			
		n	36	30	66
		Mean	2.67	2.97	2.80
		SD, SE	0.793, 0.132	0.615, 0.112	0.728, 0.090
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	2.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
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Table 2.2.8.24.8
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat <= 47.8	Week 24	Observed			
		n	36	30	66
		Mean	3.75	3.37	3.58
		SD, SE	1.228, 0.205	1.098, 0.200	1.177, 0.145
		Median	4.00	3.00	3.50
		Q1, Q3	3.00, 4.50	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	2.0, 6.0	2.0, 7.0
		GEE Estimates			
		LS Mean (SE)	4.04 (0.268)	3.65 (0.322)	
		95% CI	(3.51, 4.56)	(3.02, 4.29)	
		LS Mean Difference (SE)		-0.38 (0.271)	
		95% CI		(-0.92, 0.15)	
		p-value		0.1554	
		HedgesG (95% CI)		-0.319 (-0.806, 0.169)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.8
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8		N1	29	38	67
	Baseline	n	29	38	67
		Mean	3.45	3.34	3.39
		SD, SE	0.632, 0.117	0.582, 0.094	0.602, 0.074
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.8
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Baseline			
		n	29	37	66
		Mean	3.45	3.32	3.38
		SD, SE	0.632, 0.117	0.580, 0.095	0.602, 0.074
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.8
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 12	Observed			
		n	29	37	66
		Mean	3.52	3.68	3.61
		SD, SE	1.271, 0.236	1.180, 0.194	1.214, 0.149
		Median	3.00	4.00	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.52 (0.230)	3.66 (0.189)	
		95% CI	(3.07, 3.97)	(3.29, 4.03)	
		LS Mean Difference (SE)		0.14 (0.302)	
		95% CI		(-0.45, 0.74)	
		p-value		0.6329	
		HedgesG (95% CI)		0.126 (-0.360, 0.613)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.8
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Baseline			
		n	28	37	65
		Mean	3.43	3.32	3.37
		SD, SE	0.634, 0.120	0.580, 0.095	0.601, 0.075
		Median	3.50	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.8
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Physical Function at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Physical Function at BL cat > 47.8	Week 24	Observed			
		n	28	37	65
		Mean	3.96	3.68	3.80
		SD, SE	1.598, 0.302	1.334, 0.219	1.449, 0.180
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 5.00	3.00, 5.00	3.00, 5.00
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.95 (0.290)	3.70 (0.216)	
		95% CI	(3.38, 4.52)	(3.28, 4.13)	
		LS Mean Difference (SE)		-0.25 (0.365)	
		95% CI		(-0.96, 0.47)	
		p-value		0.5013	
		HedgesG (95% CI)		-0.193 (-0.685, 0.299)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.9
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat <= 50		N1	42	32	74
	Baseline	n	42	32	74
		Mean	2.71	2.94	2.81
		SD, SE	0.805, 0.124	0.619, 0.109	0.734, 0.085
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	2.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.9
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat <= 50	Week 12	Baseline			
		n	42	32	74
		Mean	2.71	2.94	2.81
		SD, SE	0.805, 0.124	0.619, 0.109	0.734, 0.085
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	2.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
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Table 2.2.8.24.9
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat <= 50	Week 12	Observed			
		n	42	32	74
		Mean	3.76	3.19	3.51
		SD, SE	1.031, 0.159	0.998, 0.176	1.050, 0.122
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	2.50, 4.00	3.00, 4.00
		Min, Max	2.0, 6.0	2.0, 6.0	2.0, 6.0
		GEE Estimates			
		LS Mean (SE)	3.94 (0.168)	3.38 (0.210)	
		95% CI	(3.61, 4.27)	(2.97, 3.79)	
		LS Mean Difference (SE)		-0.57 (0.236)	
		95% CI		(-1.03, -0.10)	
		p-value		0.0165	
		HedgesG (95% CI)		-0.551 (-1.020, -0.083)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.9
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat <= 50	Week 24	Baseline			
		n	41	32	73
		Mean	2.73	2.94	2.82
		SD, SE	0.807, 0.126	0.619, 0.109	0.733, 0.086
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	2.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
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Table 2.2.8.24.9
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat <= 50	Week 24	Observed			
		n	41	32	73
		Mean	3.98	3.28	3.67
		SD, SE	1.332, 0.208	1.054, 0.186	1.259, 0.147
		Median	4.00	3.00	4.00
		Q1, Q3	3.00, 5.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	4.14 (0.220)	3.47 (0.222)	
		95% CI	(3.71, 4.58)	(3.04, 3.91)	
		LS Mean Difference (SE)		-0.67 (0.271)	
		95% CI		(-1.21, -0.14)	
		p-value		0.0131	
		HedgesG (95% CI)		-0.556 (-1.027, -0.085)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.9
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat > 50		N1	24	35	59
	Baseline	n	24	35	59
		Mean	3.50	3.40	3.44
		SD, SE	0.590, 0.120	0.553, 0.093	0.565, 0.074
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.9
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat > 50	Week 12	Baseline			
		n	24	34	58
		Mean	3.50	3.38	3.43
		SD, SE	0.590, 0.120	0.551, 0.095	0.565, 0.074
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.9
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat > 50	Week 12	Observed			
		n	24	34	58
		Mean	3.33	3.79	3.60
		SD, SE	1.239, 0.253	1.250, 0.214	1.256, 0.165
		Median	3.00	4.00	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.34 (0.243)	3.78 (0.210)	
		95% CI	(2.86, 3.81)	(3.36, 4.19)	
		LS Mean Difference (SE)		0.44 (0.323)	
		95% CI		(-0.19, 1.08)	
		p-value		0.1720	
		HedgesG (95% CI)		0.359 (-0.168, 0.885)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.9
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat > 50	Week 24	Baseline			
		n	23	34	57
		Mean	3.48	3.38	3.42
		SD, SE	0.593, 0.124	0.551, 0.095	0.565, 0.075
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.9
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Pain Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Pain Score at BL cat > 50	Week 24	Observed			
		n	23	34	57
		Mean	3.61	3.79	3.72
		SD, SE	1.500, 0.313	1.366, 0.234	1.411, 0.187
		Median	3.00	3.50	3.00
		Q1, Q3	3.00, 4.00	3.00, 5.00	3.00, 5.00
		Min, Max	1.0, 7.0	2.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.60 (0.294)	3.82 (0.232)	
		95% CI	(3.02, 4.18)	(3.37, 4.28)	
		LS Mean Difference (SE)		0.22 (0.377)	
		95% CI		(-0.51, 0.96)	
		p-value		0.5507	
		HedgesG (95% CI)		0.126 (-0.403, 0.656)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.10
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5		N1	37	30	67
	Baseline	n	37	30	67
		Mean	2.65	2.93	2.78
		SD, SE	0.789, 0.130	0.583, 0.106	0.714, 0.087
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	2.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.10
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Baseline			
		n	37	30	67
		Mean	2.65	2.93	2.78
		SD, SE	0.789, 0.130	0.583, 0.106	0.714, 0.087
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	2.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.10
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 12	Observed			
		n	37	30	67
		Mean	3.68	3.40	3.55
		SD, SE	1.002, 0.165	1.133, 0.207	1.063, 0.130
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 6.0	2.0, 6.0	2.0, 6.0
		GEE Estimates			
		LS Mean (SE)	3.96 (0.247)	3.67 (0.328)	
		95% CI	(3.47, 4.44)	(3.03, 4.31)	
		LS Mean Difference (SE)		-0.29 (0.256)	
		95% CI		(-0.79, 0.21)	
		p-value		0.2592	
		HedgesG (95% CI)		-0.253 (-0.736, 0.231)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.10
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Baseline			
		n	36	30	66
		Mean	2.67	2.93	2.79
		SD, SE	0.793, 0.132	0.583, 0.106	0.713, 0.088
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	2.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.10
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat <= 49.5	Week 24	Observed			
		n	36	30	66
		Mean	3.75	3.40	3.59
		SD, SE	1.228, 0.205	1.102, 0.201	1.176, 0.145
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.50	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	2.0, 6.0	2.0, 7.0
		GEE Estimates			
		LS Mean (SE)	4.02 (0.268)	3.67 (0.321)	
		95% CI	(3.50, 4.54)	(3.04, 4.30)	
		LS Mean Difference (SE)		-0.35 (0.272)	
		95% CI		(-0.88, 0.18)	
		p-value		0.1973	
		HedgesG (95% CI)		-0.291 (-0.778, 0.197)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.10
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5		N1	29	38	67
	Baseline	n	29	38	67
		Mean	3.45	3.37	3.40
		SD, SE	0.632, 0.117	0.589, 0.096	0.605, 0.074
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
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Table 2.2.8.24.10
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Baseline			
		n	29	37	66
		Mean	3.45	3.35	3.39
		SD, SE	0.632, 0.117	0.588, 0.097	0.605, 0.074
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.10
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 12	Observed			
		n	29	37	66
		Mean	3.52	3.57	3.55
		SD, SE	1.271, 0.236	1.191, 0.196	1.218, 0.150
		Median	3.00	4.00	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.52 (0.230)	3.56 (0.190)	
		95% CI	(3.07, 3.97)	(3.18, 3.93)	
		LS Mean Difference (SE)		0.04 (0.302)	
		95% CI		(-0.55, 0.63)	
		p-value		0.8978	
		HedgesG (95% CI)		0.040 (-0.446, 0.526)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.10
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Baseline			
		n	28	37	65
		Mean	3.43	3.35	3.38
		SD, SE	0.634, 0.120	0.588, 0.097	0.604, 0.075
		Median	3.50	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.10
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: WOMAC Total Score at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
WOMAC Total Score at BL cat > 49.5	Week 24	Observed			
		n	28	37	65
		Mean	3.96	3.65	3.78
		SD, SE	1.598, 0.302	1.338, 0.220	1.452, 0.180
		Median	4.00	3.00	4.00
		Q1, Q3	3.00, 5.00	3.00, 4.00	3.00, 5.00
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.95 (0.290)	3.68 (0.217)	
		95% CI	(3.38, 4.52)	(3.26, 4.11)	
		LS Mean Difference (SE)		-0.27 (0.365)	
		95% CI		(-0.98, 0.45)	
		p-value		0.4634	
		HedgesG (95% CI)		-0.211 (-0.703, 0.281)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.11
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes		N1	44	47	91
	Baseline	n	44	47	91
		Mean	3.05	3.19	3.12
		SD, SE	0.806, 0.121	0.613, 0.089	0.712, 0.075
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.11
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	44	47	91
		Mean	3.05	3.19	3.12
		SD, SE	0.806, 0.121	0.613, 0.089	0.712, 0.075
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.11
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 12	Observed			
		n	44	47	91
		Mean	3.45	3.60	3.53
		SD, SE	1.150, 0.173	1.228, 0.179	1.186, 0.124
		Median	3.00	4.00	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 6.0	1.0, 6.0	1.0, 6.0
		GEE Estimates			
		LS Mean (SE)	3.50 (0.166)	3.65 (0.190)	
		95% CI	(3.18, 3.83)	(3.28, 4.02)	
		LS Mean Difference (SE)		0.15 (0.247)	
		95% CI		(-0.34, 0.63)	
		p-value		0.5543	
		HedgesG (95% CI)		0.116 (-0.295, 0.528)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.11
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	42	46	88
		Mean	3.05	3.17	3.11
		SD, SE	0.795, 0.123	0.608, 0.090	0.702, 0.075
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.11
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL = Yes	Week 24	Observed			
		n	42	46	88
		Mean	3.83	3.50	3.66
		SD, SE	1.378, 0.213	1.206, 0.178	1.294, 0.138
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 5.00	3.00, 4.00	3.00, 4.50
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.87 (0.201)	3.58 (0.188)	
		95% CI	(3.47, 4.26)	(3.21, 3.95)	
		LS Mean Difference (SE)		-0.29 (0.271)	
		95% CI		(-0.82, 0.24)	
		p-value		0.2824	
		HedgesG (95% CI)		-0.253 (-0.673, 0.167)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.11
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No		N1	22	21	43
	Baseline	n	22	21	43
		Mean	2.91	3.14	3.02
		SD, SE	0.868, 0.185	0.655, 0.143	0.771, 0.118
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.11
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Baseline			
		n	22	20	42
		Mean	2.91	3.10	3.00
		SD, SE	0.868, 0.185	0.641, 0.143	0.765, 0.118
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 3.50	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.11
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 12	Observed			
		n	22	20	42
		Mean	3.91	3.25	3.60
		SD, SE	1.019, 0.217	0.967, 0.216	1.037, 0.160
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	3.0, 7.0	2.0, 6.0	2.0, 7.0
		GEE Estimates			
		LS Mean (SE)	4.01 (0.253)	3.28 (0.230)	
		95% CI	(3.51, 4.50)	(2.83, 3.73)	
		LS Mean Difference (SE)		-0.73 (0.287)	
		95% CI		(-1.29, -0.17)	
		p-value		0.0108	
		HedgesG (95% CI)		-0.635 (-1.255, -0.014)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.11
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Baseline			
		n	22	21	43
		Mean	2.91	3.14	3.02
		SD, SE	0.868, 0.185	0.655, 0.143	0.771, 0.118
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	2.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.11
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Pain Medication Use at BL cat=No	Week 24	Observed			
		n	22	21	43
		Mean	3.86	3.62	3.74
		SD, SE	1.457, 0.311	1.322, 0.288	1.382, 0.211
		Median	4.00	3.00	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	2.0, 6.0	2.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.96 (0.338)	3.67 (0.308)	
		95% CI	(3.30, 4.63)	(3.07, 4.28)	
		LS Mean Difference (SE)		-0.29 (0.406)	
		95% CI		(-1.09, 0.50)	
		p-value		0.4712	
		HedgesG (95% CI)		-0.168 (-0.767, 0.431)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.12
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes		N1	13	17	30
	Baseline	n	13	17	30
		Mean	2.92	3.59	3.30
		SD, SE	0.954, 0.265	0.507, 0.123	0.794, 0.145
		Median	3.00	4.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	3.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.12
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Baseline			
		n	13	17	30
		Mean	2.92	3.59	3.30
		SD, SE	0.954, 0.265	0.507, 0.123	0.794, 0.145
		Median	3.00	4.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	3.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.12
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 12	Observed			
		n	13	17	30
		Mean	3.92	3.35	3.60
		SD, SE	1.498, 0.415	0.996, 0.242	1.248, 0.228
		Median	4.00	4.00	4.00
		Q1, Q3	3.00, 5.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 6.0	1.0, 5.0	1.0, 6.0
		GEE Estimates			
		LS Mean (SE)	4.02 (0.358)	3.40 (0.252)	
		95% CI	(3.32, 4.73)	(2.91, 3.89)	
		LS Mean Difference (SE)		-0.63 (0.433)	
		95% CI		(-1.47, 0.22)	
		p-value		0.1487	
		HedgesG (95% CI)		-0.433 (-1.164, 0.297)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.12
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Baseline			
		n	13	16	29
		Mean	2.92	3.56	3.28
		SD, SE	0.954, 0.265	0.512, 0.128	0.797, 0.148
		Median	3.00	4.00	3.00
		Q1, Q3	2.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	3.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
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The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.12
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL = Yes	Week 24	Observed			
		n	13	16	29
		Mean	4.00	3.38	3.66
		SD, SE	1.354, 0.376	1.147, 0.287	1.261, 0.234
		Median	4.00	3.00	4.00
		Q1, Q3	4.00, 5.00	3.00, 4.00	3.00, 5.00
		Min, Max	1.0, 6.0	2.0, 6.0	1.0, 6.0
		GEE Estimates			
		LS Mean (SE)	4.10 (0.314)	3.49 (0.295)	
		95% CI	(3.49, 4.72)	(2.91, 4.07)	
		LS Mean Difference (SE)		-0.61 (0.429)	
		95% CI		(-1.45, 0.23)	
		p-value		0.1547	
		HedgesG (95% CI)		-0.471 (-1.213, 0.270)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.12
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No		N1	53	51	104
	Baseline	n	53	51	104
		Mean	3.02	3.04	3.03
		SD, SE	0.796, 0.109	0.599, 0.084	0.703, 0.069
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 3.00	3.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.12
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Baseline			
		n	53	50	103
		Mean	3.02	3.02	3.02
		SD, SE	0.796, 0.109	0.589, 0.083	0.700, 0.069
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 3.00	3.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.12
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 12	Observed			
		n	53	50	103
		Mean	3.53	3.54	3.53
		SD, SE	1.012, 0.139	1.216, 0.172	1.110, 0.109
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.57 (0.144)	3.57 (0.184)	
		95% CI	(3.28, 3.85)	(3.21, 3.93)	
		LS Mean Difference (SE)		0.00 (0.217)	
		95% CI		(-0.42, 0.43)	
		p-value		0.9951	
		HedgesG (95% CI)		0.010 (-0.376, 0.397)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.12
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Baseline			
		n	51	51	102
		Mean	3.02	3.04	3.03
		SD, SE	0.787, 0.110	0.599, 0.084	0.696, 0.069
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 3.00	3.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.12
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgrooup: Opioid Pain Medication Use at Baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Opioid Pain Medication Use at BL cat = No	Week 24	Observed			
		n	51	51	102
		Mean	3.80	3.59	3.70
		SD, SE	1.414, 0.198	1.268, 0.178	1.341, 0.133
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 5.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.83 (0.198)	3.62 (0.196)	
		95% CI	(3.44, 4.21)	(3.24, 4.01)	
		LS Mean Difference (SE)		-0.20 (0.260)	
		95% CI		(-0.71, 0.31)	
		p-value		0.4375	
		HedgesG (95% CI)		-0.158 (-0.547, 0.231)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.14
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes		N1	38	32	70
	Baseline	n	38	32	70
		Mean	3.16	3.25	3.20
		SD, SE	0.718, 0.116	0.440, 0.078	0.604, 0.072
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 3.50	3.00, 4.00
		Min, Max	2.0, 4.0	3.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.14
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Baseline			
		n	38	31	69
		Mean	3.16	3.23	3.19
		SD, SE	0.718, 0.116	0.425, 0.076	0.601, 0.072
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 3.00	3.00, 4.00
		Min, Max	2.0, 4.0	3.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.14
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 12	Observed			
		n	38	31	69
		Mean	3.74	3.42	3.59
		SD, SE	1.057, 0.172	1.285, 0.231	1.167, 0.141
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	2.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.79 (0.174)	3.48 (0.233)	
		95% CI	(3.45, 4.14)	(3.03, 3.94)	
		LS Mean Difference (SE)		-0.31 (0.279)	
		95% CI		(-0.86, 0.24)	
		p-value		0.2657	
		HedgesG (95% CI)		-0.266 (-0.742, 0.211)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.14
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Baseline			
		n	36	31	67
		Mean	3.17	3.23	3.19
		SD, SE	0.697, 0.116	0.425, 0.076	0.584, 0.071
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 3.00	3.00, 4.00
		Min, Max	2.0, 4.0	3.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.14
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = Yes	Week 24	Observed			
		n	36	31	67
		Mean	3.86	3.48	3.69
		SD, SE	1.150, 0.192	1.363, 0.245	1.258, 0.154
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.89 (0.187)	3.60 (0.253)	
		95% CI	(3.52, 4.26)	(3.11, 4.10)	
		LS Mean Difference (SE)		-0.29 (0.306)	
		95% CI		(-0.89, 0.31)	
		p-value		0.3490	
		HedgesG (95% CI)		-0.293 (-0.776, 0.190)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.14
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No		N1	28	36	64
	Baseline	n	28	36	64
		Mean	2.79	3.11	2.97
		SD, SE	0.917, 0.173	0.747, 0.125	0.835, 0.104
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Baseline			
		n	28	36	64
		Mean	2.79	3.11	2.97
		SD, SE	0.917, 0.173	0.747, 0.125	0.835, 0.104
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.14
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 12	Observed			
		n	28	36	64
		Mean	3.43	3.56	3.50
		SD, SE	1.200, 0.227	1.054, 0.176	1.113, 0.139
		Median	4.00	4.00	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 6.0	1.0, 6.0	1.0, 6.0
		GEE Estimates			
		LS Mean (SE)	3.47 (0.236)	3.58 (0.194)	
		95% CI	(3.01, 3.93)	(3.20, 3.96)	
		LS Mean Difference (SE)		0.11 (0.278)	
		95% CI		(-0.44, 0.65)	
		p-value		0.6993	
		HedgesG (95% CI)		0.110 (-0.384, 0.604)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.14
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Baseline			
		n	28	36	64
		Mean	2.79	3.11	2.97
		SD, SE	0.917, 0.173	0.747, 0.125	0.835, 0.104
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
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Table 2.2.8.24.14
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: Active fractures and pseudo-fractures at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
Active fractures and pseudo-fractures at BL = No	Week 24	Observed			
		n	28	36	64
		Mean	3.82	3.58	3.69
		SD, SE	1.679, 0.317	1.131, 0.188	1.390, 0.174
		Median	4.00	3.00	4.00
		Q1, Q3	2.00, 5.00	3.00, 4.00	3.00, 5.00
		Min, Max	1.0, 7.0	2.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.86 (0.329)	3.60 (0.208)	
		95% CI	(3.22, 4.51)	(3.20, 4.01)	
		LS Mean Difference (SE)		-0.26 (0.358)	
		95% CI		(-0.96, 0.44)	
		p-value		0.4718	
		HedgesG (95% CI)		-0.166 (-0.661, 0.329)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.15
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = High		N1	29	37	66
	Baseline	n	29	37	66
		Mean	3.34	3.41	3.38
		SD, SE	0.721, 0.134	0.599, 0.098	0.651, 0.080
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.15
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = High	Week 12	Baseline			
		n	29	36	65
		Mean	3.34	3.39	3.37
		SD, SE	0.721, 0.134	0.599, 0.100	0.651, 0.081
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.15
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = High	Week 12	Observed			
		n	29	36	65
		Mean	3.76	3.50	3.62
		SD, SE	1.123, 0.209	1.108, 0.185	1.114, 0.138
		Median	3.00	3.50	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.76 (0.202)	3.49 (0.199)	
		95% CI	(3.36, 4.15)	(3.10, 3.88)	
		LS Mean Difference (SE)		-0.27 (0.282)	
		95% CI		(-0.82, 0.28)	
		p-value		0.3367	
		HedgesG (95% CI)		-0.226 (-0.716, 0.265)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.15
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = High	Week 24	Baseline			
		n	28	36	64
		Mean	3.32	3.39	3.36
		SD, SE	0.723, 0.137	0.599, 0.100	0.651, 0.081
		Median	3.00	3.00	3.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	2.0, 4.0	2.0, 4.0	2.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.15
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = High	Week 24	Observed			
		n	28	36	64
		Mean	3.93	3.53	3.70
		SD, SE	1.120, 0.212	1.253, 0.209	1.204, 0.151
		Median	4.00	3.00	3.00
		Q1, Q3	3.00, 4.50	3.00, 4.00	3.00, 4.00
		Min, Max	3.0, 7.0	1.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	3.91 (0.204)	3.55 (0.220)	
		95% CI	(3.51, 4.31)	(3.12, 3.98)	
		LS Mean Difference (SE)		-0.36 (0.297)	
		95% CI		(-0.94, 0.22)	
		p-value		0.2284	
		HedgesG (95% CI)		-0.326 (-0.823, 0.172)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.15
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = Low		N1	36	30	66
	Baseline	n	36	30	66
		Mean	2.69	2.90	2.79
		SD, SE	0.786, 0.131	0.548, 0.100	0.691, 0.085
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	3.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.15
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = Low	Week 12	Baseline			
		n	36	30	66
		Mean	2.69	2.90	2.79
		SD, SE	0.786, 0.131	0.548, 0.100	0.691, 0.085
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	3.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.15
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = Low	Week 12	Observed			
		n	36	30	66
		Mean	3.50	3.50	3.50
		SD, SE	1.134, 0.189	1.253, 0.229	1.180, 0.145
		Median	4.00	3.50	4.00
		Q1, Q3	3.00, 4.00	3.00, 4.00	3.00, 4.00
		Min, Max	1.0, 6.0	1.0, 6.0	1.0, 6.0
		GEE Estimates			
		LS Mean (SE)	3.75 (0.213)	3.65 (0.242)	
		95% CI	(3.34, 4.17)	(3.18, 4.13)	
		LS Mean Difference (SE)		-0.10 (0.292)	
		95% CI		(-0.67, 0.47)	
		p-value		0.7281	
		HedgesG (95% CI)		0.000 (-0.485, 0.485)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.15
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = Low	Week 24	Baseline			
		n	35	30	65
		Mean	2.71	2.90	2.80
		SD, SE	0.789, 0.133	0.548, 0.100	0.689, 0.085
		Median	3.00	3.00	3.00
		Q1, Q3	2.00, 3.00	3.00, 3.00	3.00, 3.00
		Min, Max	1.0, 4.0	1.0, 4.0	1.0, 4.0

