Dossier zur Nutzenbewertung gemäß § 35a SGB V

Natriumzirconiumcyclosilicat (Lokelma®)

AstraZeneca GmbH

Separater Anhang 4-G

Hyperkaliämie bei erwachsenen PatientInnen

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Ergänzende Daten zu den Studien und Metaanalysen

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Anhang 4-G1: Studie Dialize

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Table 6.1.1.1 - Study DIALIZE: Proportion of responders (subjects who maintained pre-dialysis serum potassium between 4.0-5.0 mmol/L on at least 3 out of 4 dialysis treatments following the LIDI during the evaluation period and who did not receive rescue therapy during the evaluation period), SZC (variable dose) QD vs. Placebo, overall and by subgroups (full population)

	Placebo (N=99)		Lokelma 10g QD (N=97)								
Subgroup / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Overall	99	1 (1.0%)	97	40 (41.2%)	68.77 (9.21, 513.77)	<.0001	40.82 (5.61, 296.96)	0.0002	40.2 (27.3, 53.2)	<.0001	
Sex											
Male	58	1 (1.7%)	57	28 (49.1%)	55.01 (7.13, 424.70)	0.0001	28.49 (3.88, 209.40)	0.0010	47.4 (28.9, 65.9)	<.0001	
Female	41	0 (0.0%)	40	12 (30.0%)	n/a	n/a	n/a	n/a	NC	NC	
Age (years)											
<65 years	53	1 (1.9%)	65	24 (36.9%)	30.44 (3.95, 234.49)	0.0010	19.57 (2.65, 144.65)	0.0036	35.0 (19.8, 50.3)	<.0001	
>=65 years	46	0 (0.0%)	32	16 (50.0%)	n/a	n/a	n/a	n/a	NC	NC	
Country											NC
USA	23	1 (4.3%)	21	5 (23.8%)	6.87 (0.73, 64.68)	0.0918	5.48 (0.64, 46.87)	0.1206	19.5 (-3.1, 42.0)	0.0906	
GB	15	0 (0.0%)	15	5 (33.3%)	n/a	n/a	n/a	n/a	NC	NC	
Japan	28	0 (0.0%)	28	20 (71.4%)	n/a	n/a	n/a	n/a	NC	NC	
Russia	33	0 (0.0%)	33	10 (30.3%)	n/a	n/a	n/a	n/a	NC	NC	
Region USA or Rest of world											
USA	23	1 (4.3%)	21	5 (23.8%)	6.87 (0.73, 64.68)	0.0918	5.48 (0.64, 46.87)	0.1206	19.5 (-3.1, 42.0)	0.0906	
Rest of world	76	0 (0.0%)	76	35 (46.1%)	n/a	n/a	n/a	n/a	NC	NC	
Region Japan or Not Japan											
Japan	28	0 (0.0%)	28	20 (71.4%)	n/a	n/a	n/a	n/a	NC	NC	
Not Japan	71	1 (1.4%)	69	20 (29.0%)	28.57 (3.71, 219.98)	0.0013	20.58 (2.76, 153.34)	0.0032	27.6 (14.6, 40.6)	<.0001	

OR, RR and ARR derived from model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 6.1.2.1 - Study DIALIZE: Proportion of subjects requiring rescue therapy, SZC (variable dose) QD vs. Placebo, overall and by subgroups (full population)

	Placebo (N=99)		Lokelma 10g QD (N=97)								
Subgroup / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Overall	99	5 (5.1%)	97	2 (2.1%)	0.40 (0.07, 2.09)	0.2751	0.41 (0.08, 2.10)	0.2843	-3.0 (-8.3, 2.3)	0.2663	
Sex											-
Male	58	3 (5.2%)	57	1 (1.8%)	-	-	-	-	-	-	
Female	41	2 (4.9%)	40	1 (2.5%)	-	-	-	-	-	-	
Age (years)											-
<65 years	53	2 (3.8%)	65	2 (3.1%)	-	-	-	-	-	-	
>=65 years	46	3 (6.5%)	32	0 (0.0%)	-	-	-	-	-	-	
Country											-
USA	23	1 (4.3%)	21	0 (0.0%)	-	-	-	-	-	-	
GB	15	1 (6.7%)	15	2 (13.3%)	-	-	-	-	-	-	
Japan	28	3 (10.7%)	28	0 (0.0%)	-	-	-	-	-	-	
Russia	33	0 (0.0%)	33	0 (0.0%)	-	-	-	-	-	-	
Region USA or Rest of world											-
USA	23	1 (4.3%)	21	0 (0.0%)	-	-	-	-	-	-	
Rest of world	76	4 (5.3%)	76	2 (2.6%)	-	-	-	-	-	-	
Region Japan or Not Japan											-
Japan	28	3 (10.7%)	28	0 (0.0%)	-	-	-	-	-	-	
Not Japan	71	2 (2.8%)	69	2 (2.9%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 6.1.3.1 - Study DIALIZE: Proportion of subjects able to increase dialysate K concentration at end of treatment compared to baseline, SZC (variable dose) QD vs. Placebo, overall and by subgroups (full population)

	Placebo (N=99)		Lokelma 10g QD (N=97)								
Subgroup / Category	N*	Patients meeting criteria [n (%)]	N*	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Overall	94	1 (1.1%)	87	2 (2.3%)	2.19 (0.19, 24.57)	0.5257	2.16 (0.20, 23.83)	0.5293	1.2 (-2.6, 5.0)	0.5250	
Sex											-
Male	56	1 (1.8%)	52	1 (1.9%)	-	-	-	-	-	-	
Female	38	0 (0.0%)	35	1 (2.9%)	-	-	-	-	-	-	
Age (years)											-
<65 years	51	1 (2.0%)	56	1 (1.8%)	-	-	-	-	-	-	
>=65 years	43	0 (0.0%)	31	1 (3.2%)	-	-	-	-	-	-	
Country											-
USA	19	1 (5.3%)	18	1 (5.6%)	-	-	-	-	-	-	
GB	14	0 (0.0%)	13	1 (7.7%)	-	-	-	-	-	-	
Japan	28	0 (0.0%)	26	0 (0.0%)	-	-	-	-	-	-	
Russia	33	0 (0.0%)	30	0 (0.0%)	-	-	-	-	-	-	
Region USA or Rest of world											-
USA	19	1 (5.3%)	18	1 (5.6%)	-	-	-	-	-	-	
Rest of world	75	0 (0.0%)	69	1 (1.4%)	-	-	-	-	-	-	
Region Japan or Not Japan											-
Japan	28	0 (0.0%)	26	0 (0.0%)	-	-	-	-	-	-	
Not Japan	66	1 (1.5%)	61	2 (3.3%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
Subjects with missing baseline dialysate K are not included in this analysis, therefore % of subjects is calculated out of number of subjects included in analysis (N*)
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 6.3.1.1 - Study DIALIZE: Dose of investigational product assigned by visit, SZC (variable dose) QD vs Placebo, overall and by subgroups (safety population)

	Placebo QD (N=99) [n(%)]					SZC variable dose QD (N=96) [n(%)]				
Subgroup / Category / Timepoint	**n**	**5g**	**10g**	**15g**	**Not dosed**	**n**	**5g**	**10g**	**15g**	**Not dosed**
Overall										
Unknown	5	1 (20.0%)	0 (0.0%)	4 (80.0%)	0 (0.0%)	2	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)
Visit 4 (Day 1)	99	99 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	90	90 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 5 (Day 3)	98	97 (99.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	93	93 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 6 (Day 5)	99	99 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	92	92 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 7 (Day 8)	98	25 (25.5%)	73 (74.5%)	0 (0.0%)	0 (0.0%)	91	49 (53.8%)	41 (45.1%)	0 (0.0%)	1 (1.1%)
Visit 7.5 (Day 10)	77	19 (24.7%)	57 (74.0%)	0 (0.0%)	1 (1.3%)	69	32 (46.4%)	36 (52.2%)	0 (0.0%)	1 (1.4%)
Visit 8 (Day 12)	97	24 (24.7%)	73 (75.3%)	0 (0.0%)	0 (0.0%)	92	48 (52.2%)	43 (46.7%)	0 (0.0%)	1 (1.1%)
Visit 9 (Day 15)	92	9 (9.8%)	24 (26.1%)	59 (64.1%)	0 (0.0%)	91	38 (41.8%)	39 (42.9%)	13 (14.3%)	1 (1.1%)
Visit 9.5 (Day 17)	77	9 (11.7%)	21 (27.3%)	47 (61.0%)	0 (0.0%)	75	27 (36.0%)	34 (45.3%)	13 (17.3%)	1 (1.3%)
Visit 10 (Day 22)	95	8 (8.4%)	8 (8.4%)	79 (83.2%)	0 (0.0%)	90	33 (36.7%)	39 (43.3%)	17 (18.9%)	1 (1.1%)
Visit 10.5 (Day 24)	79	9 (11.4%)	6 (7.6%)	64 (81.0%)	0 (0.0%)	75	25 (33.3%)	32 (42.7%)	17 (22.7%)	1 (1.3%)
Visit 11 (Day 29)	94	9 (9.6%)	6 (6.4%)	79 (84.0%)	0 (0.0%)	88	32 (36.4%)	39 (44.3%)	16 (18.2%)	1 (1.1%)
Visit 11.5 (Day 31)	82	9 (11.0%)	5 (6.1%)	68 (82.9%)	0 (0.0%)	77	26 (33.8%)	33 (42.9%)	17 (22.1%)	1 (1.3%)
Visit 12 (Day 36)	95	9 (9.5%)	6 (6.3%)	80 (84.2%)	0 (0.0%)	88	32 (36.4%)	38 (43.2%)	17 (19.3%)	1 (1.1%)
Visit 12.5 (Day 38)	86	9 (10.5%)	5 (5.8%)	71 (82.6%)	1 (1.2%)	78	28 (35.9%)	32 (41.0%)	17 (21.8%)	1 (1.3%)
Visit 13 (Day 43)	93	9 (9.7%)	6 (6.5%)	78 (83.9%)	0 (0.0%)	88	31 (35.2%)	39 (44.3%)	17 (19.3%)	1 (1.1%)
Visit 13.5 (Day 45)	83	9 (10.8%)	5 (6.0%)	69 (83.1%)	0 (0.0%)	78	28 (35.9%)	32 (41.0%)	17 (21.8%)	1 (1.3%)
Visit 14 (Day 50)	95	9 (9.5%)	6 (6.3%)	80 (84.2%)	0 (0.0%)	87	30 (34.5%)	39 (44.8%)	17 (19.5%)	1 (1.1%)
Visit 14.5 (Day 52)	87	9 (10.3%)	5 (5.7%)	73 (83.9%)	0 (0.0%)	80	29 (36.3%)	33 (41.3%)	17 (21.3%)	1 (1.3%)
Visit 15 (Day 57)	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3	0 (0.0%)	0 (0.0%)	3 (100.0%)	0 (0.0%)
Sex										
Male										
Unknown	3	0 (0.0%)	0 (0.0%)	3 (100.0%)	0 (0.0%)	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 4 (Day 1)	58	58 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	51	51 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 5 (Day 3)	57	57 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	55	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 6 (Day 5)	58	58 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	54	54 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 7 (Day 8)	58	15 (25.9%)	43 (74.1%)	0 (0.0%)	0 (0.0%)	55	28 (50.9%)	26 (47.3%)	0 (0.0%)	1 (1.8%)
Visit 7.5 (Day 10)	43	12 (27.9%)	30 (69.8%)	0 (0.0%)	1 (2.3%)	41	18 (43.9%)	22 (53.7%)	0 (0.0%)	1 (2.4%)
Visit 8 (Day 12)	56	14 (25.0%)	42 (75.0%)	0 (0.0%)	0 (0.0%)	55	27 (49.1%)	27 (49.1%)	0 (0.0%)	1 (1.8%)
Visit 9 (Day 15)	55	6 (10.9%)	12 (21.8%)	37 (67.3%)	0 (0.0%)	55	23 (41.8%)	24 (43.6%)	7 (12.7%)	1 (1.8%)
Visit 9.5 (Day 17)	44	6 (13.6%)	11 (25.0%)	27 (61.4%)	0 (0.0%)	47	17 (36.2%)	21 (44.7%)	8 (17.0%)	1 (2.1%)
Visit 10 (Day 22)	56	5 (8.9%)	4 (7.1%)	47 (83.9%)	0 (0.0%)	55	20 (36.4%)	22 (40.0%)	12 (21.8%)	1 (1.8%)
Visit 10.5 (Day 24)	46	5 (10.9%)	3 (6.5%)	38 (82.6%)	0 (0.0%)	47	15 (31.9%)	19 (40.4%)	12 (25.5%)	1 (2.1%)
Visit 11 (Day 29)	55	5 (9.1%)	3 (5.5%)	47 (85.5%)	0 (0.0%)	53	19 (35.8%)	21 (39.6%)	12 (22.6%)	1 (1.9%)
Visit 11.5 (Day 31)	46	5 (10.9%)	2 (4.3%)	39 (84.8%)	0 (0.0%)	49	16 (32.7%)	20 (40.8%)	12 (24.5%)	1 (2.0%)
Visit 12 (Day 36)	56	5 (8.9%)	3 (5.4%)	48 (85.7%)	0 (0.0%)	53	19 (35.8%)	21 (39.6%)	12 (22.6%)	1 (1.9%)
Visit 12.5 (Day 38)	50	5 (10.0%)	2 (4.0%)	42 (84.0%)	1 (2.0%)	50	18 (36.0%)	19 (38.0%)	12 (24.0%)	1 (2.0%)
Visit 13 (Day 43)	54	5 (9.3%)	3 (5.6%)	46 (85.2%)	0 (0.0%)	54	19 (35.2%)	22 (40.7%)	12 (22.2%)	1 (1.9%)
Visit 13.5 (Day 45)	48	5 (10.4%)	2 (4.2%)	41 (85.4%)	0 (0.0%)	51	18 (35.3%)	20 (39.2%)	12 (23.5%)	1 (2.0%)
Visit 14 (Day 50)	56	5 (8.9%)	3 (5.4%)	48 (85.7%)	0 (0.0%)	53	18 (34.0%)	22 (41.5%)	12 (22.6%)	1 (1.9%)
Visit 14.5 (Day 52)	51	5 (9.8%)	2 (3.9%)	44 (86.3%)	0 (0.0%)	52	19 (36.5%)	20 (38.5%)	12 (23.1%)	1 (1.9%)
Visit 15 (Day 57)	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2	0 (0.0%)	0 (0.0%)	2 (100.0%)	0 (0.0%)