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 2.2.8.24.15
Subgroup Analysis: Patient global impression of improvement as measured by PGI-I
Primary Analysis Set_24 Weeks Analysis
Subgroup: 6MWT at baseline

Subgroup	Visit	Statistics	Placebo (N=66)	KRN23 (N=68)	Total (N=134)
6MWT score at BL = Low	Week 24	Observed			
		n	35	30	65
		Mean	3.80	3.57	3.69
		SD, SE	1.605, 0.271	1.251, 0.228	1.446, 0.179
		Median	4.00	3.00	4.00
		Q1, Q3	2.00, 5.00	3.00, 4.00	3.00, 5.00
		Min, Max	1.0, 7.0	2.0, 6.0	1.0, 7.0
		GEE Estimates			
		LS Mean (SE)	4.04 (0.288)	3.72 (0.248)	
		95% CI	(3.48, 4.61)	(3.23, 4.21)	
		LS Mean Difference (SE)		-0.32 (0.337)	
		95% CI		(-0.98, 0.34)	
		p-value		0.3372	
		HedgesG (95% CI)		-0.156 (-0.645, 0.332)	

Patient Global Impression of Severity (PGI-S) is taken at baseline visit with 4-point scale: 1 = Normal; 2 = Mild; 3 = Moderate; 4 = Severe. The PGI-I measures the improvement from baseline at post-baseline visit with 7-point scale: 1 = Very much better; 2 = Much better; 3 = A little better; 4 = No change; 5 = A little worse; 6 = Much worse; 7 = Very much worse.
The actual randomization stratification is based on the mean of the 7 days of BPI Average Pain diary scores prior to baseline visit.
The GEE Estimates are from the GEE model which includes the PGI-I as the dependent variable, actual randomization stratification, visit, treatment and visit by treatment as fixed factors, with compound symmetry covariance structure.
The baseline summary at each post-baseline visit is based on baseline of the subjects who had non-missing results at given visit.
Data source: ADSL.sas7bdat, ADPGI.sas7bdat Program source: s_pgii.sas

Table 5.1.2.24.1
Subgroup Analysis on Treatment Emergent AE
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
BPI Worst Pain > 6.0	TEAE	Placebo (39)	37 (94.9%)				
		Burosumab (51)		0.826	0.992	0.826	-0.008
			48 (94.1%)	0.125, 5.451	0.898, 1.097	0.129, 5.308	-0.102, 0.087
				0.8412	1.0000	0.841	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.1
Subgroup Analysis on Treatment Emergent AE
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
BPI Worst Pain <= 6.0 TEAE	Placebo (27)	24 (88.9%)				
	Burosumab (17)		2.118	1.059	2.118	0.052
		16 (94.1%)	0.179, 25.097	0.886, 1.266	0.193, 23.289	-0.111, 0.215
			0.5430	1.0000	0.539	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.2
Subgroup Analysis on Treatment Emergent AE
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
BPI Average Pain > 6.0 TEAE	Placebo (17)	16 (94.1%)				
	Burosumab (20)		1.100	1.009	1.100	0.009
		19 (95.0%)	0.054, 22.273	0.864, 1.179	0.060, 20.013	-0.138, 0.156
			0.9490	1.0000	0.949	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.2
Subgroup Analysis on Treatment Emergent AE
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
BPI Average Pain <= 6.0 TEAE	Placebo (49)	45 (91.8%)				
	Burosumab (48)		1.262	1.021	1.262	0.019
		45 (93.8%)	0.258, 6.164	0.914, 1.141	0.264, 6.040	-0.084, 0.122
			0.7712	1.0000	0.771	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.3
Subgroup Analysis on Treatment Emergent AE
Subgroup: Region
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Region North America/EU	TEAE	Placebo (58)	56 (96.6%)				
		Burosumab (58)		0.482	0.964	0.482	-0.034
			54 (93.1%)	0.083, 2.801	0.885, 1.050	0.085, 2.748	-0.115, 0.046
				0.4130	0.6791	0.411	0.6791

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.3
Subgroup Analysis on Treatment Emergent AE
Subgroup: Region
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Region Asia	TEAE	Placebo (8)	5 (62.5%)				
		Burosumab (10)		>999.999	1.600	40141	0.375
			10 (100.0%)	<0.001, >999.999	0.935, 2.737	0.000, 12E102	0.040, 0.710
				0.9848	0.0686	0.927	0.0686

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.4
Subgroup Analysis on Treatment Emergent AE
Subgroup: Gender
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Sex Male	TEAE	Placebo (23)	21 (91.3%)				
		Burosumab (24)		0.705	0.958	0.705	-0.038
			21 (87.5%)	0.095, 5.225	0.787, 1.167	0.101, 4.938	-0.213, 0.137
				0.7264	1.0000	0.725	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.4
Subgroup Analysis on Treatment Emergent AE
Subgroup: Gender
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Sex Female	TEAE	Placebo (43)	40 (93.0%)				
		Burosumab (44)		3.186	1.051	3.186	0.047
			43 (97.7%)	0.300, 33.876	0.957, 1.153	0.310, 32.716	-0.041, 0.135
				0.3324	0.3604	0.330	0.3604

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.5
Subgroup Analysis on Treatment Emergent AE
Subgroup: Race
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Race White	TEAE	Placebo (53)	51 (96.2%)				
		Burosumab (55)		0.502	0.964	0.502	-0.035
			51 (92.7%)	0.086, 2.935	0.880, 1.056	0.088, 2.875	-0.121, 0.051
				0.4407	0.6788	0.439	0.6788

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.5
Subgroup Analysis on Treatment Emergent AE
Subgroup: Race
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Race Non-White	TEAE	Placebo (13)	10 (76.9%)				
		Burosumab (13)		>999.999	1.300	87414	0.231
			13 (100.0%)	<0.001, >999.999	0.965, 1.751	0.000, 17E149	0.002, 0.460
				0.9809	0.2200	0.947	0.2200

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.6
Subgroup Analysis on Treatment Emergent AE
Subgroup: Age
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Age Group <=41 years TEAE	Placebo (36)	32 (88.9%)				
	Burosumab (31)		1.813	1.052	1.813	0.047
		29 (93.5%)	0.297, 11.083	0.908, 1.220	0.307, 10.710	-0.088, 0.181
			0.5139	0.6784	0.512	0.6784

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.6
Subgroup Analysis on Treatment Emergent AE
Subgroup: Age
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Age Group >41 years	TEAE	Placebo (30)	29 (96.7%)				
		Burosumab (37)		0.587	0.979	0.587	-0.021
			35 (94.6%)	0.048, 7.233	0.884, 1.083	0.050, 6.898	-0.118, 0.076
				0.6731	1.0000	0.672	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.7
Subgroup Analysis on Treatment Emergent AE
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Stiffness <=62.5	TEAE	Placebo (41)	36 (87.8%)				
		Burosumab (39)		2.415	1.080	2.415	0.071
			37 (94.9%)	0.421, 13.861	0.944, 1.237	0.433, 13.479	-0.051, 0.192
				0.3180	0.4327	0.315	0.4327

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.7
Subgroup Analysis on Treatment Emergent AE
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Stiffness >62.5	TEAE	Placebo (25)	25 (100.0%)				
		Burosumab (29)		<0.001	0.931	0.000	0.069
			27 (93.1%)	<0.001, >999.999	0.843, 1.028	0.000, 63E125	-0.023, 0.161
				0.9785	0.4934	0.945	0.4934

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.8
Subgroup Analysis on Treatment Emergent AE
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Physical Function <=47.8	TEAE	Placebo (37)	34 (91.9%)				
		Burosumab (30)		0.991	1.016	0.991	0.014
			28 (93.3%)	0.142, 6.935	0.887, 1.163	0.147, 6.681	-0.111, 0.140
				0.9925	1.0000	0.992	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.8
Subgroup Analysis on Treatment Emergent AE
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Physical Function >47.8	TEAE	Placebo (29)	27 (93.1%)				
		Burosumab (38)		1.334	1.018	1.334	0.016
			36 (94.7%)	0.169, 10.531	0.899, 1.152	0.176, 10.121	-0.100, 0.133
				0.7816	1.0000	0.781	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.9
Subgroup Analysis on Treatment Emergent AE
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Pain Medication Use at Baseline Yes	TEAE	Placebo (44)	42 (95.5%)				
		Burosumab (47)		0.701	0.981	0.701	-0.018
			44 (93.6%)	0.107, 4.569	0.889, 1.082	0.110, 4.451	-0.111, 0.075
				0.7070	1.0000	0.706	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.9
Subgroup Analysis on Treatment Emergent AE
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Pain Medication Use at Baseline No	TEAE	Placebo (22)	19 (86.4%)				
		Burosumab (21)		1.909	1.103	1.909	0.089
			20 (95.2%)	0.152, 24.016	0.910, 1.336	0.164, 22.202	-0.081, 0.259
				0.6084	0.6069	0.605	0.6069

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.10
Subgroup Analysis on Treatment Emergent AE
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Opioid Pain Medication Use at Baseline Yes	TEAE					
	Placebo (13)	13 (100.0%)				
	Burosumab (17)		<0.001	0.941	0.000	0.059
		16 (94.1%)	<0.001, >999.999	0.836, 1.060	0.000, 15E144	-0.053, 0.171
			0.9831	1.0000	0.954	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.10
Subgroup Analysis on Treatment Emergent AE
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Opioid Pain Medication Use at Baseline	TEAE					
No	Placebo (53)	48 (90.6%)				
	Burosumab (51)		1.531	1.039	1.531	0.036
		48 (94.1%)	0.335, 6.996	0.930, 1.161	0.341, 6.868	-0.066, 0.137
			0.5797	0.7159	0.578	0.7159

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.12
Subgroup Analysis on Treatment Emergent AE
Subgroup: Active Fracture and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Active Fractures and Pseudo Fractures Baseline Yes	TEAE	Placebo (38)	35 (92.1%)				
		Burosumab (32)		1.004	1.018	1.004	0.016
			30 (93.8%)	0.144, 7.019	0.895, 1.158	0.149, 6.773	-0.103, 0.136
				0.9970	1.0000	0.997	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.12
Subgroup Analysis on Treatment Emergent AE
Subgroup: Active Fracture and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Active Fractures and Pseudo Fractures at Baseline No	TEAE	Placebo (28)	26 (92.9%)				
		Burosumab (36)		1.033	1.017	1.033	0.016
			34 (94.4%)	0.126, 8.462	0.893, 1.158	0.131, 8.110	-0.105, 0.137
				0.9757	1.0000	0.976	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.13
Subgroup Analysis on Treatment Emergent AE
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
6MWT at Baseline Low TEAE	Placebo (29)	26 (89.7%)				
	Burosumab (37)		4.383	1.085	4.383	0.076
		36 (97.3%)	0.402, 47.804	0.948, 1.242	0.421, 45.626	-0.046, 0.199
			0.2210	0.3122	0.216	0.3122

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.13
Subgroup Analysis on Treatment Emergent AE
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
6MWT at Baseline High TEAE	Placebo (36)	34 (94.4%)				
	Burosumab (30)		0.433	0.953	0.433	-0.044
		27 (90.0%)	0.057, 3.312	0.826, 1.100	0.059, 3.183	-0.175, 0.086
			0.4140	0.6525	0.411	0.6525

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.15
Subgroup Analysis on Treatment Emergent AE
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Pain Score <=50.0	TEAE	Placebo (42)	39 (92.9%)				
		Burosumab (32)		0.902	1.010	0.902	0.009
			30 (93.8%)	0.127, 6.391	0.893, 1.141	0.132, 6.178	-0.106, 0.123
				0.9165	1.0000	0.916	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.15
Subgroup Analysis on Treatment Emergent AE
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Pain Score >50.0	TEAE	Placebo (24)	22 (91.7%)				
		Burosumab (35)		1.503	1.029	1.503	0.026
			33 (94.3%)	0.186, 12.119	0.889, 1.190	0.195, 11.575	-0.108, 0.161
				0.6973	1.0000	0.696	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.16
Subgroup Analysis on Treatment Emergent AE
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Total Score <=49.5	TEAE	Placebo (37)	34 (91.9%)				
		Burosumab (30)		1.046	1.016	1.046	0.014
			28 (93.3%)	0.151, 7.237	0.887, 1.163	0.157, 6.973	-0.111, 0.140
				0.9633	1.0000	0.963	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.1.2.24.16
Subgroup Analysis on Treatment Emergent AE
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Total Score >49.5	TEAE	Placebo (29)	27 (93.1%)				
		Burosumab (38)		1.322	1.018	1.322	0.016
			36 (94.7%)	0.167, 10.437	0.899, 1.152	0.174, 10.031	-0.100, 0.133
				0.7882	1.0000	0.787	1.0000

Note: Limited to Body System Organ Class and Preferred Terms that occur in at least 10% (7 patients) in a each subgroup.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24_SUB.sas7bdat, TEAESOCPT24_SUB.sas7bdat, TEAEPT24_SUB.sas7bdat Program source: TTE_LogARD_Sum_Wk24_Sub.sas

Table 5.3.2.24.1
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
BPI Worst Pain > 6.0	TEAE	Placebo (39)	5 (12.8%)				
		Burosumab (51)		0.912	0.918	0.912	-0.011
			6 (11.8%)	0.249, 3.343	0.302, 2.788	0.253, 3.282	-0.148, 0.127
				0.8884	1.0000	0.888	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.1
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Baseline BPI Worst Pain
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
BPI Worst Pain <= 6.0 TEAE	Placebo (27)	3 (11.1%)				
	Burosumab (17)		1.021	1.059	1.021	0.007
		2 (11.8%)	0.143, 7.275	0.197, 5.699	0.152, 6.856	-0.187, 0.200
			0.9829	1.0000	0.983	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.2
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
BPI Average Pain > 6.0 TEAE	Placebo (17)	1 (5.9%)				
	Burosumab (20)		3.991	3.400	3.990	0.141
		4 (20.0%)	0.368, 43.332	0.419, 27.592	0.400, 39.785	-0.067, 0.349
			0.2464	0.3479	0.238	0.3479

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.2
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Baseline BPI Average Pain
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
BPI Average Pain <= 6.0	TEAE	Placebo (49)	7 (14.3%)				
		Burosumab (48)		0.541	0.583	0.541	-0.060
			4 (8.3%)	0.144, 2.036	0.182, 1.865	0.146, 2.002	-0.185, 0.066
				0.3600	0.5240	0.358	0.5240

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.3
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Region
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Region North America/EU	TEAE	Placebo (58)	8 (13.8%)				
		Burosumab (58)		1.001	1.000	1.001	0.000
			8 (13.8%)	0.344, 2.914	0.403, 2.484	0.348, 2.881	-0.126, 0.126
				0.9990	1.0000	0.999	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.4
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Gender
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Gender Male	TEAE	Placebo (23)	3 (13.0%)				
		Burosumab (24)		1.153	1.278	1.153	0.036
			4 (16.7%)	0.207, 6.438	0.320, 5.096	0.217, 6.134	-0.167, 0.239
				0.8678	1.0000	0.867	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.4
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Gender
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Gender Female	TEAE	Placebo (43)	5 (11.6%)				
		Burosumab (44)		0.748	0.782	0.748	-0.025
			4 (9.1%)	0.180, 3.110	0.225, 2.717	0.184, 3.046	-0.153, 0.103
				0.6863	0.7387	0.685	0.7387

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.5
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Race
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Race White	TEAE	Placebo (53)	7 (13.2%)				
		Burosumab (55)		0.965	0.964	0.965	-0.005
			7 (12.7%)	0.309, 3.014	0.363, 2.561	0.313, 2.975	-0.132, 0.122
				0.9502	1.0000	0.950	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.5
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Race
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Race Non-White	TEAE	Placebo (13)	1 (7.7%)				
		Burosumab (13)		0.882	1.000	0.882	0.000
			1 (7.7%)	0.033, 23.842	0.070, 14.340	0.039, 19.893	-0.205, 0.205
				0.9378	1.0000	0.937	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.6
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Age
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Age Group <=41 years TEAE	Placebo (36)	4 (11.1%)				
	Burosumab (31)		1.171	1.161	1.171	0.018
		4 (12.9%)	0.258, 5.313	0.316, 4.261	0.266, 5.163	-0.138, 0.174
			0.8351	1.0000	0.834	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.7
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Stiffness at Baseline <=62.5	TEAE	Placebo (41)	6 (14.6%)				
		Burosumab (39)		1.091	1.051	1.091	0.008
			6 (15.4%)	0.311, 3.826	0.370, 2.984	0.317, 3.751	-0.149, 0.164
				0.8906	1.0000	0.890	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.7
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: WOMAC Stiffness at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Stiffness at Baseline >62.5	TEAE	Placebo (25)	2 (8.0%)				
		Burosumab (29)		0.715	0.862	0.715	-0.011
			2 (6.9%)	0.083, 6.158	0.131, 5.681	0.087, 5.845	-0.152, 0.130
				0.7556	1.0000	0.754	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.8
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Physical Function at Baseline <=47.8	TEAE	Placebo (37)	6 (16.2%)				
		Burosumab (30)		0.570	0.617	0.570	-0.062
			3 (10.0%)	0.126, 2.579	0.168, 2.262	0.130, 2.506	-0.222, 0.098
				0.4596	0.7206	0.457	0.7206