5g = 1 sachet, 10g = 2 sachets, 15g = 3 sachets.
Not dosed represents subjects who have discontinued, have a drug interruption or a zero dose.
Percentages calculated from subjects analyzed at each visit, within each treatment group.
N=Number of subjects in treatment group. n = Number of subjects included in analysis.

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Table 6.3.1.1 - Study DIALIZE: Dose of investigational product assigned by visit, SZC (variable dose) QD vs Placebo, overall and by subgroups (safety population)

	Placebo QD (N=99) [n(%)]					SZC variable dose QD (N=96) [n(%)]				
Subgroup / Category / Timepoint	**n**	**5g**	**10g**	**15g**	**Not dosed**	**n**	**5g**	**10g**	**15g**	**Not dosed**
Sex *(contd.)*										
Female										
Unknown	2	1 (50.0%)	0 (0.0%)	1 (50.0%)	0 (0.0%)	2	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)
Visit 4 (Day 1)	41	41 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	39	39 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 5 (Day 3)	41	40 (97.6%)	0 (0.0%)	0 (0.0%)	1 (2.4%)	38	38 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 6 (Day 5)	41	41 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	38	38 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 7 (Day 8)	40	10 (25.0%)	30 (75.0%)	0 (0.0%)	0 (0.0%)	36	21 (58.3%)	15 (41.7%)	0 (0.0%)	0 (0.0%)
Visit 7.5 (Day 10)	34	7 (20.6%)	27 (79.4%)	0 (0.0%)	0 (0.0%)	28	14 (50.0%)	14 (50.0%)	0 (0.0%)	0 (0.0%)
Visit 8 (Day 12)	41	10 (24.4%)	31 (75.6%)	0 (0.0%)	0 (0.0%)	37	21 (56.8%)	16 (43.2%)	0 (0.0%)	0 (0.0%)
Visit 9 (Day 15)	37	3 (8.1%)	12 (32.4%)	22 (59.5%)	0 (0.0%)	36	15 (41.7%)	15 (41.7%)	6 (16.7%)	0 (0.0%)
Visit 9.5 (Day 17)	33	3 (9.1%)	10 (30.3%)	20 (60.6%)	0 (0.0%)	28	10 (35.7%)	13 (46.4%)	5 (17.9%)	0 (0.0%)
Visit 10 (Day 22)	39	3 (7.7%)	4 (10.3%)	32 (82.1%)	0 (0.0%)	35	13 (37.1%)	17 (48.6%)	5 (14.3%)	0 (0.0%)
Visit 10.5 (Day 24)	33	4 (12.1%)	3 (9.1%)	26 (78.8%)	0 (0.0%)	28	10 (35.7%)	13 (46.4%)	5 (17.9%)	0 (0.0%)
Visit 11 (Day 29)	39	4 (10.3%)	3 (7.7%)	32 (82.1%)	0 (0.0%)	35	13 (37.1%)	18 (51.4%)	4 (11.4%)	0 (0.0%)
Visit 11.5 (Day 31)	36	4 (11.1%)	3 (8.3%)	29 (80.6%)	0 (0.0%)	28	10 (35.7%)	13 (46.4%)	5 (17.9%)	0 (0.0%)
Visit 12 (Day 36)	39	4 (10.3%)	3 (7.7%)	32 (82.1%)	0 (0.0%)	35	13 (37.1%)	17 (48.6%)	5 (14.3%)	0 (0.0%)
Visit 12.5 (Day 38)	36	4 (11.1%)	3 (8.3%)	29 (80.6%)	0 (0.0%)	28	10 (35.7%)	13 (46.4%)	5 (17.9%)	0 (0.0%)
Visit 13 (Day 43)	39	4 (10.3%)	3 (7.7%)	32 (82.1%)	0 (0.0%)	34	12 (35.3%)	17 (50.0%)	5 (14.7%)	0 (0.0%)
Visit 13.5 (Day 45)	35	4 (11.4%)	3 (8.6%)	28 (80.0%)	0 (0.0%)	27	10 (37.0%)	12 (44.4%)	5 (18.5%)	0 (0.0%)
Visit 14 (Day 50)	39	4 (10.3%)	3 (7.7%)	32 (82.1%)	0 (0.0%)	34	12 (35.3%)	17 (50.0%)	5 (14.7%)	0 (0.0%)
Visit 14.5 (Day 52)	36	4 (11.1%)	3 (8.3%)	29 (80.6%)	0 (0.0%)	28	10 (35.7%)	13 (46.4%)	5 (17.9%)	0 (0.0%)
Visit 15 (Day 57)	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)
Age										
<65 years										
Unknown	4	0 (0.0%)	0 (0.0%)	4 (100.0%)	0 (0.0%)	2	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)
Visit 4 (Day 1)	53	53 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	59	59 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 5 (Day 3)	51	51 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	62	62 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 6 (Day 5)	53	53 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	61	61 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 7 (Day 8)	53	12 (22.6%)	41 (77.4%)	0 (0.0%)	0 (0.0%)	60	31 (51.7%)	29 (48.3%)	0 (0.0%)	0 (0.0%)
Visit 7.5 (Day 10)	41	9 (22.0%)	32 (78.0%)	0 (0.0%)	0 (0.0%)	47	20 (42.6%)	27 (57.4%)	0 (0.0%)	0 (0.0%)
Visit 8 (Day 12)	53	12 (22.6%)	41 (77.4%)	0 (0.0%)	0 (0.0%)	61	30 (49.2%)	31 (50.8%)	0 (0.0%)	0 (0.0%)
Visit 9 (Day 15)	50	5 (10.0%)	12 (24.0%)	33 (66.0%)	0 (0.0%)	61	25 (41.0%)	26 (42.6%)	10 (16.4%)	0 (0.0%)
Visit 9.5 (Day 17)	41	5 (12.2%)	10 (24.4%)	26 (63.4%)	0 (0.0%)	52	19 (36.5%)	23 (44.2%)	10 (19.2%)	0 (0.0%)
Visit 10 (Day 22)	52	4 (7.7%)	4 (7.7%)	44 (84.6%)	0 (0.0%)	60	22 (36.7%)	26 (43.3%)	12 (20.0%)	0 (0.0%)
Visit 10.5 (Day 24)	43	5 (11.6%)	2 (4.7%)	36 (83.7%)	0 (0.0%)	52	18 (34.6%)	22 (42.3%)	12 (23.1%)	0 (0.0%)
Visit 11 (Day 29)	51	5 (9.8%)	2 (3.9%)	44 (86.3%)	0 (0.0%)	58	21 (36.2%)	26 (44.8%)	11 (19.0%)	0 (0.0%)
Visit 11.5 (Day 31)	42	5 (11.9%)	1 (2.4%)	36 (85.7%)	0 (0.0%)	54	19 (35.2%)	23 (42.6%)	12 (22.2%)	0 (0.0%)
Visit 12 (Day 36)	51	5 (9.8%)	2 (3.9%)	44 (86.3%)	0 (0.0%)	58	21 (36.2%)	25 (43.1%)	12 (20.7%)	0 (0.0%)
Visit 12.5 (Day 38)	45	5 (11.1%)	1 (2.2%)	39 (86.7%)	0 (0.0%)	54	20 (37.0%)	22 (40.7%)	12 (22.2%)	0 (0.0%)
Visit 13 (Day 43)	49	5 (10.2%)	2 (4.1%)	42 (85.7%)	0 (0.0%)	58	20 (34.5%)	26 (44.8%)	12 (20.7%)	0 (0.0%)
Visit 13.5 (Day 45)	42	5 (11.9%)	1 (2.4%)	36 (85.7%)	0 (0.0%)	54	20 (37.0%)	22 (40.7%)	12 (22.2%)	0 (0.0%)
Visit 14 (Day 50)	51	5 (9.8%)	2 (3.9%)	44 (86.3%)	0 (0.0%)	58	20 (34.5%)	26 (44.8%)	12 (20.7%)	0 (0.0%)
Visit 14.5 (Day 52)	46	5 (10.9%)	1 (2.2%)	40 (87.0%)	0 (0.0%)	54	19 (35.2%)	23 (42.6%)	12 (22.2%)	0 (0.0%)
Visit 15 (Day 57)	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3	0 (0.0%)	0 (0.0%)	3 (100.0%)	0 (0.0%)

5g = 1 sachet, 10g = 2 sachets, 15g = 3 sachets.
Not dosed represents subjects who have discontinued, have a drug interruption or a zero dose.
Percentages calculated from subjects analyzed at each visit, within each treatment group.
N=Number of subjects in treatment group. n = Number of subjects included in analysis.

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Table 6.3.1.1 - Study DIALIZE: Dose of investigational product assigned by visit, SZC (variable dose) QD vs Placebo, overall and by subgroups (safety population)