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.8
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: WOMAC Physical Function at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Physical Function at Baseline >47.8	TEAE	Placebo (29)	2 (6.9%)				
		Burosumab (38)	5 (13.2%)	2.092 0.361, 12.119 0.4043	1.908 0.398, 9.143 0.6899	2.092 0.373, 11.723 0.401	0.063 -0.079, 0.204 0.6899

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.9
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Pain Medication Use at Baseline	TEAE	Placebo (44)	6 (13.6%)				
Yes		Burosumab (47)		0.900	0.936	0.900	-0.009
			6 (12.8%)	0.261, 3.104	0.326, 2.687	0.266, 3.051	-0.148, 0.131
				0.8664	1.0000	0.866	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.9
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Pain Medication Use at Baseline	TEAE	Placebo (22)	2 (9.1%)				
No		Burosumab (21)	2 (9.5%)	0.802 0.071, 9.014 0.8546	1.048 0.162, 6.774 1.0000	0.802 0.077, 8.362 0.854	0.004 -0.169, 0.178 1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.10
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Opioid Pain Medication Use at Baseline	TEAE					
Yes	Placebo (13)	2 (15.4%)				
	Burosumab (17)		0.678	0.765	0.678	-0.036
		2 (11.8%)	0.072, 6.426	0.124, 4.730	0.079, 5.788	-0.285, 0.213
			0.7255	1.0000	0.723	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.10
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Opioid Pain Medication Use at Baseline
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Opioid Pain Medication Use at Baseline No	Placebo (53)	6 (11.3%)				
	Burosumab (51)	6 (11.8%)	1.067 0.314, 3.633 0.9162	1.039 0.359, 3.012 1.0000	1.067 0.318, 3.579 0.916	0.004 -0.118, 0.127 1.0000
TEAE						

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.12
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Active Fracture and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Active Fractures and Pseudo-Fractures at Baseline Yes	TEAE	Placebo (38)	4 (10.5%)				
		Burosumab (32)		0.955	0.891	0.955	-0.012
			3 (9.4%)	0.184, 4.952	0.215, 3.689	0.190, 4.805	-0.152, 0.129
				0.9555	1.0000	0.955	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.12
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: Active Fracture and Pseudo-Fractures at Baseline
(Primary Analysis Set - Week 24)

		Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
Active Fractures and Pseudo-Fractures at Baseline No	TEAE	Placebo (28)	4 (14.3%)				
		Burosumab (36)	5 (13.9%)	1.000 0.230, 4.341 0.9998	0.972 0.287, 3.288 1.0000	1.000 0.237, 4.215 1.000	-0.004 -0.176, 0.168 1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.13
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
6MWT at Baseline Low TEAE	Placebo (29)	3 (10.3%)				
	Burosumab (37)		1.051	1.045	1.051	0.005
		4 (10.8%)	0.202, 5.481	0.254, 4.305	0.208, 5.307	-0.145, 0.154
			0.9521	1.0000	0.952	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.13
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: 6MWT at Baseline
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
6MWT at Baseline High TEAE	Placebo (36)	5 (13.9%)				
	Burosumab (30)		0.903	0.960	0.903	-0.006
		4 (13.3%)	0.205, 3.967	0.283, 3.259	0.211, 3.854	-0.172, 0.160
			0.8905	1.0000	0.890	1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.15
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Pain Score at Baseline <=50.0	TEAE					
	Placebo (42)	4 (9.5%)				
	Burosumab (32)	3 (9.4%)	1.018 0.203, 5.108 0.9821	0.984 0.237, 4.091 1.0000	1.018 0.209, 4.967 0.982	-0.001 -0.136, 0.133 1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.15
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: WOMAC Pain Score at Baseline
(Primary Analysis Set - Week 24)

WOMAC Pain Score at Baseline >50.0	TEAE	Placebo (24)	4 (16.7%)			
		Burosumab (35)	5 (14.3%)	0.817 0.188, 3.554 0.7836	0.857 0.256, 2.868 1.0000	0.817 0.194, 3.441 0.783	-0.024 -0.213, 0.165 1.0000

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.16
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Total Score at Baseline <=49.5	Placebo (37)	6 (16.2%)				
	Burosumab (30)	3 (10.0%)	0.587 0.128, 2.687 0.4866	0.617 0.168, 2.262 0.7206	0.587 0.132, 2.610 0.484	-0.062 -0.222, 0.098 0.7206

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

Table 5.3.2.24.16
Subgroup Analysis on Treatment Emergent Severe AE (Grade 3,4,5)
Subgroup: WOMAC Total Score at Baseline
(Primary Analysis Set - Week 24)

	Treatment Group (N)	n (%)	OR 95% C.I. p-value	RR 95% C.I. p-value	ARR 95% C.I. p-value	RD 95% C.I. p-value
WOMAC Total Score at Baseline >49.5	Placebo (29)	2 (6.9%)				
	Burosumab (38)	5 (13.2%)	2.082 0.356, 12.168 0.4097	1.908 0.398, 9.143 0.6899	2.082 0.368, 11.761 0.407	0.063 -0.079, 0.204 0.6899

Note: Includes all severe Grade 3-5 AE up to Week 24.
N is the number of subjects in each subgroup and treatment group.
OR: Odds Ratio; RR: Relative Risk; ARR: Adjusted Relative Risk; RD: Risk Difference
OR is from logistic regression model.
Data source: ADSL.sas7bdat, ADTTEAE24S35.sas7bdat, SER35TEAESOCPT24.sas7bdat, SER35TEAEPT24.sas7bdat Program source: TTESAE_LogARD_Sum_Wk24.sas

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Table 14.3.1.2.9.1
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by BPI Worst Pain (<= 6.0 vs. > 6.0)
Double-Blind Period

BPI Worst Pain <= 6.0

Statistics	KRN23 (N=17)	Placebo (N=27)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	0 (2.8%) *	4 (14.8%)
Difference (KRN23 vs Placebo) - %	12.0%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	<0.001	
95% C.I. of odds ratio	<0.001, >999.999	
P-value	0.9804	
RR[2] (95% CI), P-value	0.188 (0.011, 3.336), 0.1873	
ARR[3] (95% CI), P-value	0.151 (0.009, 2.441), 0.1830**	
ARD[4]		
Difference (95% C.I.)	0.120 (-0.034, 0.274)	
P-value	0.1873	

* In the event of zero cells, the correction value of 0.5 is added to each cell frequency of the corresponding fourfold table
** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Table 14.3.1.2.9.1
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by BPI Worst Pain (<= 6.0 vs. > 6.0)
Double-Blind Period

BPI Worst Pain > 6.0

Statistics	KRN23 (N=51)	Placebo (N=39)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	6 (11.8%)	12 (30.8%)
Difference (KRN23 vs Placebo) - %	19.0%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.316	
95% C.I. of odds ratio	0.103, 0.972	
P-value	0.0445	
RR[2] (95% CI), P-value	0.382 (0.158, 0.928), 0.0340	
ARR[3] (95% CI), P-value	0.343 (0.120, 0.981), 0.0460**	
ARD[4]		
Difference (95% C.I.)	0.190 (0.020, 0.360)	
P-value	0.0340	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Table 14.3.1.2.9.2
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by BPI Average Pain (<= 6.0 vs. > 6.0)
Double-Blind Period

BPI Average Pain <= 6.0

Statistics	KRN23 (N=48)	Placebo (N=49)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	3 (6.3%)	11 (22.4%)
Difference (KRN23 vs Placebo) - %	16.2%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.221	
95% C.I. of odds ratio	0.055, 0.881	
P-value	0.0327	
RR[2] (95% CI), P-value	0.278 (0.083, 0.936), 0.0404	
ARR[3] (95% CI), P-value	0.252 (0.071, 0.889), 0.0322**	
ARD[4]		
Difference (95% C.I.)	0.162 (0.027, 0.297)	
P-value	0.0404	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Table 14.3.1.2.9.2
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by BPI Average Pain (<= 6.0 vs. > 6.0)
Double-Blind Period

BPI Average Pain > 6.0

Statistics	KRN23 (N=20)	Placebo (N=17)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	3 (15.0%)	5 (29.4%)
Difference (KRN23 vs Placebo) - %	14.4%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.480	
95% C.I. of odds ratio	0.089, 2.580	
P-value	0.3810	
RR[2] (95% CI), P-value	0.510 (0.142, 1.829), 0.4283	
ARR[3] (95% CI), P-value	0.513 (0.106, 2.483), 0.4069**	
ARD[4]		
Difference (95% C.I.)	0.144 (-0.123, 0.411)	
P-value	0.4283	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Table 14.3.1.2.9.3
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by Region (North America/EU vs. Asia)
Double-Blind Period

Region = North America/EU

Statistics	KRN23 (N=58)	Placebo (N=58)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	6 (10.3%)	16 (27.6%)
Difference (KRN23 vs Placebo) - %	17.2%	
Logistic Regression[1]		
Percentage of Patients - %	10.9%	29.1%
95% C.I.	4.9%, 22.5%	18.2%, 43.0%
Odds ratio (KRN23 vs Placebo)	0.299	
95% C.I. of odds ratio	0.106, 0.843	
P-value	0.0229	
RR[2] (95% CI), P-value	0.375 (0.158, 0.890), 0.0314	
ARR[3] (95% CI), P-value	0.299 (0.107, 0.834), 0.0211	
ARD[4]		
Difference (95% C.I.)	0.172 (0.033, 0.312)	
P-value	0.0314	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Table 14.3.1.2.9.3
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by Region (North America/EU vs. Asia)
Double-Blind Period

Region = Asia

Statistics	KRN23 (N=10)	Placebo (N=8)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	0 (4.5%) *	0 (5.6%) *
Difference (KRN23 vs Placebo) - %	1.0%	
Logistic Regression[1]		
Percentage of Patients - %	-	-
95% C.I.	-	-
Odds ratio (KRN23 vs Placebo)	-	
95% C.I. of odds ratio	-	
P-value	-	
RR[2] (95% CI), P-value	0.818 (0.018, 37.300), 0.9179	
ARR[3] (95% CI), P-value	-	
ARD[4]		
Difference (95% C.I.)	0.010 (-0.184, 0.204)	
P-value	0.9179	

* In the event of zero cells, the correction value of 0.5 is added to each cell frequency of the corresponding fourfold table

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Table 14.3.1.2.9.4
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by Sex (Male vs. Female)
Double-Blind Period

Sex = Male

Statistics	KRN23 (N=24)	Placebo (N=23)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	2 (8.3%)	3 (13.0%)
Difference (KRN23 vs Placebo) - %	4.7%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.457	
95% C.I. of odds ratio	0.054, 3.894	
P-value	0.4645	
RR[2] (95% CI), P-value	0.639 (0.117, 3.481), 0.6662	
ARR[3] (95% CI), P-value	0.540 (0.090, 3.233), 0.4994**	
ARD[4]		
Difference (95% C.I.)	0.047 (-0.129, 0.224)	
P-value	0.6662	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Table 14.3.1.2.9.4
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by Sex (Male vs. Female)
Double-Blind Period

Sex = Female

Statistics	KRN23 (N=44)	Placebo (N=43)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	4 (9.1%)	13 (30.2%)
Difference (KRN23 vs Placebo) - %	21.1%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.227	
95% C.I. of odds ratio	0.065, 0.794	
P-value	0.0208	
RR[2] (95% CI), P-value	0.301 (0.106, 0.850), 0.0158	
ARR[3] (95% CI), P-value	0.259 (0.082, 0.819), 0.0215**	
ARD[4]		
Difference (95% C.I.)	0.211 (0.050, 0.373)	
P-value	0.0158	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Table 14.3.1.2.9.5
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by Race (WHITE vs. NON-WHITE)
Double-Blind Period

Race = WHITE

Statistics	KRN23 (N=55)	Placebo (N=53)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	4 (7.3%)	14 (26.4%)
Difference (KRN23 vs Placebo) - %	19.1%	
Logistic Regression[1]		
Percentage of Patients - %	7.7%	28.0%
95% C.I.	2.9%, 19.0%	16.7%, 43.0%
Odds ratio (KRN23 vs Placebo)	0.214	
95% C.I. of odds ratio	0.064, 0.713	
P-value	0.0126	
RR[2] (95% CI), P-value	0.275 (0.097, 0.783), 0.0096	
ARR[3] (95% CI), P-value	0.214 (0.065, 0.704), 0.0111	
ARD[4]		
Difference (95% C.I.)	0.191 (0.054, 0.329)	
P-value	0.0096	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Table 14.3.1.2.9.5
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term
-
Safety Analysis Set by Race (WHITE vs. NON-WHITE)
Double-Blind Period

Race = NON-WHITE

Statistics	KRN23 (N=13)	Placebo (N=13)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	2 (15.4%)	2 (15.4%)
Difference (KRN23 vs Placebo) - %	0.0%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	3.278	
95% C.I. of odds ratio	0.117, 91.728	
P-value	0.4668	
RR[2] (95% CI), P-value	1.000 (0.165, 6.067), 1.0000	
ARR[3] (95% CI), P-value	2.119 (0.186, 24.187), 0.5454**	
ARD[4]		
Difference (95% C.I.)	0.000 (-0.277, 0.277)	
Difference (95% C.I.)	0.000 (-0.277, 0.277)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Table 14.3.1.2.9.6
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by Age (18 to 50 vs. >50 to 65)
Double-Blind Period

Age 18 to 50

Statistics	KRN23 (N=52)	Placebo (N=56)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	5 (9.6%)	13 (23.2%)
Difference (KRN23 vs Placebo) - %	13.6%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.365	
95% C.I. of odds ratio	0.117, 1.143	
P-value	0.0829	
RR[2] (95% CI), P-value	0.414 (0.159, 1.082), 0.0727	
ARR[3] (95% CI), P-value	0.395 (0.137, 1.143), 0.0866**	
ARD[4]		
Difference (95% C.I.)	0.136 (-0.001, 0.273)	
P-value	0.0727	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Table 14.3.1.2.9.6
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term
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Safety Analysis Set by Age (18 to 50 vs. >50 to 65)
Double-Blind Period