	Placebo QD (N=99) [n(%)]					SZC variable dose QD (N=96) [n(%)]				
Subgroup / Category / Timepoint	**n**	**5g**	**10g**	**15g**	**Not dosed**	**n**	**5g**	**10g**	**15g**	**Not dosed**
Age *(contd.)*										
>= 65 years										
Unknown	1	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 4 (Day 1)	46	46 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	31	31 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 5 (Day 3)	47	46 (97.9%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	31	31 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 6 (Day 5)	46	46 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	31	31 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 7 (Day 8)	45	13 (28.9%)	32 (71.1%)	0 (0.0%)	0 (0.0%)	31	18 (58.1%)	12 (38.7%)	0 (0.0%)	1 (3.2%)
Visit 7.5 (Day 10)	36	10 (27.8%)	25 (69.4%)	0 (0.0%)	1 (2.8%)	22	12 (54.5%)	9 (40.9%)	0 (0.0%)	1 (4.5%)
Visit 8 (Day 12)	44	12 (27.3%)	32 (72.7%)	0 (0.0%)	0 (0.0%)	31	18 (58.1%)	12 (38.7%)	0 (0.0%)	1 (3.2%)
Visit 9 (Day 15)	42	4 (9.5%)	12 (28.6%)	26 (61.9%)	0 (0.0%)	30	13 (43.3%)	13 (43.3%)	3 (10.0%)	1 (3.3%)
Visit 9.5 (Day 17)	36	4 (11.1%)	11 (30.6%)	21 (58.3%)	0 (0.0%)	23	8 (34.8%)	11 (47.8%)	3 (13.0%)	1 (4.3%)
Visit 10 (Day 22)	43	4 (9.3%)	4 (9.3%)	35 (81.4%)	0 (0.0%)	30	11 (36.7%)	13 (43.3%)	5 (16.7%)	1 (3.3%)
Visit 10.5 (Day 24)	36	4 (11.1%)	4 (11.1%)	28 (77.8%)	0 (0.0%)	23	7 (30.4%)	10 (43.5%)	5 (21.7%)	1 (4.3%)
Visit 11 (Day 29)	43	4 (9.3%)	4 (9.3%)	35 (81.4%)	0 (0.0%)	30	11 (36.7%)	13 (43.3%)	5 (16.7%)	1 (3.3%)
Visit 11.5 (Day 31)	40	4 (10.0%)	4 (10.0%)	32 (80.0%)	0 (0.0%)	23	7 (30.4%)	10 (43.5%)	5 (21.7%)	1 (4.3%)
Visit 12 (Day 36)	44	4 (9.1%)	4 (9.1%)	36 (81.8%)	0 (0.0%)	30	11 (36.7%)	13 (43.3%)	5 (16.7%)	1 (3.3%)
Visit 12.5 (Day 38)	41	4 (9.8%)	4 (9.8%)	32 (78.0%)	1 (2.4%)	24	8 (33.3%)	10 (41.7%)	5 (20.8%)	1 (4.2%)
Visit 13 (Day 43)	44	4 (9.1%)	4 (9.1%)	36 (81.8%)	0 (0.0%)	30	11 (36.7%)	13 (43.3%)	5 (16.7%)	1 (3.3%)
Visit 13.5 (Day 45)	41	4 (9.8%)	4 (9.8%)	33 (80.5%)	0 (0.0%)	24	8 (33.3%)	10 (41.7%)	5 (20.8%)	1 (4.2%)
Visit 14 (Day 50)	44	4 (9.1%)	4 (9.1%)	36 (81.8%)	0 (0.0%)	29	10 (34.5%)	13 (44.8%)	5 (17.2%)	1 (3.4%)
Visit 14.5 (Day 52)	41	4 (9.8%)	4 (9.8%)	33 (80.5%)	0 (0.0%)	26	10 (38.5%)	10 (38.5%)	5 (19.2%)	1 (3.8%)
Country										
USA										
Unknown	1	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	1	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)
Visit 4 (Day 1)	23	23 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	20	20 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 5 (Day 3)	22	22 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	19	19 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 6 (Day 5)	23	23 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	18	18 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 7 (Day 8)	23	12 (52.2%)	11 (47.8%)	0 (0.0%)	0 (0.0%)	18	7 (38.9%)	11 (61.1%)	0 (0.0%)	0 (0.0%)
Visit 7.5 (Day 10)	21	10 (47.6%)	11 (52.4%)	0 (0.0%)	0 (0.0%)	18	6 (33.3%)	12 (66.7%)	0 (0.0%)	0 (0.0%)
Visit 8 (Day 12)	22	11 (50.0%)	11 (50.0%)	0 (0.0%)	0 (0.0%)	19	7 (36.8%)	12 (63.2%)	0 (0.0%)	0 (0.0%)
Visit 9 (Day 15)	19	6 (31.6%)	6 (31.6%)	7 (36.8%)	0 (0.0%)	19	6 (31.6%)	11 (57.9%)	2 (10.5%)	0 (0.0%)
Visit 9.5 (Day 17)	20	6 (30.0%)	6 (30.0%)	8 (40.0%)	0 (0.0%)	19	6 (31.6%)	11 (57.9%)	2 (10.5%)	0 (0.0%)
Visit 10 (Day 22)	21	6 (28.6%)	1 (4.8%)	14 (66.7%)	0 (0.0%)	18	7 (38.9%)	7 (38.9%)	4 (22.2%)	0 (0.0%)
Visit 10.5 (Day 24)	20	6 (30.0%)	1 (5.0%)	13 (65.0%)	0 (0.0%)	17	6 (35.3%)	7 (41.2%)	4 (23.5%)	0 (0.0%)
Visit 11 (Day 29)	20	6 (30.0%)	1 (5.0%)	13 (65.0%)	0 (0.0%)	16	6 (37.5%)	7 (43.8%)	3 (18.8%)	0 (0.0%)
Visit 11.5 (Day 31)	19	6 (31.6%)	1 (5.3%)	12 (63.2%)	0 (0.0%)	18	6 (33.3%)	8 (44.4%)	4 (22.2%)	0 (0.0%)
Visit 12 (Day 36)	21	6 (28.6%)	1 (4.8%)	14 (66.7%)	0 (0.0%)	16	6 (37.5%)	6 (37.5%)	4 (25.0%)	0 (0.0%)
Visit 12.5 (Day 38)	20	6 (30.0%)	1 (5.0%)	13 (65.0%)	0 (0.0%)	17	6 (35.3%)	7 (41.2%)	4 (23.5%)	0 (0.0%)
Visit 13 (Day 43)	18	6 (33.3%)	1 (5.6%)	11 (61.1%)	0 (0.0%)	17	5 (29.4%)	8 (47.1%)	4 (23.5%)	0 (0.0%)
Visit 13.5 (Day 45)	17	6 (35.3%)	1 (5.9%)	10 (58.8%)	0 (0.0%)	17	6 (35.3%)	7 (41.2%)	4 (23.5%)	0 (0.0%)
Visit 14 (Day 50)	20	6 (30.0%)	1 (5.0%)	13 (65.0%)	0 (0.0%)	17	5 (29.4%)	8 (47.1%)	4 (23.5%)	0 (0.0%)
Visit 14.5 (Day 52)	19	6 (31.6%)	1 (5.3%)	12 (63.2%)	0 (0.0%)	17	5 (29.4%)	8 (47.1%)	4 (23.5%)	0 (0.0%)
GB										
Unknown	1	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

5g = 1 sachet, 10g = 2 sachets, 15g = 3 sachets.
Not dosed represents subjects who have discontinued, have a drug interruption or a zero dose.
Percentages calculated from subjects analyzed at each visit, within each treatment group.
N=Number of subjects in treatment group. n = Number of subjects included in analysis.

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Table 6.3.1.1 - Study DIALIZE: Dose of investigational product assigned by visit, SZC (variable dose) QD vs Placebo, overall and by subgroups (safety population)

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	Placebo QD (N=99) [n(%)]					SZC variable dose QD (N=96) [n(%)]				
Subgroup / Category / Timepoint	**n**	**5g**	**10g**	**15g**	**Not dosed**	**n**	**5g**	**10g**	**15g**	**Not dosed**
Country *(contd.)*										
GB *(contd.)*										
Visit 4 (Day 1)	15	15 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	13	13 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 5 (Day 3)	14	14 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	13	13 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 6 (Day 5)	15	15 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	13	13 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 7 (Day 8)	14	2 (14.3%)	12 (85.7%)	0 (0.0%)	0 (0.0%)	12	9 (75.0%)	3 (25.0%)	0 (0.0%)	0 (0.0%)
Visit 7.5 (Day 10)	14	2 (14.3%)	12 (85.7%)	0 (0.0%)	0 (0.0%)	12	9 (75.0%)	3 (25.0%)	0 (0.0%)	0 (0.0%)
Visit 8 (Day 12)	14	2 (14.3%)	12 (85.7%)	0 (0.0%)	0 (0.0%)	12	9 (75.0%)	3 (25.0%)	0 (0.0%)	0 (0.0%)
Visit 9 (Day 15)	14	0 (0.0%)	6 (42.9%)	8 (57.1%)	0 (0.0%)	11	5 (45.5%)	5 (45.5%)	1 (9.1%)	0 (0.0%)
Visit 9.5 (Day 17)	14	1 (7.1%)	6 (42.9%)	7 (50.0%)	0 (0.0%)	11	5 (45.5%)	5 (45.5%)	1 (9.1%)	0 (0.0%)
Visit 10 (Day 22)	13	0 (0.0%)	2 (15.4%)	11 (84.6%)	0 (0.0%)	11	4 (36.4%)	6 (54.5%)	1 (9.1%)	0 (0.0%)
Visit 10.5 (Day 24)	14	0 (0.0%)	2 (14.3%)	12 (85.7%)	0 (0.0%)	11	4 (36.4%)	6 (54.5%)	1 (9.1%)	0 (0.0%)
Visit 11 (Day 29)	14	0 (0.0%)	1 (7.1%)	13 (92.9%)	0 (0.0%)	11	4 (36.4%)	6 (54.5%)	1 (9.1%)	0 (0.0%)
Visit 11.5 (Day 31)	14	0 (0.0%)	1 (7.1%)	13 (92.9%)	0 (0.0%)	11	4 (36.4%)	6 (54.5%)	1 (9.1%)	0 (0.0%)
Visit 12 (Day 36)	14	0 (0.0%)	1 (7.1%)	13 (92.9%)	0 (0.0%)	11	4 (36.4%)	6 (54.5%)	1 (9.1%)	0 (0.0%)
Visit 12.5 (Day 38)	14	0 (0.0%)	1 (7.1%)	13 (92.9%)	0 (0.0%)	11	4 (36.4%)	6 (54.5%)	1 (9.1%)	0 (0.0%)
Visit 13 (Day 43)	14	0 (0.0%)	1 (7.1%)	13 (92.9%)	0 (0.0%)	11	4 (36.4%)	6 (54.5%)	1 (9.1%)	0 (0.0%)
Visit 13.5 (Day 45)	14	0 (0.0%)	1 (7.1%)	13 (92.9%)	0 (0.0%)	11	4 (36.4%)	6 (54.5%)	1 (9.1%)	0 (0.0%)
Visit 14 (Day 50)	14	0 (0.0%)	1 (7.1%)	13 (92.9%)	0 (0.0%)	10	3 (30.0%)	6 (60.0%)	1 (10.0%)	0 (0.0%)
Visit 14.5 (Day 52)	14	0 (0.0%)	1 (7.1%)	13 (92.9%)	0 (0.0%)	11	4 (36.4%)	6 (54.5%)	1 (9.1%)	0 (0.0%)
Japan										
Visit 4 (Day 1)	28	28 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	28	28 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 5 (Day 3)	29	28 (96.6%)	0 (0.0%)	0 (0.0%)	1 (3.4%)	28	28 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 6 (Day 5)	28	28 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	28	28 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 7 (Day 8)	28	4 (14.3%)	24 (85.7%)	0 (0.0%)	0 (0.0%)	28	17 (60.7%)	10 (35.7%)	0 (0.0%)	1 (3.6%)
Visit 7.5 (Day 10)	15	2 (13.3%)	12 (80.0%)	0 (0.0%)	1 (6.7%)	13	7 (53.8%)	5 (38.5%)	0 (0.0%)	1 (7.7%)
Visit 8 (Day 12)	28	4 (14.3%)	24 (85.7%)	0 (0.0%)	0 (0.0%)	28	17 (60.7%)	10 (35.7%)	0 (0.0%)	1 (3.6%)
Visit 9 (Day 15)	28	2 (7.1%)	4 (14.3%)	22 (78.6%)	0 (0.0%)	28	15 (53.6%)	9 (32.1%)	3 (10.7%)	1 (3.6%)
Visit 9.5 (Day 17)	18	1 (5.6%)	3 (16.7%)	14 (77.8%)	0 (0.0%)	16	7 (43.8%)	6 (37.5%)	2 (12.5%)	1 (6.3%)
Visit 10 (Day 22)	28	1 (3.6%)	3 (10.7%)	24 (85.7%)	0 (0.0%)	28	12 (42.9%)	14 (50.0%)	1 (3.6%)	1 (3.6%)
Visit 10.5 (Day 24)	18	2 (11.1%)	1 (5.6%)	15 (83.3%)	0 (0.0%)	18	7 (38.9%)	9 (50.0%)	1 (5.6%)	1 (5.6%)
Visit 11 (Day 29)	28	2 (7.1%)	2 (7.1%)	24 (85.7%)	0 (0.0%)	28	12 (42.9%)	14 (50.0%)	1 (3.6%)	1 (3.6%)
Visit 11.5 (Day 31)	21	2 (9.5%)	1 (4.8%)	18 (85.7%)	0 (0.0%)	19	8 (42.1%)	9 (47.4%)	1 (5.3%)	1 (5.3%)
Visit 12 (Day 36)	28	2 (7.1%)	2 (7.1%)	24 (85.7%)	0 (0.0%)	28	12 (42.9%)	14 (50.0%)	1 (3.6%)	1 (3.6%)
Visit 12.5 (Day 38)	23	2 (8.7%)	1 (4.3%)	19 (82.6%)	1 (4.3%)	21	10 (47.6%)	9 (42.9%)	1 (4.8%)	1 (4.8%)
Visit 13 (Day 43)	28	2 (7.1%)	2 (7.1%)	24 (85.7%)	0 (0.0%)	27	12 (44.4%)	13 (48.1%)	1 (3.7%)	1 (3.7%)
Visit 13.5 (Day 45)	23	2 (8.7%)	1 (4.3%)	20 (87.0%)	0 (0.0%)	21	10 (47.6%)	9 (42.9%)	1 (4.8%)	1 (4.8%)
Visit 14 (Day 50)	28	2 (7.1%)	2 (7.1%)	24 (85.7%)	0 (0.0%)	27	12 (44.4%)	13 (48.1%)	1 (3.7%)	1 (3.7%)
Visit 14.5 (Day 52)	25	2 (8.0%)	1 (4.0%)	22 (88.0%)	0 (0.0%)	23	12 (52.2%)	9 (39.1%)	1 (4.3%)	1 (4.3%)
Russia										
Unknown	3	1 (33.3%)	0 (0.0%)	2 (66.7%)	0 (0.0%)	1	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)
Visit 4 (Day 1)	33	33 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	29	29 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 5 (Day 3)	33	33 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	33	33 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 6 (Day 5)	33	33 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	33	33 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

5g = 1 sachet, 10g = 2 sachets, 15g = 3 sachets.
Not dosed represents subjects who have discontinued, have a drug interruption or a zero dose.
Percentages calculated from subjects analyzed at each visit, within each treatment group.
N=Number of subjects in treatment group. n = Number of subjects included in analysis.