Age >50 to 65

Statistics	KRN23 (N=16)	Placebo (N=10)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	1 (6.3%)	3 (30.0%)
Difference (KRN23 vs Placebo) - %	23.8%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	37.5%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	<0.001	
95% C.I. of odds ratio	<0.001, >999.999	
P-value	0.9569	
RR[2] (95% CI), P-value	0.208 (0.025, 1.737), 0.2642	
ARR[3] (95% CI), P-value	0.083 (0.004, 1.768), 0.1106**	
ARD[4]		
Difference (95% C.I.)	0.238 (-0.070, 0.545)	
P-value	0.2642	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Table 14.3.1.2.9.7
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by WOMAC Stiffness (<=62.5 vs. >62.5)
Double-Blind Period

WOMAC Stiffness <=62.5

Statistics	KRN23 (N=39)	Placebo (N=41)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	4 (10.3%)	10 (24.4%)
Difference (KRN23 vs Placebo) - %	14.1%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.341	
95% C.I. of odds ratio	0.093, 1.253	
P-value	0.1037	
RR[2] (95% CI), P-value	0.421 (0.144, 1.230), 0.1415	
ARR[3] (95% CI), P-value	0.378 (0.114, 1.247), 0.1101**	
ARD[4]		
Difference (95% C.I.)	0.141 (-0.021, 0.304)	
P-value	0.1415	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Table 14.3.1.2.9.7
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by WOMAC Stiffness (<=62.5 vs. >62.5)
Double-Blind Period

WOMAC Stiffness >62.5

Statistics	KRN23 (N=29)	Placebo (N=25)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	2 (6.9%)	6 (24.0%)
Difference (KRN23 vs Placebo) - %	17.1%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.197	
95% C.I. of odds ratio	0.031, 1.251	
P-value	0.0835	
RR[2] (95% CI), P-value	0.287 (0.064, 1.299), 0.1252	
ARR[3] (95% CI), P-value	0.245 (0.049, 1.223), 0.0864**	
ARD[4]		
Difference (95% C.I.)	0.171 (-0.020, 0.362)	
P-value	0.1252	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.2.9.8
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by WOMAC Physical Function (<=47.8 vs. >47.8)
Double-Blind Period

WOMAC Physical Function <=47.8

Statistics	KRN23 (N=30)	Placebo (N=37)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	2 (6.7%)	10 (27.0%)
Difference (KRN23 vs Placebo) - %	20.4%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.175	
95% C.I. of odds ratio	0.033, 0.923	
P-value	0.0403	
RR[2] (95% CI), P-value	0.247 (0.058, 1.041), 0.0521	
ARR[3] (95% CI), P-value	0.220 (0.051, 0.943), 0.0415**	
ARD[4]		
Difference (95% C.I.)	0.204 (0.035, 0.372)	
P-value	0.0521	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.2.9.8
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by WOMAC Physical Function (<=47.8 vs. >47.8)
Double-Blind Period

WOMAC Physical Function >47.8

Statistics	KRN23 (N=38)	Placebo (N=29)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	4 (10.5%)	6 (20.7%)
Difference (KRN23 vs Placebo) - %	10.2%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.518	
95% C.I. of odds ratio	0.123, 2.175	
P-value	0.3627	
RR[2] (95% CI), P-value	0.509 (0.158, 1.638), 0.3093	
ARR[3] (95% CI), P-value	0.543 (0.144, 2.050), 0.3675**	
ARD[4]		
Difference (95% C.I.)	0.102 (-0.075, 0.278)	
P-value	0.3093	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.2.9.9
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term
-
Safety Analysis Set by WOMAC Pain (<=50.0 vs. >50.0)
Double-Blind Period

WOMAC Pain <=50.0

Statistics	KRN23 (N=32)	Placebo (N=42)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	2 (6.3%)	12 (28.6%)
Difference (KRN23 vs Placebo) - %	22.3%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.166	
95% C.I. of odds ratio	0.033, 0.847	
P-value	0.0313	
RR[2] (95% CI), P-value	0.219 (0.053, 0.909), 0.0176	
ARR[3] (95% CI), P-value	0.211 (0.051, 0.869), 0.0313**	
ARD[4]		
Difference (95% C.I.)	0.223 (0.063, 0.384)	
P-value	0.0176	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.2.9.9
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term
-
Safety Analysis Set by WOMAC Pain (<=50.0 vs. >50.0)
Double-Blind Period

WOMAC Pain >50.0

Statistics	KRN23 (N=35)	Placebo (N=24)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	4 (11.4%)	4 (16.7%)
Difference (KRN23 vs Placebo) - %	5.2%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.696	
95% C.I. of odds ratio	0.142, 3.407	
P-value	0.6492	
RR[2] (95% CI), P-value	0.686 (0.190, 2.478), 0.7037	
ARR[3] (95% CI), P-value	0.692 (0.163, 2.941), 0.6184**	
ARD[4]		
Difference (95% C.I.)	0.052 (-0.130, 0.235)	
P-value	0.7037	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.2.9.10
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by WOMAC Total Score (<=49.5 vs. >49.5)
Double-Blind Period

WOMAC Total Score <=49.5

Statistics	KRN23 (N=30)	Placebo (N=37)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	2 (6.7%)	10 (27.0%)
Difference (KRN23 vs Placebo) - %	20.4%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.175	
95% C.I. of odds ratio	0.033, 0.923	
P-value	0.0403	
RR[2] (95% CI), P-value	0.247 (0.058, 1.041), 0.0521	
ARR[3] (95% CI), P-value	0.220 (0.051, 0.943), 0.0415**	
ARD[4]		
Difference (95% C.I.)	0.204 (0.035, 0.372)	
P-value	0.0521	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.2.9.10
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by WOMAC Total Score (<=49.5 vs. >49.5)
Double-Blind Period

WOMAC Total Score >49.5

Statistics	KRN23 (N=38)	Placebo (N=29)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	4 (10.5%)	6 (20.7%)
Difference (KRN23 vs Placebo) - %	10.2%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.518	
95% C.I. of odds ratio	0.123, 2.175	
P-value	0.3627	
RR[2] (95% CI), P-value	0.509 (0.158, 1.638), 0.3093	
ARR[3] (95% CI), P-value	0.543 (0.144, 2.050), 0.3675**	
ARD[4]		
Difference (95% C.I.)	0.102 (-0.075, 0.278)	
P-value	0.3093	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.2.9.11
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by 6MWT (Low vs. High)
Double-Blind Period

6MWT = Low

Statistics	KRN23 (N=37)	Placebo (N=29)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	4 (10.8%)	8 (27.6%)
Difference (KRN23 vs Placebo) - %	16.8%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.346	
95% C.I. of odds ratio	0.087, 1.368	
P-value	0.1278	
RR[2] (95% CI), P-value	0.392 (0.131, 1.174), 0.1105	
ARR[3] (95% CI), P-value	0.385 (0.110, 1.348), 0.1355**	
ARD[4]		
Difference (95% C.I.)	0.168 (-0.023, 0.359)	
P-value	0.1105	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.2.9.11
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by 6MWT (Low vs. High)
Double-Blind Period

6MWT = High

Statistics	KRN23 (N=30)	Placebo (N=36)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	2 (6.7%)	7 (19.4%)
Difference (KRN23 vs Placebo) - %	12.8%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.303	
95% C.I. of odds ratio	0.054, 1.693	
P-value	0.1703	
RR[2] (95% CI), P-value	0.343 (0.077, 1.529), 0.1659	
ARR[3] (95% CI), P-value	0.363 (0.080, 1.642), 0.1883**	
ARD[4]		
Difference (95% C.I.)	0.128 (-0.029, 0.285)	
P-value	0.1659	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.2.9.12
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by Pain Medication Use at Baseline (No vs. Yes)
Double-Blind Period

Pain Medication Use at Baseline = No

Statistics	KRN23 (N=21)	Placebo (N=22)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	1 (4.8%)	5 (22.7%)
Difference (KRN23 vs Placebo) - %	18.0%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.147	
95% C.I. of odds ratio	0.013, 1.660	
P-value	0.1176	
RR[2] (95% CI), P-value	0.210 (0.027, 1.647), 0.1853	
ARR[3] (95% CI), P-value	0.228 (0.034, 1.526), 0.1274**	
ARD[4]		
Difference (95% C.I.)	0.180 (-0.018, 0.377)	
P-value	0.1853	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.2.9.12
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by Pain Medication Use at Baseline (No vs. Yes)
Double-Blind Period

Pain Medication Use at Baseline = Yes

Statistics	KRN23 (N=47)	Placebo (N=44)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	5 (10.6%)	11 (25.0%)
Difference (KRN23 vs Placebo) - %	14.4%	
Logistic Regression[1]		
Percentage of Patients - %	0.1%	0.2%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.378	
95% C.I. of odds ratio	0.117, 1.222	
P-value	0.1030	
RR[2] (95% CI), P-value	0.426 (0.161, 1.127), 0.0991	
ARR[3] (95% CI), P-value	0.403 (0.131, 1.239), 0.1128**	
ARD[4]		
Difference (95% C.I.)	0.144 (-0.012, 0.299)	
P-value	0.0991	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.2.9.13
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by Opioid Pain Medication Use at Baseline (No vs. Yes)
Double-Blind Period

Opioid Pain Medication Use at Baseline = No

Statistics	KRN23 (N=51)	Placebo (N=53)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	5 (9.8%)	12 (22.6%)
Difference (KRN23 vs Placebo) - %	12.8%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.383	
95% C.I. of odds ratio	0.120, 1.226	
P-value	0.1048	
RR[2] (95% CI), P-value	0.433 (0.164, 1.142), 0.1111	
ARR[3] (95% CI), P-value	0.414 (0.140, 1.219), 0.1095**	
ARD[4]		
Difference (95% C.I.)	0.128 (-0.011, 0.268)	
P-value	0.1111	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.2.9.13
Logistic Regression on Treatment Emergent Adverse Events by System Organ Class and Preferred Term

Safety Analysis Set by Opioid Pain Medication Use at Baseline (No vs. Yes)
Double-Blind Period

Opioid Pain Medication Use at Baseline = Yes

Statistics	KRN23 (N=17)	Placebo (N=13)
System Organ Class = Musculoskeletal and connective tissue disorders, and Preferred Term = Arthralgia		
Patients with TEAE - n(%)	1 (5.9%)	4 (30.8%)
Difference (KRN23 vs Placebo) - %	24.9%	
Logistic Regression[1]		
Percentage of Patients - %	6.0%	32.4%
95% C.I.	0.8%, 34.6%	11.7%, 63.5%
Odds ratio (KRN23 vs Placebo)	0.133	
95% C.I. of odds ratio	0.011, 1.587	
P-value	0.1065	
RR[2] (95% CI), P-value	0.191 (0.024, 1.513), 0.1377	
ARR[3] (95% CI), P-value	0.133 (0.012, 1.420), 0.0949	
ARD[4]		
Difference (95% C.I.)	0.249 (-0.026, 0.524)	
P-value	0.1377	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, region and actual randomization stratification as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE. Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-ae-soc-pt-sub.sas

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Adhoc Analysis of UX023-CL303

Table 14.3.1.13.1.9.2.1
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by BPI Worst Pain
Double Blind Period
Safety Analysis Set

BPI Worst Pain: <= 6.0

Statistics	KRN23 (N=17)	Placebo (N=27)
Patients with TEAE - n(%)	2 (11.8%)	4 (14.8%)
Difference (KRN23 vs Placebo) - %	3.1%	
Logistic Regression[1]		
Percentage of Patients - %	0.3%	0.4%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.705	
95% C.I. of odds ratio	0.094, 5.260	
P-value	0.7269	
RR[2] (95% CI), P-value	0.794 (0.163, 3.875), 1.0000	
ARR[3] (95% CI), P-value	0.797 (0.131, 4.857), 0.8052**	
ARD[4]		
Difference (95% C.I.)	0.031 (-0.173, 0.234)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.1.9.2.1
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by BPI Worst Pain
Double Blind Period
Safety Analysis Set

BPI Worst Pain: > 6.0

Statistics	KRN23 (N=51)	Placebo (N=39)
Patients with TEAE - n(%)	6 (11.8%)	4 (10.3%)
Difference (KRN23 vs Placebo) - %	1.5%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.258	
95% C.I. of odds ratio	0.320, 4.953	
P-value	0.7396	
RR[2] (95% CI), P-value	1.147 (0.347, 3.787), 1.0000	
ARR[3] (95% CI), P-value	1.208 (0.346, 4.213), 0.7673**	
ARD[4]		
Difference (95% C.I.)	0.015 (-0.115, 0.145)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.1.9.2.2
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by BPI Average Pain
Double Blind Period
Safety Analysis Set

BPI Average Pain: <= 6.0

Statistics	KRN23 (N=48)	Placebo (N=49)
Patients with TEAE - n(%)	7 (14.6%)	5 (10.2%)
Difference (KRN23 vs Placebo) - %	4.4%	
Logistic Regression[1]		
Percentage of Patients - %	18.2%	12.9%
95% C.I.	7.1%, 39.4%	4.4%, 32.2%
Odds ratio (KRN23 vs Placebo)	1.504	
95% C.I. of odds ratio	0.433, 5.221	
P-value	0.5169	
RR[2] (95% CI), P-value	1.429 (0.487, 4.193), 0.5529	
ARR[3] (95% CI), P-value	1.504 (0.440, 5.137), 0.5153	
ARD[4]		
Difference (95% C.I.)	0.044 (-0.087, 0.175)	
P-value	0.5529	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

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Table 14.3.1.13.1.9.2.2
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by BPI Average Pain
Double Blind Period
Safety Analysis Set

BPI Average Pain: > 6.0

Statistics	KRN23 (N=20)	Placebo (N=17)
Patients with TEAE - n(%)	1 (5.0%)	3 (17.6%)
Difference (KRN23 vs Placebo) - %	12.6%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.275	
95% C.I. of odds ratio	0.023, 3.217	
P-value	0.2930	
RR[2] (95% CI), P-value	0.283 (0.032, 2.479), 0.3153	
ARR[3] (95% CI), P-value	0.355 (0.044, 2.879), 0.3324**	
ARD[4]		
Difference (95% C.I.)	0.126 (-0.078, 0.331)	
P-value	0.3153	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
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Table 14.3.1.13.1.9.2.3
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Region
Double Blind Period
Safety Analysis Set

Region = North America/EU

Statistics	KRN23 (N=58)	Placebo (N=58)
Patients with TEAE - n(%)	6 (10.3%)	7 (12.1%)
Difference (KRN23 vs Placebo) - %	1.7%	
Logistic Regression[1]		
Percentage of Patients - %	10.4%	12.1%
95% C.I.	4.6%, 22.0%	5.6%, 24.2%
Odds ratio (KRN23 vs Placebo)	0.840	
95% C.I. of odds ratio	0.261, 2.706	
P-value	0.7685	
RR[2] (95% CI), P-value	0.857 (0.307, 2.396), 1.0000	
ARR[3] (95% CI), P-value	0.840 (0.264, 2.672), 0.7679	
ARD[4]		
Difference (95% C.I.)	0.017 (-0.098, 0.132)	
P-value	1.0000	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

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Table 14.3.1.13.1.9.2.3
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Region
Double Blind Period
Safety Analysis Set

Asia

Statistics	KRN23 (N=10)	Placebo (N=8)
Patients with TEAE - n(%)	2 (20.0%)	1 (12.5%)
Difference (KRN23 vs Placebo) - %	7.5%	
Logistic Regression[1]		
Percentage of Patients - %	0.1%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	2.337	
95% C.I. of odds ratio	0.130, 41.951	
P-value	0.5386	
RR[2] (95% CI), P-value	1.600 (0.175, 14.631), 1.0000	
ARR[3] (95% CI), P-value	1.862 (0.175, 19.783), 0.6061**	
ARD[4]		
Difference (95% C.I.)	0.075 (-0.263, 0.413)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

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Table 14.3.1.13.1.9.2.4
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Sex
Double Blind Period
Safety Analysis Set

Sex = Male

Statistics	KRN23 (N=24)	Placebo (N=23)
Patients with TEAE - n(%)	1 (4.2%)	1 (4.3%)
Difference (KRN23 vs Placebo) - %	0.2%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.076	
95% C.I. of odds ratio	0.049, 23.397	
P-value	0.9622	
RR[2] (95% CI), P-value	0.958 (0.064, 14.434), 1.0000	
ARR[3] (95% CI), P-value	1.044 (0.114, 9.594), 0.9699**	
ARD[4]		
Difference (95% C.I.)	0.002 (-0.114, 0.117)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
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Table 14.3.1.13.1.9.2.4
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Sex
Double Blind Period
Safety Analysis Set

Sex = Female

Statistics	KRN23 (N=44)	Placebo (N=43)
Patients with TEAE - n(%)	7 (15.9%)	7 (16.3%)
Difference (KRN23 vs Placebo) - %	0.4%	
Logistic Regression[1]		
Percentage of Patients - %	0.5%	0.5%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.996	
95% C.I. of odds ratio	0.308, 3.223	
P-value	0.9940	
RR[2] (95% CI), P-value	0.977 (0.374, 2.551), 1.0000	
ARR[3] (95% CI), P-value	0.997 (0.329, 3.023), 0.9952**	
ARD[4]		
Difference (95% C.I.)	0.004 (-0.151, 0.158)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
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Table 14.3.1.13.1.9.2.5
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Race
Double Blind Period
Safety Analysis Set

Race = WHITE

Statistics	KRN23 (N=55)	Placebo (N=53)
Patients with TEAE - n(%)	6 (10.9%)	6 (11.3%)
Difference (KRN23 vs Placebo) - %	0.4%	
Logistic Regression[1]		
Percentage of Patients - %	10.5%	10.8%
95% C.I.	4.5%, 22.6%	4.5%, 23.6%
Odds ratio (KRN23 vs Placebo)	0.968	
95% C.I. of odds ratio	0.287, 3.266	
P-value	0.9577	
RR[2] (95% CI), P-value	0.964 (0.332, 2.801), 1.0000	
ARR[3] (95% CI), P-value	0.968 (0.291, 3.220), 0.9576	
ARD[4]		
Difference (95% C.I.)	0.004 (-0.114, 0.123)	
P-value	1.0000	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

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Table 14.3.1.13.1.9.2.5
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Race
Double Blind Period
Safety Analysis Set

Race = NON-WHITE

Statistics	KRN23 (N=13)	Placebo (N=13)
Patients with TEAE - n(%)	2 (15.4%)	2 (15.4%)
Difference (KRN23 vs Placebo) - %	0.0%	
Logistic Regression[1]		
Percentage of Patients - %	15.4%	16.6%
95% C.I.	3.1%, 51.0%	3.1%, 55.1%
Odds ratio (KRN23 vs Placebo)	0.921	
95% C.I. of odds ratio	0.089, 9.509	
P-value	0.9422	
RR[2] (95% CI), P-value	1.000 (0.165, 6.067), 1.0000	
ARR[3] (95% CI), P-value	0.921 (0.102, 8.314), 0.9415	
ARD[4]		
Difference (95% C.I.)	0.000 (-0.277, 0.277)	
Difference (95% C.I.)	0.000 (-0.277, 0.277)	
P-value	1.0000	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
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Table 14.3.1.13.1.9.2.6
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Age Group
Double Blind Period
Safety Analysis Set

Age = 18 to 50 Years

Statistics	KRN23 (N=52)	Placebo (N=56)
Patients with TEAE - n(%)	4 (7.7%)	8 (14.3%)
Difference (KRN23 vs Placebo) - %	6.6%	
Logistic Regression[1]		
Percentage of Patients - %	9.3%	17.2%
95% C.I.	2.6%, 27.9%	5.7%, 41.6%
Odds ratio (KRN23 vs Placebo)	0.490	
95% C.I. of odds ratio	0.135, 1.775	
P-value	0.2739	
RR[2] (95% CI), P-value	0.538 (0.172, 1.683), 0.3636	
ARR[3] (95% CI), P-value	0.490 (0.137, 1.748), 0.2714	
ARD[4]		
Difference (95% C.I.)	0.066 (-0.051, 0.183)	
P-value	0.3636	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
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Table 14.3.1.13.1.9.2.6
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Age Group
Double Blind Period
Safety Analysis Set

Age = >50 to 65 Years

Statistics	KRN23 (N=16)	Placebo (N=10)
Patients with TEAE - n(%)	4 (25.0%)	0 (4.5%) *
Difference (KRN23 vs Placebo) - %	20.5%	
Logistic Regression[1]		
Percentage of Patients - %	23.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	>999.999	
95% C.I. of odds ratio	<0.001, >999.999	
P-value	0.9465	
RR[2] (95% CI), P-value	5.500 (0.322, 93.944), 0.1611	
ARR[3] (95% CI), P-value	11.750 (0.443, 311.932), 0.1408**	
ARD[4]		
Difference (95% C.I.)	0.205 (-0.041, 0.450)	
P-value	0.1611	

* In the event of zero cells, the correction value of 0.5 is added to each cell frequency of the corresponding fourfold table
** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
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Table 14.3.1.13.1.9.2.7
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by WOMAC Stiffness
Double Blind Period
Safety Analysis Set

WOMAC Stiffness = <=62.5

Statistics	KRN23 (N=39)	Placebo (N=41)
Patients with TEAE - n(%)	5 (12.8%)	5 (12.2%)
Difference (KRN23 vs Placebo) - %	0.6%	
Logistic Regression[1]		
Percentage of Patients - %	26.3%	24.2%
95% C.I.	8.6%, 57.7%	7.8%, 54.7%
Odds ratio (KRN23 vs Placebo)	1.118	
95% C.I. of odds ratio	0.280, 4.470	
P-value	0.8731	
RR[2] (95% CI), P-value	1.051 (0.330, 3.352), 1.0000	
ARR[3] (95% CI), P-value	1.118 (0.286, 4.372), 0.8727	
ARD[4]		
Difference (95% C.I.)	0.006 (-0.139, 0.151)	
P-value	1.0000	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

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Table 14.3.1.13.1.9.2.7
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by WOMAC Stiffness
Double Blind Period
Safety Analysis Set

WOMAC Stiffness = >62.5

Statistics	KRN23 (N=29)	Placebo (N=25)
Patients with TEAE - n(%)	3 (10.3%)	3 (12.0%)
Difference (KRN23 vs Placebo) - %	1.7%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.006	
95% C.I. of odds ratio	0.168, 6.008	
P-value	0.9949	
RR[2] (95% CI), P-value	0.862 (0.191, 3.896), 1.0000	
ARR[3] (95% CI), P-value	1.029 (0.216, 4.909), 0.9714**	
ARD[4]		
Difference (95% C.I.)	0.017 (-0.152, 0.185)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

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Table 14.3.1.13.1.9.2.8
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by WOMAC Physical Function
Double Blind Period
Safety Analysis Set

WOMAC Physical Function: <=47.8

Statistics	KRN23 (N=30)	Placebo (N=37)
Patients with TEAE - n(%)	4 (13.3%)	4 (10.8%)
Difference (KRN23 vs Placebo) - %	2.5%	
Logistic Regression[1]		
Percentage of Patients - %	0.1%	0.1%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.355	
95% C.I. of odds ratio	0.288, 6.374	
P-value	0.6962	
RR[2] (95% CI), P-value	1.233 (0.336, 4.523), 1.0000	
ARR[3] (95% CI), P-value	1.316 (0.323, 5.367), 0.7021**	
ARD[4]		
Difference (95% C.I.)	0.025 (-0.132, 0.183)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

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Table 14.3.1.13.1.9.2.8
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by WOMAC Physical Function
Double Blind Period
Safety Analysis Set

WOMAC Physical Function: >47.8

Statistics	KRN23 (N=38)	Placebo (N=29)
Patients with TEAE - n(%)	4 (10.5%)	4 (13.8%)
Difference (KRN23 vs Placebo) - %	3.3%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.832	
95% C.I. of odds ratio	0.182, 3.798	
P-value	0.8089	
RR[2] (95% CI), P-value	0.763 (0.208, 2.797), 0.7188	
ARR[3] (95% CI), P-value	0.838 (0.209, 3.357), 0.8030**	
ARD[4]		
Difference (95% C.I.)	0.033 (-0.126, 0.192)	
P-value	0.7188	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

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Table 14.3.1.13.1.9.2.9
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by WOMAC Pain
Double Blind Period
Safety Analysis Set

WOMAC Pain at BL cat: <=50.0

Statistics	KRN23 (N=32)	Placebo (N=42)
Patients with TEAE - n(%)	4 (12.5%)	4 (9.5%)
Difference (KRN23 vs Placebo) - %	3.0%	
Logistic Regression[1]		
Percentage of Patients - %	0.1%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.270	
95% C.I. of odds ratio	0.264, 6.102	
P-value	0.7620	
RR[2] (95% CI), P-value	1.313 (0.355, 4.852), 0.7200	
ARR[3] (95% CI), P-value	1.256 (0.303, 5.202), 0.7534**	
ARD[4]		
Difference (95% C.I.)	0.030 (-0.115, 0.175)	
P-value	0.7200	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

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Table 14.3.1.13.1.9.2.9
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by WOMAC Pain
Double Blind Period
Safety Analysis Set

WOMAC Pain at BL cat: >50.0

Statistics	KRN23 (N=35)	Placebo (N=24)
Patients with TEAE - n(%)	4 (11.4%)	4 (16.7%)
Difference (KRN23 vs Placebo) - %	5.2%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.670	
95% C.I. of odds ratio	0.143, 3.143	
P-value	0.6058	
RR[2] (95% CI), P-value	0.686 (0.190, 2.478), 0.7037	
ARR[3] (95% CI), P-value	0.689 (0.167, 2.839), 0.6060**	
ARD[4]		
Difference (95% C.I.)	0.052 (-0.130, 0.235)	
P-value	0.7037	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

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Table 14.3.1.13.1.9.2.10
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by WOMAC Total Score
Double Blind Period
Safety Analysis Set

WOMAC Total Score at BL: <=49.5

Statistics	KRN23 (N=30)	Placebo (N=37)
Patients with TEAE - n(%)	4 (13.3%)	4 (10.8%)
Difference (KRN23 vs Placebo) - %	2.5%	
Logistic Regression[1]		
Percentage of Patients - %	0.1%	0.1%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.355	
95% C.I. of odds ratio	0.288, 6.374	
P-value	0.6962	
RR[2] (95% CI), P-value	1.233 (0.336, 4.523), 1.0000	
ARR[3] (95% CI), P-value	1.316 (0.323, 5.367), 0.7021**	
ARD[4]		
Difference (95% C.I.)	0.025 (-0.132, 0.183)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

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Table 14.3.1.13.1.9.2.10
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by WOMAC Total Score
Double Blind Period
Safety Analysis Set

WOMAC Total Score at BL: >49.5

Statistics	KRN23 (N=38)	Placebo (N=29)
Patients with TEAE - n(%)	4 (10.5%)	4 (13.8%)
Difference (KRN23 vs Placebo) - %	3.3%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.832	
95% C.I. of odds ratio	0.182, 3.798	
P-value	0.8089	
RR[2] (95% CI), P-value	0.763 (0.208, 2.797), 0.7188	
ARR[3] (95% CI), P-value	0.838 (0.209, 3.357), 0.8030**	
ARD[4]		
Difference (95% C.I.)	0.033 (-0.126, 0.192)	
P-value	0.7188	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.1.9.2.14
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Active fractures and pseudo-fractures at BL
Double Blind Period
Safety Analysis Set

Active fractures and pseudo-fractures at BL = Yes

Statistics	KRN23 (N=32)	Placebo (N=38)
Patients with TEAE - n(%)	2 (6.3%)	5 (13.2%)
Difference (KRN23 vs Placebo) - %	6.9%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.518	
95% C.I. of odds ratio	0.088, 3.061	
P-value	0.4622	
RR[2] (95% CI), P-value	0.475 (0.099, 2.285), 0.4415	
ARR[3] (95% CI), P-value	0.591 (0.131, 2.662), 0.4931**	
ARD[4]		
Difference (95% C.I.)	0.069 (-0.067, 0.205)	
P-value	0.4415	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.1.9.2.14
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Active fractures and pseudo-fractures at BL
Double Blind Period
Safety Analysis Set