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Table 6.3.1.1 - Study DIALIZE: Dose of investigational product assigned by visit, SZC (variable dose) QD vs Placebo, overall and by subgroups (safety population)

	Placebo QD (N=99) [n(%)]					SZC variable dose QD (N=96) [n(%)]				
Subgroup / Category / Timepoint	**n**	**5g**	**10g**	**15g**	**Not dosed**	**n**	**5g**	**10g**	**15g**	**Not dosed**
Country *(contd.)*										
Russia *(contd.)*										
Visit 7 (Day 8)	33	7 (21.2%)	26 (78.8%)	0 (0.0%)	0 (0.0%)	33	16 (48.5%)	17 (51.5%)	0 (0.0%)	0 (0.0%)
Visit 7.5 (Day 10)	27	5 (18.5%)	22 (81.5%)	0 (0.0%)	0 (0.0%)	26	10 (38.5%)	16 (61.5%)	0 (0.0%)	0 (0.0%)
Visit 8 (Day 12)	33	7 (21.2%)	26 (78.8%)	0 (0.0%)	0 (0.0%)	33	15 (45.5%)	18 (54.5%)	0 (0.0%)	0 (0.0%)
Visit 9 (Day 15)	31	1 (3.2%)	8 (25.8%)	22 (71.0%)	0 (0.0%)	33	12 (36.4%)	14 (42.4%)	7 (21.2%)	0 (0.0%)
Visit 9.5 (Day 17)	25	1 (4.0%)	6 (24.0%)	18 (72.0%)	0 (0.0%)	29	9 (31.0%)	12 (41.4%)	8 (27.6%)	0 (0.0%)
Visit 10 (Day 22)	33	1 (3.0%)	2 (6.1%)	30 (90.9%)	0 (0.0%)	33	10 (30.3%)	12 (36.4%)	11 (33.3%)	0 (0.0%)
Visit 10.5 (Day 24)	27	1 (3.7%)	2 (7.4%)	24 (88.9%)	0 (0.0%)	29	8 (27.6%)	10 (34.5%)	11 (37.9%)	0 (0.0%)
Visit 11 (Day 29)	32	1 (3.1%)	2 (6.3%)	29 (90.6%)	0 (0.0%)	33	10 (30.3%)	12 (36.4%)	11 (33.3%)	0 (0.0%)
Visit 11.5 (Day 31)	28	1 (3.6%)	2 (7.1%)	25 (89.3%)	0 (0.0%)	29	8 (27.6%)	10 (34.5%)	11 (37.9%)	0 (0.0%)
Visit 12 (Day 36)	32	1 (3.1%)	2 (6.3%)	29 (90.6%)	0 (0.0%)	33	10 (30.3%)	12 (36.4%)	11 (33.3%)	0 (0.0%)
Visit 12.5 (Day 38)	29	1 (3.4%)	2 (6.9%)	26 (89.7%)	0 (0.0%)	29	8 (27.6%)	10 (34.5%)	11 (37.9%)	0 (0.0%)
Visit 13 (Day 43)	33	1 (3.0%)	2 (6.1%)	30 (90.9%)	0 (0.0%)	33	10 (30.3%)	12 (36.4%)	11 (33.3%)	0 (0.0%)
Visit 13.5 (Day 45)	29	1 (3.4%)	2 (6.9%)	26 (89.7%)	0 (0.0%)	29	8 (27.6%)	10 (34.5%)	11 (37.9%)	0 (0.0%)
Visit 14 (Day 50)	33	1 (3.0%)	2 (6.1%)	30 (90.9%)	0 (0.0%)	33	10 (30.3%)	12 (36.4%)	11 (33.3%)	0 (0.0%)
Visit 14.5 (Day 52)	29	1 (3.4%)	2 (6.9%)	26 (89.7%)	0 (0.0%)	29	8 (27.6%)	10 (34.5%)	11 (37.9%)	0 (0.0%)
Visit 15 (Day 57)	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3	0 (0.0%)	0 (0.0%)	3 (100.0%)	0 (0.0%)
Region USA or Rest of World										
USA										
Unknown	1	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	1	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)
Visit 4 (Day 1)	23	23 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	20	20 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 5 (Day 3)	22	22 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	19	19 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 6 (Day 5)	23	23 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	18	18 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 7 (Day 8)	23	12 (52.2%)	11 (47.8%)	0 (0.0%)	0 (0.0%)	18	7 (38.9%)	11 (61.1%)	0 (0.0%)	0 (0.0%)
Visit 7.5 (Day 10)	21	10 (47.6%)	11 (52.4%)	0 (0.0%)	0 (0.0%)	18	6 (33.3%)	12 (66.7%)	0 (0.0%)	0 (0.0%)
Visit 8 (Day 12)	22	11 (50.0%)	11 (50.0%)	0 (0.0%)	0 (0.0%)	19	7 (36.8%)	12 (63.2%)	0 (0.0%)	0 (0.0%)
Visit 9 (Day 15)	19	6 (31.6%)	6 (31.6%)	7 (36.8%)	0 (0.0%)	19	6 (31.6%)	11 (57.9%)	2 (10.5%)	0 (0.0%)
Visit 9.5 (Day 17)	20	6 (30.0%)	6 (30.0%)	8 (40.0%)	0 (0.0%)	19	6 (31.6%)	11 (57.9%)	2 (10.5%)	0 (0.0%)
Visit 10 (Day 22)	21	6 (28.6%)	1 (4.8%)	14 (66.7%)	0 (0.0%)	18	7 (38.9%)	7 (38.9%)	4 (22.2%)	0 (0.0%)
Visit 10.5 (Day 24)	20	6 (30.0%)	1 (5.0%)	13 (65.0%)	0 (0.0%)	17	6 (35.3%)	7 (41.2%)	4 (23.5%)	0 (0.0%)
Visit 11 (Day 29)	20	6 (30.0%)	1 (5.0%)	13 (65.0%)	0 (0.0%)	16	6 (37.5%)	7 (43.8%)	3 (18.8%)	0 (0.0%)
Visit 11.5 (Day 31)	19	6 (31.6%)	1 (5.3%)	12 (63.2%)	0 (0.0%)	18	6 (33.3%)	8 (44.4%)	4 (22.2%)	0 (0.0%)
Visit 12 (Day 36)	21	6 (28.6%)	1 (4.8%)	14 (66.7%)	0 (0.0%)	16	6 (37.5%)	6 (37.5%)	4 (25.0%)	0 (0.0%)
Visit 12.5 (Day 38)	20	6 (30.0%)	1 (5.0%)	13 (65.0%)	0 (0.0%)	17	6 (35.3%)	7 (41.2%)	4 (23.5%)	0 (0.0%)
Visit 13 (Day 43)	18	6 (33.3%)	1 (5.6%)	11 (61.1%)	0 (0.0%)	17	5 (29.4%)	8 (47.1%)	4 (23.5%)	0 (0.0%)
Visit 13.5 (Day 45)	17	6 (35.3%)	1 (5.9%)	10 (58.8%)	0 (0.0%)	17	6 (35.3%)	7 (41.2%)	4 (23.5%)	0 (0.0%)
Visit 14 (Day 50)	20	6 (30.0%)	1 (5.0%)	13 (65.0%)	0 (0.0%)	17	5 (29.4%)	8 (47.1%)	4 (23.5%)	0 (0.0%)
Visit 14.5 (Day 52)	19	6 (31.6%)	1 (5.3%)	12 (63.2%)	0 (0.0%)	17	5 (29.4%)	8 (47.1%)	4 (23.5%)	0 (0.0%)
Rest of World										
Unknown	4	1 (25.0%)	0 (0.0%)	3 (75.0%)	0 (0.0%)	1	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)
Visit 4 (Day 1)	76	76 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	70	70 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 5 (Day 3)	76	75 (98.7%)	0 (0.0%)	0 (0.0%)	1 (1.3%)	74	74 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 6 (Day 5)	76	76 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	74	74 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

5g = 1 sachet, 10g = 2 sachets, 15g = 3 sachets.
Not dosed represents subjects who have discontinued, have a drug interruption or a zero dose.
Percentages calculated from subjects analyzed at each visit, within each treatment group.
N=Number of subjects in treatment group. n = Number of subjects included in analysis.

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Table 6.3.1.1 - Study DIALIZE: Dose of investigational product assigned by visit, SZC (variable dose) QD vs Placebo, overall and by subgroups (safety population)

	Placebo QD (N=99) [n(%)]					SZC variable dose QD (N=96) [n(%)]				
Subgroup / Category / Timepoint	**n**	**5g**	**10g**	**15g**	**Not dosed**	**n**	**5g**	**10g**	**15g**	**Not dosed**
Region USA or Rest of World *(contd.)*										
Rest of World *(contd.)*										
Visit 7 (Day 8)	75	13 (17.3%)	62 (82.7%)	0 (0.0%)	0 (0.0%)	73	42 (57.5%)	30 (41.1%)	0 (0.0%)	1 (1.4%)
Visit 7.5 (Day 10)	56	9 (16.1%)	46 (82.1%)	0 (0.0%)	1 (1.8%)	51	26 (51.0%)	24 (47.1%)	0 (0.0%)	1 (2.0%)
Visit 8 (Day 12)	75	13 (17.3%)	62 (82.7%)	0 (0.0%)	0 (0.0%)	73	41 (56.2%)	31 (42.5%)	0 (0.0%)	1 (1.4%)
Visit 9 (Day 15)	73	3 (4.1%)	18 (24.7%)	52 (71.2%)	0 (0.0%)	72	32 (44.4%)	28 (38.9%)	11 (15.3%)	1 (1.4%)
Visit 9.5 (Day 17)	57	3 (5.3%)	15 (26.3%)	39 (68.4%)	0 (0.0%)	56	21 (37.5%)	23 (41.1%)	11 (19.6%)	1 (1.8%)
Visit 10 (Day 22)	74	2 (2.7%)	7 (9.5%)	65 (87.8%)	0 (0.0%)	72	26 (36.1%)	32 (44.4%)	13 (18.1%)	1 (1.4%)
Visit 10.5 (Day 24)	59	3 (5.1%)	5 (8.5%)	51 (86.4%)	0 (0.0%)	58	19 (32.8%)	25 (43.1%)	13 (22.4%)	1 (1.7%)
Visit 11 (Day 29)	74	3 (4.1%)	5 (6.8%)	66 (89.2%)	0 (0.0%)	72	26 (36.1%)	32 (44.4%)	13 (18.1%)	1 (1.4%)
Visit 11.5 (Day 31)	63	3 (4.8%)	4 (6.3%)	56 (88.9%)	0 (0.0%)	59	20 (33.9%)	25 (42.4%)	13 (22.0%)	1 (1.7%)
Visit 12 (Day 36)	74	3 (4.1%)	5 (6.8%)	66 (89.2%)	0 (0.0%)	72	26 (36.1%)	32 (44.4%)	13 (18.1%)	1 (1.4%)
Visit 12.5 (Day 38)	66	3 (4.5%)	4 (6.1%)	58 (87.9%)	1 (1.5%)	61	22 (36.1%)	25 (41.0%)	13 (21.3%)	1 (1.6%)
Visit 13 (Day 43)	75	3 (4.0%)	5 (6.7%)	67 (89.3%)	0 (0.0%)	71	26 (36.6%)	31 (43.7%)	13 (18.3%)	1 (1.4%)
Visit 13.5 (Day 45)	66	3 (4.5%)	4 (6.1%)	59 (89.4%)	0 (0.0%)	61	22 (36.1%)	25 (41.0%)	13 (21.3%)	1 (1.6%)
Visit 14 (Day 50)	75	3 (4.0%)	5 (6.7%)	67 (89.3%)	0 (0.0%)	70	25 (35.7%)	31 (44.3%)	13 (18.6%)	1 (1.4%)
Visit 14.5 (Day 52)	68	3 (4.4%)	4 (5.9%)	61 (89.7%)	0 (0.0%)	63	24 (38.1%)	25 (39.7%)	13 (20.6%)	1 (1.6%)
Visit 15 (Day 57)	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3	0 (0.0%)	0 (0.0%)	3 (100.0%)	0 (0.0%)
Region Japan or Not Japan										
Japan										
Visit 4 (Day 1)	28	28 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	28	28 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 5 (Day 3)	29	28 (96.6%)	0 (0.0%)	0 (0.0%)	1 (3.4%)	28	28 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 6 (Day 5)	28	28 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	28	28 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 7 (Day 8)	28	4 (14.3%)	24 (85.7%)	0 (0.0%)	0 (0.0%)	28	17 (60.7%)	10 (35.7%)	0 (0.0%)	1 (3.6%)
Visit 7.5 (Day 10)	15	2 (13.3%)	12 (80.0%)	0 (0.0%)	1 (6.7%)	13	7 (53.8%)	5 (38.5%)	0 (0.0%)	1 (7.7%)
Visit 8 (Day 12)	28	4 (14.3%)	24 (85.7%)	0 (0.0%)	0 (0.0%)	28	17 (60.7%)	10 (35.7%)	0 (0.0%)	1 (3.6%)
Visit 9 (Day 15)	28	2 (7.1%)	4 (14.3%)	22 (78.6%)	0 (0.0%)	28	15 (53.6%)	9 (32.1%)	3 (10.7%)	1 (3.6%)
Visit 9.5 (Day 17)	18	1 (5.6%)	3 (16.7%)	14 (77.8%)	0 (0.0%)	16	7 (43.8%)	6 (37.5%)	2 (12.5%)	1 (6.3%)
Visit 10 (Day 22)	28	1 (3.6%)	3 (10.7%)	24 (85.7%)	0 (0.0%)	28	12 (42.9%)	14 (50.0%)	1 (3.6%)	1 (3.6%)
Visit 10.5 (Day 24)	18	2 (11.1%)	1 (5.6%)	15 (83.3%)	0 (0.0%)	18	7 (38.9%)	9 (50.0%)	1 (5.6%)	1 (5.6%)
Visit 11 (Day 29)	28	2 (7.1%)	2 (7.1%)	24 (85.7%)	0 (0.0%)	28	12 (42.9%)	14 (50.0%)	1 (3.6%)	1 (3.6%)
Visit 11.5 (Day 31)	21	2 (9.5%)	1 (4.8%)	18 (85.7%)	0 (0.0%)	19	8 (42.1%)	9 (47.4%)	1 (5.3%)	1 (5.3%)
Visit 12 (Day 36)	28	2 (7.1%)	2 (7.1%)	24 (85.7%)	0 (0.0%)	28	12 (42.9%)	14 (50.0%)	1 (3.6%)	1 (3.6%)
Visit 12.5 (Day 38)	23	2 (8.7%)	1 (4.3%)	19 (82.6%)	1 (4.3%)	21	10 (47.6%)	9 (42.9%)	1 (4.8%)	1 (4.8%)
Visit 13 (Day 43)	28	2 (7.1%)	2 (7.1%)	24 (85.7%)	0 (0.0%)	27	12 (44.4%)	13 (48.1%)	1 (3.7%)	1 (3.7%)
Visit 13.5 (Day 45)	23	2 (8.7%)	1 (4.3%)	20 (87.0%)	0 (0.0%)	21	10 (47.6%)	9 (42.9%)	1 (4.8%)	1 (4.8%)
Visit 14 (Day 50)	28	2 (7.1%)	2 (7.1%)	24 (85.7%)	0 (0.0%)	27	12 (44.4%)	13 (48.1%)	1 (3.7%)	1 (3.7%)
Visit 14.5 (Day 52)	25	2 (8.0%)	1 (4.0%)	22 (88.0%)	0 (0.0%)	23	12 (52.2%)	9 (39.1%)	1 (4.3%)	1 (4.3%)
Not Japan										
Unknown	5	1 (20.0%)	0 (0.0%)	4 (80.0%)	0 (0.0%)	2	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)
Visit 4 (Day 1)	71	71 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	62	62 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 5 (Day 3)	69	69 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	65	65 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 6 (Day 5)	71	71 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	64	64 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Visit 7 (Day 8)	70	21 (30.0%)	49 (70.0%)	0 (0.0%)	0 (0.0%)	63	32 (50.8%)	31 (49.2%)	0 (0.0%)	0 (0.0%)

5g = 1 sachet, 10g = 2 sachets, 15g = 3 sachets.
Not dosed represents subjects who have discontinued, have a drug interruption or a zero dose.
Percentages calculated from subjects analyzed at each visit, within each treatment group.
N=Number of subjects in treatment group. n = Number of subjects included in analysis.

t_dialize_vardose.pdf generated by t_dialize_vardose.sas at 16:37:49 on 15 September 2020

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Table 6.3.1.1 - Study DIALIZE: Dose of investigational product assigned by visit, SZC (variable dose) QD vs Placebo, overall and by subgroups (safety population)

	Placebo QD (N=99) [n(%)]					SZC variable dose QD (N=96) [n(%)]				
Subgroup / Category / Timepoint	**n**	**5g**	**10g**	**15g**	**Not dosed**	**n**	**5g**	**10g**	**15g**	**Not dosed**
Region Japan or Not Japan *(contd.)*										
Not Japan *(contd.)*										
Visit 7.5 (Day 10)	62	17 (27.4%)	45 (72.6%)	0 (0.0%)	0 (0.0%)	56	25 (44.6%)	31 (55.4%)	0 (0.0%)	0 (0.0%)
Visit 8 (Day 12)	69	20 (29.0%)	49 (71.0%)	0 (0.0%)	0 (0.0%)	64	31 (48.4%)	33 (51.6%)	0 (0.0%)	0 (0.0%)
Visit 9 (Day 15)	64	7 (10.9%)	20 (31.3%)	37 (57.8%)	0 (0.0%)	63	23 (36.5%)	30 (47.6%)	10 (15.9%)	0 (0.0%)
Visit 9.5 (Day 17)	59	8 (13.6%)	18 (30.5%)	33 (55.9%)	0 (0.0%)	59	20 (33.9%)	28 (47.5%)	11 (18.6%)	0 (0.0%)
Visit 10 (Day 22)	67	7 (10.4%)	5 (7.5%)	55 (82.1%)	0 (0.0%)	62	21 (33.9%)	25 (40.3%)	16 (25.8%)	0 (0.0%)
Visit 10.5 (Day 24)	61	7 (11.5%)	5 (8.2%)	49 (80.3%)	0 (0.0%)	57	18 (31.6%)	23 (40.4%)	16 (28.1%)	0 (0.0%)
Visit 11 (Day 29)	66	7 (10.6%)	4 (6.1%)	55 (83.3%)	0 (0.0%)	60	20 (33.3%)	25 (41.7%)	15 (25.0%)	0 (0.0%)
Visit 11.5 (Day 31)	61	7 (11.5%)	4 (6.6%)	50 (82.0%)	0 (0.0%)	58	18 (31.0%)	24 (41.4%)	16 (27.6%)	0 (0.0%)
Visit 12 (Day 36)	67	7 (10.4%)	4 (6.0%)	56 (83.6%)	0 (0.0%)	60	20 (33.3%)	24 (40.0%)	16 (26.7%)	0 (0.0%)
Visit 12.5 (Day 38)	63	7 (11.1%)	4 (6.3%)	52 (82.5%)	0 (0.0%)	57	18 (31.6%)	23 (40.4%)	16 (28.1%)	0 (0.0%)
Visit 13 (Day 43)	65	7 (10.8%)	4 (6.2%)	54 (83.1%)	0 (0.0%)	61	19 (31.1%)	26 (42.6%)	16 (26.2%)	0 (0.0%)
Visit 13.5 (Day 45)	60	7 (11.7%)	4 (6.7%)	49 (81.7%)	0 (0.0%)	57	18 (31.6%)	23 (40.4%)	16 (28.1%)	0 (0.0%)
Visit 14 (Day 50)	67	7 (10.4%)	4 (6.0%)	56 (83.6%)	0 (0.0%)	60	18 (30.0%)	26 (43.3%)	16 (26.7%)	0 (0.0%)
Visit 14.5 (Day 52)	62	7 (11.3%)	4 (6.5%)	51 (82.3%)	0 (0.0%)	57	17 (29.8%)	24 (42.1%)	16 (28.1%)	0 (0.0%)
Visit 15 (Day 57)	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3	0 (0.0%)	0 (0.0%)	3 (100.0%)	0 (0.0%)

5g = 1 sachet, 10g = 2 sachets, 15g = 3 sachets.
Not dosed represents subjects who have discontinued, have a drug interruption or a zero dose.
Percentages calculated from subjects analyzed at each visit, within each treatment group.
N=Number of subjects in treatment group. n = Number of subjects included in analysis.

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Table 6.2.1.1 - Study DIALIZE: Subjects experiencing any adverse event (AE), SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	99	46 (46.5%)	96	40 (41.7%)	0.82 (0.47 , 1.45)	0.5001	0.90 (0.65 , 1.23)	0.5009	-4.80 (-18.72 , 9.12)	0.4993	
Sex											0.3097
Male	58	27 (46.6%)	56	20 (35.7%)	0.64 (0.30 , 1.35)	0.2410	0.77 (0.49 , 1.20)	0.2449	-10.84 (-28.79 , 7.11)	0.2367	
Female	41	19 (46.3%)	40	20 (50.0%)	1.16 (0.48 , 2.77)	0.7419	1.08 (0.69 , 1.70)	0.7419	3.66 (-18.09 , 25.41)	0.7416	
Age (years)											0.0386
<65 years	53	21 (39.6%)	64	30 (46.9%)	1.34 (0.64 , 2.81)	0.4315	1.18 (0.78 , 1.80)	0.4355	7.25 (-10.72 , 25.22)	0.4289	
>=65 years	46	25 (54.3%)	32	10 (31.3%)	0.38 (0.15 , 0.98)	0.0461	0.58 (0.32 , 1.03)	0.0607	-23.10 (-44.66 , -1.53)	0.0358	
Country											0.9160
USA	23	12 (52.2%)	21	11 (52.4%)	1.01 (0.31 , 3.30)	0.9890	1.00 (0.57 , 1.77)	0.9890	0.21 (-29.34 , 29.75)	0.9890	
GB	15	10 (66.7%)	14	9 (64.3%)	0.90 (0.19 , 4.17)	0.8928	0.96 (0.57 , 1.64)	0.8929	-2.38 (-37.01 , 32.25)	0.8928	
Japan	28	16 (57.1%)	28	15 (53.6%)	0.87 (0.30 , 2.48)	0.7881	0.94 (0.59 , 1.50)	0.7882	-3.57 (-29.59 , 22.45)	0.7879	
Russia	33	8 (24.2%)	33	5 (15.2%)	0.56 (0.16 , 1.93)	0.3568	0.63 (0.23 , 1.71)	0.3607	-9.09 (-28.16 , 9.97)	0.3500	
Region USA or Rest of world											0.7076
USA	23	12 (52.2%)	21	11 (52.4%)	1.01 (0.31 , 3.30)	0.9890	1.00 (0.57 , 1.77)	0.9890	0.21 (-29.34 , 29.75)	0.9890	
Rest of world	76	34 (44.7%)	75	29 (38.7%)	0.78 (0.41 , 1.49)	0.4498	0.86 (0.59 , 1.26)	0.4509	-6.07 (-21.77 , 9.63)	0.4485	
Region Japan or Not Japan											0.8940
Japan	28	16 (57.1%)	28	15 (53.6%)	0.87 (0.30 , 2.48)	0.7881	0.94 (0.59 , 1.50)	0.7882	-3.57 (-29.59 , 22.45)	0.7879	
Not Japan	71	30 (42.3%)	68	25 (36.8%)	0.79 (0.40 , 1.57)	0.5085	0.87 (0.58 , 1.32)	0.5097	-5.49 (-21.72 , 10.74)	0.5074	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_dialize_ae_any.pdf generated by dialize_ae_soc_pt.sas at 18:57:37 on 24 February 2021