Active fractures and pseudo-fractures at BL = No

Statistics	KRN23 (N=36)	Placebo (N=28)
Patients with TEAE - n(%)	6 (16.7%)	3 (10.7%)
Difference (KRN23 vs Placebo) - %	6.0%	
Logistic Regression[1]		
Percentage of Patients - %	23.7%	12.6%
95% C.I.	6.2%, 59.5%	2.2%, 47.8%
Odds ratio (KRN23 vs Placebo)	2.161	
95% C.I. of odds ratio	0.426, 10.965	
P-value	0.3462	
RR[2] (95% CI), P-value	1.556 (0.426, 5.679), 0.7197	
ARR[3] (95% CI), P-value	2.161 (0.440, 10.606), 0.3423	
ARD[4]		
Difference (95% C.I.)	0.060 (-0.108, 0.227)	
P-value	0.7197	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.1.9.2.12
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Pain Medication Use at BL
Double Blind Period
Safety Analysis Set

Pain Medication Use at BL = Yes

Statistics	KRN23 (N=47)	Placebo (N=44)
Patients with TEAE - n(%)	6 (12.8%)	7 (15.9%)
Difference (KRN23 vs Placebo) - %	3.1%	
Logistic Regression[1]		
Percentage of Patients - %	0.1%	0.1%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.817	
95% C.I. of odds ratio	0.247, 2.703	
P-value	0.7373	
RR[2] (95% CI), P-value	0.802 (0.292, 2.203), 0.7684	
ARR[3] (95% CI), P-value	0.828 (0.264, 2.600), 0.7462**	
ARD[4]		
Difference (95% C.I.)	0.031 (-0.113, 0.176)	
P-value	0.7684	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.1.9.2.12
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Pain Medication Use at BL
Double Blind Period
Safety Analysis Set

Pain Medication Use at BL = No

Statistics	KRN23 (N=21)	Placebo (N=22)
Patients with TEAE - n(%)	2 (9.5%)	1 (4.5%)
Difference (KRN23 vs Placebo) - %	5.0%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	2.883	
95% C.I. of odds ratio	0.181, 45.825	
P-value	0.4431	
RR[2] (95% CI), P-value	2.095 (0.205, 21.423), 0.6069	
ARR[3] (95% CI), P-value	2.097 (0.246, 17.910), 0.4985**	
ARD[4]		
Difference (95% C.I.)	0.050 (-0.103, 0.203)	
P-value	0.6069	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.1.9.2.13
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Opioid Pain Medication Use at BL
Double Blind Period
Safety Analysis Set

Opioid Pain Medication Use at BL = Yes

Statistics	KRN23 (N=17)	Placebo (N=13)
Patients with TEAE - n(%)	1 (5.9%)	3 (23.1%)
Difference (KRN23 vs Placebo) - %	17.2%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.1%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.222	
95% C.I. of odds ratio	0.016, 3.005	
P-value	0.2464	
RR[2] (95% CI), P-value	0.255 (0.030, 2.177), 0.2903	
ARR[3] (95% CI), P-value	0.300 (0.036, 2.496), 0.2656**	
ARD[4]		
Difference (95% C.I.)	0.172 (-0.083, 0.427)	
P-value	0.2903	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.1.9.2.13
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by Opioid Pain Medication Use at BL
Double Blind Period
Safety Analysis Set

Opioid Pain Medication Use at BL = No

Statistics	KRN23 (N=51)	Placebo (N=53)
Patients with TEAE - n(%)	7 (13.7%)	5 (9.4%)
Difference (KRN23 vs Placebo) - %	4.3%	
Logistic Regression[1]		
Percentage of Patients - %	18.5%	13.4%
95% C.I.	7.1%, 40.3%	4.2%, 35.0%
Odds ratio (KRN23 vs Placebo)	1.470	
95% C.I. of odds ratio	0.424, 5.105	
P-value	0.5403	
RR[2] (95% CI), P-value	1.455 (0.493, 4.290), 0.5513	
ARR[3] (95% CI), P-value	1.470 (0.430, 5.028), 0.5389	
ARD[4]		
Difference (95% C.I.)	0.043 (-0.080, 0.166)	
P-value	0.5513	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

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Adhoc Analysis of UX023-CL303

Table 14.3.1.13.1.9.2.11
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by 6MWT score at BL
Double Blind Period
Safety Analysis Set

6MWT score at BL cat = High

Statistics	KRN23 (N=30)	Placebo (N=36)
Patients with TEAE - n(%)	5 (16.7%)	3 (8.3%)
Difference (KRN23 vs Placebo) - %	8.3%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	2.785	
95% C.I. of odds ratio	0.560, 13.849	
P-value	0.2066	
RR[2] (95% CI), P-value	2.000 (0.520, 7.691), 0.4525	
ARR[3] (95% CI), P-value	2.504 (0.574, 10.927), 0.2220**	
ARD[4]		
Difference (95% C.I.)	0.083 (-0.078, 0.244)	
P-value	0.4525	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.1.9.2.11
Logistic Regression on Tretment-Emergent AESI-Any Injection Site Reaction by 6MWT score at BL
Double Blind Period
Safety Analysis Set

6MWT score at BL cat = Low

Statistics	KRN23 (N=37)	Placebo (N=29)
Patients with TEAE - n(%)	3 (8.1%)	5 (17.2%)
Difference (KRN23 vs Placebo) - %	9.1%	
Logistic Regression[1]		
Percentage of Patients - %	0.3%	0.6%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.432	
95% C.I. of odds ratio	0.089, 2.099	
P-value	0.2925	
RR[2] (95% CI), P-value	0.470 (0.122, 1.807), 0.2852	
ARR[3] (95% CI), P-value	0.483 (0.118, 1.980), 0.3119**	
ARD[4]		
Difference (95% C.I.)	0.091 (-0.072, 0.255)	
P-value	0.2852	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-isr-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.5.9.2.1
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by BPI Worst Pain
Double Blind Period
Safety Analysis Set

BPI Worst Pain: <= 6.0

Statistics	KRN23 (N=17)	Placebo (N=27)
Patients with TEAE - n(%)	2 (11.8%)	2 (7.4%)
Difference (KRN23 vs Placebo) - %	4.4%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.583	
95% C.I. of odds ratio	0.183, 13.672	
P-value	0.6687	
RR[2] (95% CI), P-value	1.588 (0.246, 10.240), 0.6337	
ARR[3] (95% CI), P-value	1.517 (0.249, 9.244), 0.6516**	
ARD[4]		
Difference (95% C.I.)	0.044 (-0.139, 0.226)	
P-value	0.6337	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.5.9.2.1
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by BPI Worst Pain
Double Blind Period
Safety Analysis Set

BPI Worst Pain: > 6.0

Statistics	KRN23 (N=51)	Placebo (N=39)
Patients with TEAE - n(%)	6 (11.8%)	4 (10.3%)
Difference (KRN23 vs Placebo) - %	1.5%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.280	
95% C.I. of odds ratio	0.325, 5.052	
P-value	0.7212	
RR[2] (95% CI), P-value	1.147 (0.347, 3.787), 1.0000	
ARR[3] (95% CI), P-value	1.223 (0.349, 4.284), 0.7531**	
ARD[4]		
Difference (95% C.I.)	0.015 (-0.115, 0.145)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.5.9.2.2
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by BPI Average Pain
Double Blind Period
Safety Analysis Set

BPI Average Pain: <= 6.0

Statistics	KRN23 (N=48)	Placebo (N=49)
Patients with TEAE - n(%)	5 (10.4%)	4 (8.2%)
Difference (KRN23 vs Placebo) - %	2.3%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.321	
95% C.I. of odds ratio	0.322, 5.423	
P-value	0.6960	
RR[2] (95% CI), P-value	1.276 (0.364, 4.468), 0.7404	
ARR[3] (95% CI), P-value	1.284 (0.356, 4.632), 0.7024**	
ARD[4]		
Difference (95% C.I.)	0.023 (-0.093, 0.138)	
P-value	0.7404	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.5.9.2.2
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by BPI Average Pain
Double Blind Period
Safety Analysis Set

BPI Average Pain: > 6.0

Statistics	KRN23 (N=20)	Placebo (N=17)
Patients with TEAE - n(%)	3 (15.0%)	2 (11.8%)
Difference (KRN23 vs Placebo) - %	3.2%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.500	
95% C.I. of odds ratio	0.203, 11.087	
P-value	0.6827	
RR[2] (95% CI), P-value	1.275 (0.240, 6.761), 1.0000	
ARR[3] (95% CI), P-value	1.400 (0.227, 8.636), 0.7167**	
ARD[4]		
Difference (95% C.I.)	0.032 (-0.187, 0.251)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.5.9.2.3
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Region
Double Blind Period
Safety Analysis Set

Region = North America/EU

Statistics	KRN23 (N=58)	Placebo (N=58)
Patients with TEAE - n(%)	8 (13.8%)	6 (10.3%)
Difference (KRN23 vs Placebo) - %	3.4%	
Logistic Regression[1]		
Percentage of Patients - %	14.4%	10.8%
95% C.I.	7.2%, 26.7%	4.8%, 22.6%
Odds ratio (KRN23 vs Placebo)	1.381	
95% C.I. of odds ratio	0.441, 4.320	
P-value	0.5766	
RR[2] (95% CI), P-value	1.333 (0.493, 3.603), 0.7767	
ARR[3] (95% CI), P-value	1.380 (0.447, 4.267), 0.5755	
ARD[4]		
Difference (95% C.I.)	0.034 (-0.084, 0.153)	
P-value	0.7767	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.5.9.2.3
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Region
Double Blind Period
Safety Analysis Set

Asia

Statistics	KRN23 (N=10)	Placebo (N=8)
Patients with TEAE - n(%)	0 (4.5%) *	0 (5.6%) *
Difference (KRN23 vs Placebo) - %	1.0%	
Logistic Regression[1]		
Percentage of Patients - %	-	-
95% C.I.	-	-
Odds ratio (KRN23 vs Placebo)	-	
95% C.I. of odds ratio	-	
P-value	-	
RR[2] (95% CI), P-value	0.818 (0.018, 37.300), 0.9179	
ARR[3] (95% CI), P-value	-	
ARD[4]		
Difference (95% C.I.)	0.010 (-0.184, 0.204)	
P-value	0.9179	

* In the event of zero cells, the correction value of 0.5 is added to each cell frequency of the corresponding fourfold table
** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
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Table 14.3.1.13.5.9.2.4
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Sex
Double Blind Period
Safety Analysis Set

Sex = Male

Statistics	KRN23 (N=24)	Placebo (N=23)
Patients with TEAE - n(%)	4 (16.7%)	1 (4.3%)
Difference (KRN23 vs Placebo) - %	12.3%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	5.818	
95% C.I. of odds ratio	0.533, 63.543	
P-value	0.1446	
RR[2] (95% CI), P-value	3.833 (0.462, 31.788), 0.3475	
ARR[3] (95% CI), P-value	3.971 (0.609, 25.874), 0.1493**	
ARD[4]		
Difference (95% C.I.)	0.123 (-0.048, 0.294)	
P-value	0.3475	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
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Table 14.3.1.13.5.9.2.4
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Sex
Double Blind Period
Safety Analysis Set

Sex = Female

Statistics	KRN23 (N=44)	Placebo (N=43)
Patients with TEAE - n(%)	4 (9.1%)	5 (11.6%)
Difference (KRN23 vs Placebo) - %	2.5%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.792	
95% C.I. of odds ratio	0.189, 3.312	
P-value	0.7460	
RR[2] (95% CI), P-value	0.782 (0.225, 2.717), 0.7387	
ARR[3] (95% CI), P-value	0.807 (0.222, 2.939), 0.7451**	
ARD[4]		
Difference (95% C.I.)	0.025 (-0.103, 0.153)	
P-value	0.7387	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
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Table 14.3.1.13.5.9.2.5
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Race
Double Blind Period
Safety Analysis Set

Race = WHITE

Statistics	KRN23 (N=55)	Placebo (N=53)
Patients with TEAE - n(%)	8 (14.5%)	6 (11.3%)
Difference (KRN23 vs Placebo) - %	3.2%	
Logistic Regression[1]		
Percentage of Patients - %	15.3%	12.1%
95% C.I.	7.7%, 28.2%	5.4%, 25.0%
Odds ratio (KRN23 vs Placebo)	1.312	
95% C.I. of odds ratio	0.416, 4.141	
P-value	0.6404	
RR[2] (95% CI), P-value	1.285 (0.478, 3.454), 0.7762	
ARR[3] (95% CI), P-value	1.312 (0.421, 4.087), 0.6394	
ARD[4]		
Difference (95% C.I.)	0.032 (-0.094, 0.159)	
P-value	0.7762	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
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Table 14.3.1.13.5.9.2.5
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Race
Double Blind Period
Safety Analysis Set

Race = NON-WHITE

Statistics	KRN23 (N=13)	Placebo (N=13)
Patients with TEAE - n(%)	0 (3.6%) *	0 (3.6%) *
Difference (KRN23 vs Placebo) - %	0.0%	
Logistic Regression[1]		
Percentage of Patients - %	-	-
95% C.I.	-	-
Odds ratio (KRN23 vs Placebo)	-	
95% C.I. of odds ratio	-	
P-value	-	
RR[2] (95% CI), P-value	1.000 (0.021, 46.960), 1.0000	
ARR[3] (95% CI), P-value	-	
ARD[4]		
Difference (95% C.I.)	0.000 (-0.137, 0.137)	
Difference (95% C.I.)	0.000 (-0.137, 0.137)	
P-value	1.0000	

* In the event of zero cells, the correction value of 0.5 is added to each cell frequency of the corresponding fourfold table
** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

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Table 14.3.1.13.5.9.2.6
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Age Group
Double Blind Period
Safety Analysis Set

Age = 18 to 50 Years

Statistics	KRN23 (N=52)	Placebo (N=56)
Patients with TEAE - n(%)	3 (5.8%)	5 (8.9%)
Difference (KRN23 vs Placebo) - %	3.2%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.664	
95% C.I. of odds ratio	0.146, 3.017	
P-value	0.5931	
RR[2] (95% CI), P-value	0.646 (0.162, 2.570), 0.7175	
ARR[3] (95% CI), P-value	0.710 (0.188, 2.677), 0.6133**	
ARD[4]		
Difference (95% C.I.)	0.032 (-0.066, 0.130)	
P-value	0.7175	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

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Table 14.3.1.13.5.9.2.6
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Age Group
Double Blind Period
Safety Analysis Set

Age = >50 to 65 Years

Statistics	KRN23 (N=16)	Placebo (N=10)
Patients with TEAE - n(%)	5 (31.3%)	1 (10.0%)
Difference (KRN23 vs Placebo) - %	21.3%	
Logistic Regression[1]		
Percentage of Patients - %	0.2%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	3.774	
95% C.I. of odds ratio	0.302, 47.166	
P-value	0.2873	
RR[2] (95% CI), P-value	3.125 (0.424, 23.007), 0.3524	
ARR[3] (95% CI), P-value	2.647 (0.337, 20.793), 0.3546**	
ARD[4]		
Difference (95% C.I.)	0.213 (-0.081, 0.506)	
P-value	0.3524	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

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Table 14.3.1.13.5.9.2.12
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Pain Medication Use at BL
Double Blind Period
Safety Analysis Set

Pain Medication Use at BL = Yes

Statistics	KRN23 (N=47)	Placebo (N=44)
Patients with TEAE - n(%)	5 (10.6%)	5 (11.4%)
Difference (KRN23 vs Placebo) - %	0.7%	
Logistic Regression[1]		
Percentage of Patients - %	0.1%	0.1%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.994	
95% C.I. of odds ratio	0.260, 3.799	
P-value	0.9926	
RR[2] (95% CI), P-value	0.936 (0.291, 3.015), 1.0000	
ARR[3] (95% CI), P-value	0.993 (0.280, 3.519), 0.9910**	
ARD[4]		
Difference (95% C.I.)	0.007 (-0.121, 0.136)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

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Table 14.3.1.13.5.9.2.12
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Pain Medication Use at BL
Double Blind Period
Safety Analysis Set

Pain Medication Use at BL = No

Statistics	KRN23 (N=21)	Placebo (N=22)
Patients with TEAE - n(%)	3 (14.3%)	1 (4.5%)
Difference (KRN23 vs Placebo) - %	9.7%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	4.668	
95% C.I. of odds ratio	0.363, 60.078	
P-value	0.2297	
RR[2] (95% CI), P-value	3.143 (0.354, 27.879), 0.3449	
ARR[3] (95% CI), P-value	3.210 (0.452, 22.786), 0.2434**	
ARD[4]		
Difference (95% C.I.)	0.097 (-0.076, 0.271)	
P-value	0.3449	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

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Table 14.3.1.13.5.9.2.13
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Opioid Pain Medication Use at BL
Double Blind Period
Safety Analysis Set

Opioid Pain Medication Use at BL = Yes

Statistics	KRN23 (N=17)	Placebo (N=13)
Patients with TEAE - n(%)	2 (11.8%)	2 (15.4%)
Difference (KRN23 vs Placebo) - %	3.6%	
Logistic Regression[1]		
Percentage of Patients - %	11.9%	16.7%
95% C.I.	2.8%, 39.1%	3.9%, 49.8%
Odds ratio (KRN23 vs Placebo)	0.677	
95% C.I. of odds ratio	0.072, 6.370	
P-value	0.7240	
RR[2] (95% CI), P-value	0.765 (0.124, 4.730), 1.0000	
ARR[3] (95% CI), P-value	0.677 (0.080, 5.762), 0.7212	
ARD[4]		
Difference (95% C.I.)	0.036 (-0.213, 0.285)	
P-value	1.0000	

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

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Adhoc Analysis of UX023-CL303

Table 14.3.1.13.5.9.2.13
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Opioid Pain Medication Use at BL
Double Blind Period
Safety Analysis Set

Opioid Pain Medication Use at BL = No

Statistics	KRN23 (N=51)	Placebo (N=53)
Patients with TEAE - n(%)	6 (11.8%)	4 (7.5%)
Difference (KRN23 vs Placebo) - %	4.2%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.762	
95% C.I. of odds ratio	0.452, 6.870	
P-value	0.4105	
RR[2] (95% CI), P-value	1.559 (0.467, 5.203), 0.5219	
ARR[3] (95% CI), P-value	1.669 (0.487, 5.716), 0.4148**	
ARD[4]		
Difference (95% C.I.)	0.042 (-0.071, 0.156)	
P-value	0.5219	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

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Table 14.3.1.13.5.9.2.7
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by WOMAC Stiffness
Double Blind Period
Safety Analysis Set

WOMAC Stiffness = <=62.5

Statistics	KRN23 (N=39)	Placebo (N=41)
Patients with TEAE - n(%)	3 (7.7%)	4 (9.8%)
Difference (KRN23 vs Placebo) - %	2.1%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.717	
95% C.I. of odds ratio	0.140, 3.674	
P-value	0.6866	
RR[2] (95% CI), P-value	0.788 (0.188, 3.299), 1.0000	
ARR[3] (95% CI), P-value	0.754 (0.183, 3.103), 0.6961**	
ARD[4]		
Difference (95% C.I.)	0.021 (-0.103, 0.144)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.5.9.2.7
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by WOMAC Stiffness
Double Blind Period
Safety Analysis Set

WOMAC Stiffness = >62.5

Statistics	KRN23 (N=29)	Placebo (N=25)
Patients with TEAE - n(%)	5 (17.2%)	2 (8.0%)
Difference (KRN23 vs Placebo) - %	9.2%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	2.414	
95% C.I. of odds ratio	0.380, 15.354	
P-value	0.3430	
RR[2] (95% CI), P-value	2.155 (0.457, 10.155), 0.4305	
ARR[3] (95% CI), P-value	2.006 (0.396, 10.162), 0.4003**	
ARD[4]		
Difference (95% C.I.)	0.092 (-0.081, 0.266)	
P-value	0.4305	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

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Table 14.3.1.13.5.9.2.8
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by WOMAC Physical Function
Double Blind Period
Safety Analysis Set

WOMAC Physical Function: <=47.8

Statistics	KRN23 (N=30)	Placebo (N=37)
Patients with TEAE - n(%)	3 (10.0%)	4 (10.8%)
Difference (KRN23 vs Placebo) - %	0.8%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.879	
95% C.I. of odds ratio	0.171, 4.511	
P-value	0.8752	
RR[2] (95% CI), P-value	0.925 (0.224, 3.817), 1.0000	
ARR[3] (95% CI), P-value	0.915 (0.217, 3.851), 0.9034**	
ARD[4]		
Difference (95% C.I.)	0.008 (-0.139, 0.155)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

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Table 14.3.1.13.5.9.2.8
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by WOMAC Physical Function
Double Blind Period
Safety Analysis Set

WOMAC Physical Function: >47.8

Statistics	KRN23 (N=38)	Placebo (N=29)
Patients with TEAE - n(%)	5 (13.2%)	2 (6.9%)
Difference (KRN23 vs Placebo) - %	6.3%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	2.384	
95% C.I. of odds ratio	0.408, 13.941	
P-value	0.3294	
RR[2] (95% CI), P-value	1.908 (0.398, 9.143), 0.6899	
ARR[3] (95% CI), P-value	2.038 (0.429, 9.678), 0.3703**	
ARD[4]		
Difference (95% C.I.)	0.063 (-0.079, 0.204)	
P-value	0.6899	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

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Table 14.3.1.13.5.9.2.9
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by WOMAC Pain
Double Blind Period
Safety Analysis Set

WOMAC Pain at BL cat: <=50.0

Statistics	KRN23 (N=32)	Placebo (N=42)
Patients with TEAE - n(%)	4 (12.5%)	3 (7.1%)
Difference (KRN23 vs Placebo) - %	5.4%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.997	
95% C.I. of odds ratio	0.395, 10.089	
P-value	0.3974	
RR[2] (95% CI), P-value	1.750 (0.421, 7.273), 0.4570	
ARR[3] (95% CI), P-value	1.858 (0.445, 7.750), 0.3955**	
ARD[4]		
Difference (95% C.I.)	0.054 (-0.085, 0.192)	
P-value	0.4570	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

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Table 14.3.1.13.5.9.2.9
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by WOMAC Pain
Double Blind Period
Safety Analysis Set

WOMAC Pain at BL cat: >50.0

Statistics	KRN23 (N=35)	Placebo (N=24)
Patients with TEAE - n(%)	4 (11.4%)	3 (12.5%)
Difference (KRN23 vs Placebo) - %	1.1%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.959	
95% C.I. of odds ratio	0.184, 5.001	
P-value	0.9597	
RR[2] (95% CI), P-value	0.914 (0.225, 3.722), 1.0000	
ARR[3] (95% CI), P-value	0.929 (0.210, 4.112), 0.9231**	
ARD[4]		
Difference (95% C.I.)	0.011 (-0.158, 0.180)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

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Table 14.3.1.13.5.9.2.10
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by WOMAC Total Score
Double Blind Period
Safety Analysis Set

WOMAC Total Score at BL: <=49.5

Statistics	KRN23 (N=30)	Placebo (N=37)
Patients with TEAE - n(%)	3 (10.0%)	4 (10.8%)
Difference (KRN23 vs Placebo) - %	0.8%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.879	
95% C.I. of odds ratio	0.171, 4.511	
P-value	0.8752	
RR[2] (95% CI), P-value	0.925 (0.224, 3.817), 1.0000	
ARR[3] (95% CI), P-value	0.915 (0.217, 3.851), 0.9034**	
ARD[4]		
Difference (95% C.I.)	0.008 (-0.139, 0.155)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

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Table 14.3.1.13.5.9.2.10
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by WOMAC Total Score
Double Blind Period
Safety Analysis Set

WOMAC Total Score at BL: >49.5

Statistics	KRN23 (N=38)	Placebo (N=29)
Patients with TEAE - n(%)	5 (13.2%)	2 (6.9%)
Difference (KRN23 vs Placebo) - %	6.3%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	2.384	
95% C.I. of odds ratio	0.408, 13.941	
P-value	0.3294	
RR[2] (95% CI), P-value	1.908 (0.398, 9.143), 0.6899	
ARR[3] (95% CI), P-value	2.038 (0.429, 9.678), 0.3703**	
ARD[4]		
Difference (95% C.I.)	0.063 (-0.079, 0.204)	
P-value	0.6899	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.5.9.2.11
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by6MWT score at BL
Double Blind Period
Safety Analysis Set

6MWT score at BL cat = High

Statistics	KRN23 (N=30)	Placebo (N=36)
Patients with TEAE - n(%)	3 (10.0%)	3 (8.3%)
Difference (KRN23 vs Placebo) - %	1.7%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.500	
95% C.I. of odds ratio	0.259, 8.680	
P-value	0.6459	
RR[2] (95% CI), P-value	1.200 (0.261, 5.515), 1.0000	
ARR[3] (95% CI), P-value	1.464 (0.313, 6.845), 0.6282**	
ARD[4]		
Difference (95% C.I.)	0.017 (-0.124, 0.157)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.5.9.2.11
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by6MWT score at BL
Double Blind Period
Safety Analysis Set

6MWT score at BL cat = Low

Statistics	KRN23 (N=37)	Placebo (N=29)
Patients with TEAE - n(%)	5 (13.5%)	3 (10.3%)
Difference (KRN23 vs Placebo) - %	3.2%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.695	
95% C.I. of odds ratio	0.338, 8.497	
P-value	0.5150	
RR[2] (95% CI), P-value	1.306 (0.340, 5.020), 1.0000	
ARR[3] (95% CI), P-value	1.538 (0.365, 6.474), 0.5573**	
ARD[4]		
Difference (95% C.I.)	0.032 (-0.125, 0.188)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.5.9.2.14
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Active fractures and pseudo-fractures at BL
Double Blind Period
Safety Analysis Set

Active fractures and pseudo-fractures at BL = Yes

Statistics	KRN23 (N=32)	Placebo (N=38)
Patients with TEAE - n(%)	4 (12.5%)	3 (7.9%)
Difference (KRN23 vs Placebo) - %	4.6%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	1.882	
95% C.I. of odds ratio	0.366, 9.692	
P-value	0.4437	
RR[2] (95% CI), P-value	1.583 (0.382, 6.558), 0.6946	
ARR[3] (95% CI), P-value	1.748 (0.416, 7.351), 0.4458**	
ARD[4]		
Difference (95% C.I.)	0.046 (-0.097, 0.189)	
P-value	0.6946	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas

Kyowa Kirin Pharmaceutical Development, Inc.
Adhoc Analysis of UX023-CL303

Table 14.3.1.13.5.9.2.14
Logistic Regression on Tretment-Emergent AESI-Any Restless Legs Syn-drome by Active fractures and pseudo-fractures at BL
Double Blind Period
Safety Analysis Set

Active fractures and pseudo-fractures at BL = No

Statistics	KRN23 (N=36)	Placebo (N=28)
Patients with TEAE - n(%)	4 (11.1%)	3 (10.7%)
Difference (KRN23 vs Placebo) - %	0.4%	
Logistic Regression[1]		
Percentage of Patients - %	0.0%	0.0%
95% C.I.	0.0%, 100.0%	0.0%, 100.0%
Odds ratio (KRN23 vs Placebo)	0.888	
95% C.I. of odds ratio	0.166, 4.745	
P-value	0.8874	
RR[2] (95% CI), P-value	1.037 (0.252, 4.261), 1.0000	
ARR[3] (95% CI), P-value	0.881 (0.201, 3.853), 0.8664**	
ARD[4]		
Difference (95% C.I.)	0.004 (-0.150, 0.158)	
P-value	1.0000	

** Penalized likelihood is used to deal with quasi-complete separation problem.

Note: All safety events that occurred before first treatment were excluded from the analysis of logistic regression.
1. The logistic regression includes treatment, actual randomization stratification, and country group as factors.
2. RR: Relative Risk
3. ARR: Adjusted Relative Risk
4. ARD: Absolute Risk Difference
Data Source: ADSL, ADAE . Program Source: S:\KKPD\ux023\CL303\analysis\develpool\program\Table\t-aesi-leg-db-subg.sas