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Table 6.2.1.2 - Study DIALIZE: Subjects experiencing any serious adverse event (SAE), SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	99	8 (8.1%)	96	7 (7.3%)	0.89 (0.31 , 2.57)	0.8363	0.90 (0.34 , 2.39)	0.8363	-0.79 (-8.26 , 6.69)	0.8361	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_dialize_ae_sae.pdf generated by dialize_ae_soc_pt.sas at 18:57:42 on 24 February 2021

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Table 6.2.1.3 - Study DIALIZE: Subjects experiencing any AE leading to discontinuation of study medication (DAE), SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	99	2 (2.0%)	96	4 (4.2%)	2.11 (0.38 , 11.79)	0.3956	2.06 (0.39 , 11.00)	0.3967	2.15 (-2.72 , 7.01)	0.3871	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_dialize_ae_dae.pdf generated by dialize_ae_soc_pt.sas at 18:57:46 on 24 February 2021

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Table 6.2.1.4 - Study DIALIZE: Subjects experiencing any AE graded as severe, SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	99	1 (1.0%)	96	3 (3.1%)	3.16 (0.32 , 30.93)	0.3226	3.09 (0.33 , 29.23)	0.3243	2.11 (-1.88 , 6.11)	0.3000	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_dialize_ae_sev.pdf generated by dialize_ae_soc_pt.sas at 18:57:50 on 24 February 2021

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Table 6.2.1.5 - Study DIALIZE: Subjects experiencing any AE graded as non-severe, SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	99	46 (46.5%)	96	39 (40.6%)	0.79 (0.45 , 1.39)	0.4113	0.87 (0.63 , 1.21)	0.4125	-5.84 (-19.73 , 8.05)	0.4101	
Sex											0.3982
Male	58	27 (46.6%)	56	20 (35.7%)	0.64 (0.30 , 1.35)	0.2410	0.77 (0.49 , 1.20)	0.2449	-10.84 (-28.79 , 7.11)	0.2367	
Female	41	19 (46.3%)	40	19 (47.5%)	1.05 (0.44 , 2.51)	0.9168	1.03 (0.64 , 1.63)	0.9168	1.16 (-20.58 , 22.89)	0.9168	
Age (years)											0.0496
<65 years	53	21 (39.6%)	64	29 (45.3%)	1.26 (0.60 , 2.64)	0.5360	1.14 (0.75 , 1.75)	0.5386	5.69 (-12.26 , 23.64)	0.5344	
>=65 years	46	25 (54.3%)	32	10 (31.3%)	0.38 (0.15 , 0.98)	0.0461	0.58 (0.32 , 1.03)	0.0607	-23.10 (-44.66 , -1.53)	0.0358	
Country											0.9477
USA	23	12 (52.2%)	21	10 (47.6%)	0.83 (0.25 , 2.72)	0.7629	0.91 (0.50 , 1.66)	0.7636	-4.55 (-34.10 , 24.99)	0.7625	
GB	15	10 (66.7%)	14	9 (64.3%)	0.90 (0.19 , 4.17)	0.8928	0.96 (0.57 , 1.64)	0.8929	-2.38 (-37.01 , 32.25)	0.8928	
Japan	28	16 (57.1%)	28	15 (53.6%)	0.87 (0.30 , 2.48)	0.7881	0.94 (0.59 , 1.50)	0.7882	-3.57 (-29.59 , 22.45)	0.7879	
Russia	33	8 (24.2%)	33	5 (15.2%)	0.56 (0.16 , 1.93)	0.3568	0.63 (0.23 , 1.71)	0.3607	-9.09 (-28.16 , 9.97)	0.3500	
Region USA or Rest of world											0.9217
USA	23	12 (52.2%)	21	10 (47.6%)	0.83 (0.25 , 2.72)	0.7629	0.91 (0.50 , 1.66)	0.7636	-4.55 (-34.10 , 24.99)	0.7625	
Rest of world	76	34 (44.7%)	75	29 (38.7%)	0.78 (0.41 , 1.49)	0.4498	0.86 (0.59 , 1.26)	0.4509	-6.07 (-21.77 , 9.63)	0.4485	
Region Japan or Not Japan											0.8161
Japan	28	16 (57.1%)	28	15 (53.6%)	0.87 (0.30 , 2.48)	0.7881	0.94 (0.59 , 1.50)	0.7882	-3.57 (-29.59 , 22.45)	0.7879	
Not Japan	71	30 (42.3%)	68	24 (35.3%)	0.75 (0.38 , 1.48)	0.4006	0.84 (0.55 , 1.27)	0.4025	-6.96 (-23.12 , 9.20)	0.3985	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 6.2.1.6 - Study DIALIZE: Subjects experiencing any AE resulting in death, SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	99	0 (0.0%)	96	1 (1.0%)	3.13 (0.13 , 77.68)	0.4869	3.09 (0.13 , 75.00)	0.4876	1.04 (-0.99 , 3.07)	0.3148	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_dialize_ae_death.pdf generated by dialize_ae_soc_pt.sas at 18:57:57 on 24 February 2021

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Table 6.2.1.7 - Study DIALIZE: Adverse events leading to discontinuation (DAE) by SOC and PT, SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)	
Subgroup / Category / SOC / PT	**N**	**n (%)**	**N**	**n (%)**
Overall				
Any AE	99	2 (2.0%)	96	4 (4.2%)
Gastrointestinal disorders	99	1 (1.0%)	96	2 (2.1%)
Diarrhoea	99	1 (1.0%)	96	0 (0.0%)
Gastrointestinal haemorrhage	99	0 (0.0%)	96	1 (1.0%)
Small intestinal obstruction	99	0 (0.0%)	96	1 (1.0%)
General disorders and administration site conditions	99	1 (1.0%)	96	0 (0.0%)
Peripheral swelling	99	1 (1.0%)	96	0 (0.0%)
Metabolism and nutrition disorders	99	0 (0.0%)	96	1 (1.0%)
Hyperkalaemia	99	0 (0.0%)	96	1 (1.0%)
Vascular disorders	99	0 (0.0%)	96	1 (1.0%)
Peripheral arterial occlusive disease	99	0 (0.0%)	96	1 (1.0%)
Sex				
Male				
Any AE	58	1 (1.7%)	56	0 (0.0%)
General disorders and administration site conditions	58	1 (1.7%)	56	0 (0.0%)
Peripheral swelling	58	1 (1.7%)	56	0 (0.0%)
Female				
Any AE	41	1 (2.4%)	40	4 (10.0%)
Gastrointestinal disorders	41	1 (2.4%)	40	2 (5.0%)
Diarrhoea	41	1 (2.4%)	40	0 (0.0%)
Gastrointestinal haemorrhage	41	0 (0.0%)	40	1 (2.5%)
Small intestinal obstruction	41	0 (0.0%)	40	1 (2.5%)
Metabolism and nutrition disorders	41	0 (0.0%)	40	1 (2.5%)
Hyperkalaemia	41	0 (0.0%)	40	1 (2.5%)
Vascular disorders	41	0 (0.0%)	40	1 (2.5%)
Peripheral arterial occlusive disease	41	0 (0.0%)	40	1 (2.5%)
Age (years)				
<65 years				
Any AE	53	1 (1.9%)	64	4 (6.3%)
Gastrointestinal disorders	53	0 (0.0%)	64	2 (3.1%)
Gastrointestinal haemorrhage	53	0 (0.0%)	64	1 (1.6%)
Small intestinal obstruction	53	0 (0.0%)	64	1 (1.6%)
General disorders and administration site conditions	53	1 (1.9%)	64	0 (0.0%)
Peripheral swelling	53	1 (1.9%)	64	0 (0.0%)
Metabolism and nutrition disorders	53	0 (0.0%)	64	1 (1.6%)
Hyperkalaemia	53	0 (0.0%)	64	1 (1.6%)
Vascular disorders	53	0 (0.0%)	64	1 (1.6%)
Peripheral arterial occlusive disease	53	0 (0.0%)	64	1 (1.6%)
>=65 years				
Any AE	46	1 (2.2%)	32	0 (0.0%)
Gastrointestinal disorders	46	1 (2.2%)	32	0 (0.0%)
Diarrhoea	46	1 (2.2%)	32	0 (0.0%)

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Table 6.2.1.7 - Study DIALIZE: Adverse events leading to discontinuation (DAE) by SOC and PT, SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)	
Subgroup / Category / SOC / PT	**N**	**n (%)**	**N**	**n (%)**
Country				
USA				
Any AE	23	1 (4.3%)	21	1 (4.8%)
Gastrointestinal disorders	23	1 (4.3%)	21	0 (0.0%)
Diarrhoea	23	1 (4.3%)	21	0 (0.0%)
Vascular disorders	23	0 (0.0%)	21	1 (4.8%)
Peripheral arterial occlusive disease	23	0 (0.0%)	21	1 (4.8%)
GB				
Any AE	15	1 (6.7%)	14	2 (14.3%)
Gastrointestinal disorders	15	0 (0.0%)	14	1 (7.1%)
Small intestinal obstruction	15	0 (0.0%)	14	1 (7.1%)
General disorders and administration site conditions	15	1 (6.7%)	14	0 (0.0%)
Peripheral swelling	15	1 (6.7%)	14	0 (0.0%)
Metabolism and nutrition disorders	15	0 (0.0%)	14	1 (7.1%)
Hyperkalaemia	15	0 (0.0%)	14	1 (7.1%)
Japan				
Any AE	28	0 (0.0%)	28	1 (3.6%)
Gastrointestinal disorders	28	0 (0.0%)	28	1 (3.6%)
Gastrointestinal haemorrhage	28	0 (0.0%)	28	1 (3.6%)
Russia				
Any AE	33	0 (0.0%)	33	0 (0.0%)
Region USA or Rest of world				
USA				
Any AE	23	1 (4.3%)	21	1 (4.8%)
Gastrointestinal disorders	23	1 (4.3%)	21	0 (0.0%)
Diarrhoea	23	1 (4.3%)	21	0 (0.0%)
Vascular disorders	23	0 (0.0%)	21	1 (4.8%)
Peripheral arterial occlusive disease	23	0 (0.0%)	21	1 (4.8%)
Rest of world				
Any AE	76	1 (1.3%)	75	3 (4.0%)
Gastrointestinal disorders	76	0 (0.0%)	75	2 (2.7%)
Gastrointestinal haemorrhage	76	0 (0.0%)	75	1 (1.3%)
Small intestinal obstruction	76	0 (0.0%)	75	1 (1.3%)
General disorders and administration site conditions	76	1 (1.3%)	75	0 (0.0%)
Peripheral swelling	76	1 (1.3%)	75	0 (0.0%)
Metabolism and nutrition disorders	76	0 (0.0%)	75	1 (1.3%)
Hyperkalaemia	76	0 (0.0%)	75	1 (1.3%)
Region Japan or Not Japan				
Japan				
Any AE	28	0 (0.0%)	28	1 (3.6%)
Gastrointestinal disorders	28	0 (0.0%)	28	1 (3.6%)
Gastrointestinal haemorrhage	28	0 (0.0%)	28	1 (3.6%)

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Table 6.2.1.7 - Study DIALIZE: Adverse events leading to discontinuation (DAE) by SOC and PT, SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)	
Subgroup / Category / SOC / PT	**N**	**n (%)**	**N**	**n (%)**
Region Japan or Not Japan *(contd.)*				
Not Japan				
Any AE	71	2 (2.8%)	68	3 (4.4%)
Gastrointestinal disorders	71	1 (1.4%)	68	1 (1.5%)
Diarrhoea	71	1 (1.4%)	68	0 (0.0%)
Small intestinal obstruction	71	0 (0.0%)	68	1 (1.5%)
General disorders and administration site conditions	71	1 (1.4%)	68	0 (0.0%)
Peripheral swelling	71	1 (1.4%)	68	0 (0.0%)
Metabolism and nutrition disorders	71	0 (0.0%)	68	1 (1.5%)
Hyperkalaemia	71	0 (0.0%)	68	1 (1.5%)
Vascular disorders	71	0 (0.0%)	68	1 (1.5%)
Peripheral arterial occlusive disease	71	0 (0.0%)	68	1 (1.5%)

t_dialize_ae_dae_socpt.pdf generated by dialize_ae_soc_pt.sas at 18:58:17 on 24 February 2021

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Table 6.2.1.8 - Study DIALIZE: Adverse events (AE) by SOC and PT occurring in at least 10% of subjects in any treatment group, SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)								
Subgroup / SOC :PT / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	99	46 (46.5%)	96	40 (41.7%)	0.82 (0.47 , 1.45)	0.5001	0.90 (0.65 , 1.23)	0.5009	-4.80 (-18.72 , 9.12)	0.4993	
Gastrointestinal disorders: All	99	15 (15.2%)	96	15 (15.6%)	1.04 (0.48 , 2.26)	0.9270	1.03 (0.53 , 1.99)	0.9270	0.47 (-9.66 , 10.60)	0.9270	
Infections and infestations: All	99	9 (9.1%)	96	10 (10.4%)	1.16 (0.45 , 3.00)	0.7551	1.15 (0.49 , 2.70)	0.7552	1.33 (-7.01 , 9.66)	0.7551	
Injury, poisoning and procedural complications: All	99	13 (13.1%)	96	4 (4.2%)	0.29 (0.09 , 0.92)	0.0350	0.32 (0.11 , 0.94)	0.0381	-8.96 (-16.73 , -1.20)	0.0236	
Sex											
Injury, poisoning and procedural complications: All											0.4598
Male	58	9 (15.5%)	56	2 (3.6%)	0.20 (0.04 , 0.98)	0.0470	0.23 (0.05 , 1.02)	0.0529	-11.95 (-22.46 , -1.44)	0.0259	
Female	41	4 (9.8%)	40	2 (5.0%)	0.49 (0.08 , 2.82)	0.4219	0.51 (0.10 , 2.64)	0.4245	-4.76 (-16.07 , 6.56)	0.4102	
Age (years)											
Injury, poisoning and procedural complications: All											0.5563
<65 years	53	6 (11.3%)	64	3 (4.7%)	0.39 (0.09 , 1.62)	0.1933	0.41 (0.11 , 1.58)	0.1962	-6.63 (-16.61 , 3.35)	0.1926	
>=65 years	46	7 (15.2%)	32	1 (3.1%)	0.18 (0.02 , 1.54)	0.1173	0.21 (0.03 , 1.59)	0.1294	-12.09 (-24.10 , -0.09)	0.0483	
Country											
Injury, poisoning and procedural complications: All											0.5034
USA	23	4 (17.4%)	21	0 (0.0%)	0.10 (0.01 , 1.99)	0.1319	0.12 (0.01 , 2.12)	0.1487	-17.39 (-32.88 , -1.90)	0.0278	
GB	15	1 (6.7%)	14	1 (7.1%)	1.08 (0.06 , 19.05)	0.9597	1.07 (0.07 , 15.54)	0.9597	0.48 (-18.00 , 18.95)	0.9597	
Japan	28	6 (21.4%)	28	2 (7.1%)	0.28 (0.05 , 1.54)	0.1440	0.33 (0.07 , 1.51)	0.1545	-14.29 (-32.23 , 3.66)	0.1187	
Russia	33	2 (6.1%)	33	1 (3.0%)	0.48 (0.04 , 5.62)	0.5621	0.50 (0.05 , 5.25)	0.5634	-3.03 (-13.05 , 6.99)	0.5535	
Region USA or Rest of world											
Injury, poisoning and procedural complications: All											0.2048
USA	23	4 (17.4%)	21	0 (0.0%)	0.10 (0.01 , 1.99)	0.1319	0.12 (0.01 , 2.12)	0.1487	-17.39 (-32.88 , -1.90)	0.0278	
Rest of world	76	9 (11.8%)	75	4 (5.3%)	0.42 (0.12 , 1.43)	0.1642	0.45 (0.14 , 1.40)	0.1679	-6.51 (-15.38 , 2.36)	0.1502	
Region Japan or Not Japan											
Injury, poisoning and procedural complications: All											0.9880
Japan	28	6 (21.4%)	28	2 (7.1%)	0.28 (0.05 , 1.54)	0.1440	0.33 (0.07 , 1.51)	0.1545	-14.29 (-32.23 , 3.66)	0.1187	
Not Japan	71	7 (9.9%)	68	2 (2.9%)	0.28 (0.06 , 1.38)	0.1179	0.30 (0.06 , 1.39)	0.1227	-6.92 (-14.93 , 1.10)	0.0906	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

t_dialize_ae_any_socpt.pdf generated by dialize_ae_soc_pt.sas at 18:58:02 on 24 February 2021

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Table 6.2.1.9 - Study DIALIZE: Serious adverse events (SAE) by SOC and PT occurring in at least 5% of subjects in any treatment group, SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	99	8 (8.1%)	96	7 (7.3%)	0.89 (0.31 , 2.57)	0.8363	0.90 (0.34 , 2.39)	0.8363	-0.79 (-8.26 , 6.69)	0.8361	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

t_dialize_ae_sae_socpt.pdf generated by dialize_ae_soc_pt.sas at 18:58:06 on 24 February 2021

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Table 6.2.1.10 - Study DIALIZE: AEs graded as severe by SOC and PT occurring in at least 5% of subjects in any treatment group, SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	99	1 (1.0%)	96	3 (3.1%)	3.16 (0.32 , 30.93)	0.3226	3.09 (0.33 , 29.23)	0.3243	2.11 (-1.88 , 6.11)	0.3000	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

t_dialize_ae_sev_socpt.pdf generated by dialize_ae_soc_pt.sas at 18:58:09 on 24 February 2021

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Table 6.2.1.11 - Study DIALIZE: AEs graded as non-severe by SOC and PT occurring in at least 10% of subjects in any treatment group, SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)								
Subgroup / SOC :PT / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	99	46 (46.5%)	96	39 (40.6%)	0.79 (0.45 , 1.39)	0.4113	0.87 (0.63 , 1.21)	0.4125	-5.84 (-19.73 , 8.05)	0.4101	
Gastrointestinal disorders: All	99	14 (14.1%)	96	15 (15.6%)	1.12 (0.51 , 2.48)	0.7711	1.10 (0.56 , 2.16)	0.7711	1.48 (-8.51 , 11.48)	0.7711	
Injury, poisoning and procedural complications: All	99	13 (13.1%)	96	4 (4.2%)	0.29 (0.09 , 0.92)	0.0350	0.32 (0.11 , 0.94)	0.0381	-8.96 (-16.73 , -1.20)	0.0236	
Sex											
Injury, poisoning and procedural complications: All											0.4598
Male	58	9 (15.5%)	56	2 (3.6%)	0.20 (0.04 , 0.98)	0.0470	0.23 (0.05 , 1.02)	0.0529	-11.95 (-22.46 , -1.44)	0.0259	
Female	41	4 (9.8%)	40	2 (5.0%)	0.49 (0.08 , 2.82)	0.4219	0.51 (0.10 , 2.64)	0.4245	-4.76 (-16.07 , 6.56)	0.4102	
Age (years)											
Injury, poisoning and procedural complications: All											0.5563
<65 years	53	6 (11.3%)	64	3 (4.7%)	0.39 (0.09 , 1.62)	0.1933	0.41 (0.11 , 1.58)	0.1962	-6.63 (-16.61 , 3.35)	0.1926	
>=65 years	46	7 (15.2%)	32	1 (3.1%)	0.18 (0.02 , 1.54)	0.1173	0.21 (0.03 , 1.59)	0.1294	-12.09 (-24.10 , -0.09)	0.0483	
Country											
Injury, poisoning and procedural complications: All											0.5034
USA	23	4 (17.4%)	21	0 (0.0%)	0.10 (0.01 , 1.99)	0.1319	0.12 (0.01 , 2.12)	0.1487	-17.39 (-32.88 , -1.90)	0.0278	
GB	15	1 (6.7%)	14	1 (7.1%)	1.08 (0.06 , 19.05)	0.9597	1.07 (0.07 , 15.54)	0.9597	0.48 (-18.00 , 18.95)	0.9597	
Japan	28	6 (21.4%)	28	2 (7.1%)	0.28 (0.05 , 1.54)	0.1440	0.33 (0.07 , 1.51)	0.1545	-14.29 (-32.23 , 3.66)	0.1187	
Russia	33	2 (6.1%)	33	1 (3.0%)	0.48 (0.04 , 5.62)	0.5621	0.50 (0.05 , 5.25)	0.5634	-3.03 (-13.05 , 6.99)	0.5535	
Region USA or Rest of world											
Injury, poisoning and procedural complications: All											0.2048
USA	23	4 (17.4%)	21	0 (0.0%)	0.10 (0.01 , 1.99)	0.1319	0.12 (0.01 , 2.12)	0.1487	-17.39 (-32.88 , -1.90)	0.0278	
Rest of world	76	9 (11.8%)	75	4 (5.3%)	0.42 (0.12 , 1.43)	0.1642	0.45 (0.14 , 1.40)	0.1679	-6.51 (-15.38 , 2.36)	0.1502	
Region Japan or Not Japan											
Injury, poisoning and procedural complications: All											0.9880
Japan	28	6 (21.4%)	28	2 (7.1%)	0.28 (0.05 , 1.54)	0.1440	0.33 (0.07 , 1.51)	0.1545	-14.29 (-32.23 , 3.66)	0.1187	
Not Japan	71	7 (9.9%)	68	2 (2.9%)	0.28 (0.06 , 1.38)	0.1179	0.30 (0.06 , 1.39)	0.1227	-6.92 (-14.93 , 1.10)	0.0906	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

t_dialize_ae_nsev_socpt.pdf generated by dialize_ae_soc_pt.sas at 18:58:13 on 24 February 2021

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Table 6.2.1.12 - Study DIALIZE: Adverse events resulting in death by SOC and PT, SZC (variable dose) QD vs. placebo, overall and by subgroups (safety population)

	Placebo (N=99)		Lokelma 10g TID (N=96)	
Subgroup / Category / SOC / PT	**N**	**n (%)**	**N**	**n (%)**
Overall				
Any AE	99	0 (0.0%)	96	1 (1.0%)
Vascular disorders	99	0 (0.0%)	96	1 (1.0%)
Peripheral arterial occlusive disease	99	0 (0.0%)	96	1 (1.0%)
Sex				
Male				
Any AE	58	0 (0.0%)	56	0 (0.0%)
Female				
Any AE	41	0 (0.0%)	40	1 (2.5%)
Vascular disorders	41	0 (0.0%)	40	1 (2.5%)
Peripheral arterial occlusive disease	41	0 (0.0%)	40	1 (2.5%)
Age (years)				
<65 years				
Any AE	53	0 (0.0%)	64	1 (1.6%)
Vascular disorders	53	0 (0.0%)	64	1 (1.6%)
Peripheral arterial occlusive disease	53	0 (0.0%)	64	1 (1.6%)
>=65 years				
Any AE	46	0 (0.0%)	32	0 (0.0%)
Country				
USA				
Any AE	23	0 (0.0%)	21	1 (4.8%)
Vascular disorders	23	0 (0.0%)	21	1 (4.8%)
Peripheral arterial occlusive disease	23	0 (0.0%)	21	1 (4.8%)
GB				
Any AE	15	0 (0.0%)	14	0 (0.0%)
Japan				
Any AE	28	0 (0.0%)	28	0 (0.0%)
Russia				
Any AE	33	0 (0.0%)	33	0 (0.0%)
Region USA or Rest of world				
USA				
Any AE	23	0 (0.0%)	21	1 (4.8%)
Vascular disorders	23	0 (0.0%)	21	1 (4.8%)
Peripheral arterial occlusive disease	23	0 (0.0%)	21	1 (4.8%)
Rest of world				
Any AE	76	0 (0.0%)	75	0 (0.0%)
Region Japan or Not Japan				
Japan				
Any AE	28	0 (0.0%)	28	0 (0.0%)
Not Japan				
Any AE	71	0 (0.0%)	68	1 (1.5%)
Vascular disorders	71	0 (0.0%)	68	1 (1.5%)
Peripheral arterial occlusive disease	71	0 (0.0%)	68	1 (1.5%)

t_dialize_ae_death_socpt.pdf generated by dialize_ae_soc_pt.sas at 18:58:23 on 24 February 2021

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Anhang 4-G2: Studie ZS002

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Table 1.1.1.1 - Study ZS-002: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours, ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value
Overall	30	24					
Through 24 hours							
Time			-0.00228	0.000672	-3.39	0.0014	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00130	0.000996	-1.31	0.1918	
Through 48 hours							
Time			-0.00090	0.000325	-2.78	0.0076	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00266	0.000475	-5.60	<.0001	
Acute Baseline S-K value							0.2559
<=5.3 mmol/L	25	19					
Through 24 hours							
Time			-0.00209	0.000658	-3.18	0.0028	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00063	0.000994	-0.64	0.5250	
Through 48 hours							
Time			-0.00089	0.000350	-2.55	0.0146	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00222	0.000531	-4.17	<.0001	
5.4-5.5 mmol/L	2	3					
Through 24 hours							
Time			-0.00287	0.003632	-0.79	0.4877	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00599	0.003852	-1.56	0.1303	
Through 48 hours							
Time			-0.00056	0.000778	-0.72	0.5244	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00451	0.000652	-6.93	<.0001	
>5.5 mmol/L	3	2					
Through 24 hours							
Time			-0.00365	0.002481	-1.47	0.2373	
10g ZS time-treatment interaction (Ref: Placebo*Time)			0.00026	0.003902	0.07	0.9466	
Through 48 hours							
Time			-0.00179	0.001091	-1.64	0.1987	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00294	0.001104	-2.67	0.0100	
Chronic kidney disease							0.3159
Yes	6	7					
Through 24 hours							
Time			-0.00098	0.001204	-0.81	0.4330	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00073	0.001595	-0.46	0.6470	
Through 48 hours							
Time			-0.00033	0.000507	-0.66	0.5249	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00252	0.000621	-4.05	<.0001	

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.

Interaction p-values are based on analysis through 48 hours.

t_zs002_sk_exp.pdf generated by zs002_zs002j_zs003ac_zsiss_sk_exp.sas at 12:51:03 on 17 February 2021

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Table 1.1.1.1 - Study ZS-002: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours, ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value
Chronic kidney disease *(contd.)*							
No	24	17					
Through 24 hours							
Time			-0.00265	0.000777	-3.41	0.0015	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00162	0.001200	-1.35	0.1780	
Through 48 hours							
Time			-0.00106	0.000388	-2.74	0.0093	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00277	0.000593	-4.67	<.0001	
Congestive Heart Disease							0.4072
Yes	11	13					
Through 24 hours							
Time			-0.00384	0.001074	-3.58	0.0017	
10g ZS time-treatment interaction (Ref: Placebo*Time)			0.00031	0.001394	0.22	0.8224	
Through 48 hours							
Time			-0.00117	0.000468	-2.50	0.0202	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00202	0.000615	-3.29	0.0011	
No	19	11					
Through 24 hours							
Time			-0.00155	0.000843	-1.84	0.0761	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00177	0.001382	-1.28	0.2013	
Through 48 hours							
Time			-0.00073	0.000456	-1.59	0.1228	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00331	0.000723	-4.58	<.0001	
Diabetes mellitus							0.5853
Yes	19	11					
Through 24 hours							
Time			-0.00115	0.000754	-1.52	0.1397	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00152	0.001242	-1.22	0.2234	
Through 48 hours							
Time			-0.00070	0.000347	-2.01	0.0540	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00266	0.000559	-4.77	<.0001	
No	11	13					
Through 24 hours							
Time			-0.00412	0.001091	-3.78	0.0010	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00034	0.001406	-0.24	0.8085	
Through 48 hours							
Time			-0.00126	0.000625	-2.01	0.0564	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00249	0.000817	-3.04	0.0026	

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.

Interaction p-values are based on analysis through 48 hours.

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Table 1.1.1.1 - Study ZS-002: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours, ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value
RAASi Medications							0.0006
Yes	19	20					
Through 24 hours							
Time			-0.00250	0.000861	-2.90	0.0063	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00172	0.001199	-1.44	0.1525	
Through 48 hours							
Time			-0.00119	0.000385	-3.08	0.0039	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00288	0.000532	-5.41	<.0001	
No	11	4					
Through 24 hours							
Time			-0.00181	0.000930	-1.95	0.0736	
10g ZS time-treatment interaction (Ref: Placebo*Time)			0.00115	0.001697	0.68	0.4996	
Through 48 hours							
Time			-0.00042	0.000409	-1.03	0.3198	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00065	0.000734	-0.89	0.3757	
Acute Baseline eGFR							
<15	0	0					
Through 24 hours							
Time			NC	NC	NC	NC	
10g ZS time-treatment interaction (Ref: Placebo*Time)			NC	NC	NC	NC	
Through 48 hours							
Time			NC	NC	NC	NC	
10g ZS time-treatment interaction (Ref: Placebo*Time)			NC	NC	NC	NC	
15-29+	1	1					
Through 24 hours							
Time			-0.00730	0.044102	-0.17	NC	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00080	0.062315	-0.01	0.9900	
Through 48 hours							
Time			-0.00169	0.010605	-0.16	NC	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00375	0.014962	-0.25	0.8045	
30-59+	28	22					
Through 24 hours							
Time			-0.00213	0.000699	-3.04	0.0038	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00117	0.001044	-1.12	0.2635	
Through 48 hours							
Time			-0.00086	0.000342	-2.52	0.0150	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00264	0.000501	-5.26	<.0001	

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.

Interaction p-values are based on analysis through 48 hours.

t_zs002_sk_exp.pdf generated by zs002_zs002j_zs003ac_zsiss_sk_exp.sas at 12:51:03 on 17 February 2021

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Table 1.1.1.1 - Study ZS-002: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours, ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

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Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value
Acute Baseline eGFR *(contd.)*							
>=60	1	1					
Through 24 hours							
Time			-0.00386	0.013444	-0.29	NC	
10g ZS time-treatment interaction (Ref: Placebo*Time)			0.00110	0.018947	0.06	0.9548	
Through 48 hours							
Time			-0.00223	0.012476	-0.18	NC	
10g ZS time-treatment interaction (Ref: Placebo*Time)			0.00009	0.017633	0.01	0.9959	
Sex							0.1514
Male	23	9					
Through 24 hours							
Time			-0.00265	0.000807	-3.29	0.0026	
10g ZS time-treatment interaction (Ref: Placebo*Time)			0.00000	0.001506	0.00	0.9988	
Through 48 hours							
Time			-0.00109	0.000387	-2.82	0.0084	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00165	0.000706	-2.34	0.0198	
Female	7	15					
Through 24 hours							
Time			-0.00136	0.001285	-1.06	0.3016	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00263	0.001545	-1.70	0.0912	
Through 48 hours							
Time			-0.00045	0.000588	-0.76	0.4580	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00354	0.000705	-5.03	<.0001	
Age							0.2170
<65 years	9	7					
Through 24 hours							
Time			-0.00191	0.000943	-2.03	0.0619	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00034	0.001421	-0.24	0.8122	
Through 48 hours							
Time			-0.00068	0.000461	-1.47	0.1627	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00189	0.000676	-2.80	0.0056	
>=65 years	21	17					
Through 24 hours							
Time			-0.00243	0.000872	-2.79	0.0085	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00170	0.001283	-1.33	0.1856	
Through 48 hours							
Time			-0.00101	0.000413	-2.44	0.0199	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00296	0.000604	-4.90	<.0001	

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.

Interaction p-values are based on analysis through 48 hours.

t_zs002_sk_exp.pdf generated by zs002_zs002j_zs003ac_zsiss_sk_exp.sas at 12:51:03 on 17 February 2021

26/02/2021

Lokelma

Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Overall																
Baseline																
Absolute value	30	5.14 (0.358)	5.1 (4.9, 5.3)	4.6, 6.1			24	5.05 (0.359)	4.9 (4.8, 5.2)	4.6, 6.0						
Day 1 / 30-min Post 1st																
Absolute value	29	5.17 (0.419)	5.2 (4.9, 5.4)	4.3, 6.0			24	5.03 (0.456)	4.9 (4.7, 5.4)	4.5, 6.2						
Change from baseline	29	0.03 (0.311)	0.0 (-0.1, 0.2)	-0.6, 0.6	0.05 (0.054)	(-0.06, 0.16)	24	-0.02 (0.243)	-0.1 (-0.2, 0.2)	-0.5, 0.5	-0.03 (0.059)	(-0.15, 0.09)	-0.08 (-0.24, 0.08)	0.3209	-0.19 (-0.73, 0.35)	
Percent change from baseline	29	0.73 (6.037)	0.0 (-2.1, 3.9)	-11.3, 11.9			24	-0.44 (4.791)	-1.4 (-3.8, 3.1)	-8.7, 11.2						
Day 1 / 1-hr Post 1st																
Absolute value	30	5.26 (0.524)	5.3 (4.9, 5.5)	4.4, 7.1			24	4.94 (0.438)	4.8 (4.7, 5.2)	4.4, 6.3						
Change from baseline	30	0.12 (0.362)	0.1 (-0.1, 0.3)	-0.5, 1.1	0.13 (0.073)	(-0.02, 0.28)	24	-0.11 (0.461)	-0.2 (-0.3, 0.0)	-0.9, 1.5	-0.12 (0.082)	(-0.29, 0.04)	-0.25 (-0.47, -0.03)	0.0258	-0.57 (-1.11, -0.02)	
Percent change from baseline	30	2.32 (6.787)	2.3 (-2.4, 6.1)	-10.2, 17.4			24	-1.96 (9.179)	-3.4 (-5.1, 0.9)	-14.8, 32.2						
Day 1 / 2-hr Post 1st																
Absolute value	30	5.12 (0.532)	5.0 (4.8, 5.3)	4.5, 6.7			23	4.93 (0.429)	4.8 (4.5, 5.4)	4.2, 5.7						
Change from baseline	30	-0.02 (0.341)	-0.1 (-0.2, 0.2)	-1.0, 0.7	-0.01 (0.064)	(-0.14, 0.12)	23	-0.13 (0.345)	-0.1 (-0.3, -0.1)	-0.7, 0.7	-0.14 (0.073)	(-0.29, 0.01)	-0.13 (-0.33, 0.06)	0.1770	-0.34 (-0.89, 0.21)	
Percent change from baseline	30	-0.40 (6.157)	-1.1 (-4.2, 4.2)	-16.5, 10.9			23	-2.54 (6.918)	-2.8 (-6.6, -1.7)	-12.6, 14.3						
Day 1 / 4-hr Post 1st																
Absolute value	30	4.97 (0.564)	4.9 (4.7, 5.3)	3.7, 6.2			24	4.80 (0.466)	4.8 (4.5, 5.0)	4.0, 5.6						
Change from baseline	30	-0.16 (0.541)	-0.1 (-0.4, 0.2)	-1.8, 1.1	-0.15 (0.086)	(-0.33, 0.02)	24	-0.25 (0.408)	-0.3 (-0.6, 0.0)	-0.8, 0.7	-0.27 (0.096)	(-0.46, -0.07)	-0.11 (-0.37, 0.15)	0.3925	-0.18 (-0.72, 0.35)	
Percent change from baseline	30	-3.02 (10.417)	-2.6 (-8.0, 2.5)	-32.7, 21.2			24	-4.90 (8.116)	-5.1 (-11.8, 0.3)	-17.0, 14.3						
Day 1 / 4-hr Post 2nd																
Absolute value	28	4.91 (0.465)	4.9 (4.6, 5.3)	3.9, 5.8			24	4.68 (0.420)	4.6 (4.4, 5.0)	4.1, 5.6						
Change from baseline	28	-0.24 (0.463)	-0.2 (-0.5, 0.0)	-1.3, 0.7	-0.22 (0.075)	(-0.38, -0.07)	24	-0.37 (0.379)	-0.4 (-0.5, -0.2)	-1.1, 0.3	-0.38 (0.082)	(-0.55, -0.22)	-0.16 (-0.38, 0.07)	0.1616	-0.31 (-0.86, 0.24)	
Percent change from baseline	28	-4.42 (8.895)	-5.0 (-9.9, 0.3)	-25.2, 13.2			24	-7.18 (7.418)	-7.6 (-11.0, -3.5)	-21.5, 6.2						
Day 1 / 4-hr Post 3rd																
Absolute value	30	4.82 (0.558)	4.8 (4.4, 5.1)	4.0, 6.3			24	4.50 (0.397)	4.6 (4.2, 4.8)	3.9, 5.2						
Change from baseline	30	-0.32 (0.503)	-0.3 (-0.5, -0.0)	-1.5, 0.6	-0.31 (0.085)	(-0.48, -0.14)	24	-0.55 (0.469)	-0.4 (-0.9, -0.2)	-1.5, 0.3	-0.56 (0.095)	(-0.75, -0.37)	-0.25 (-0.51, 0.00)	0.0544	-0.47 (-1.01, 0.08)	
Percent change from baseline	30	-6.14 (9.436)	-6.0 (-11.3, -0.4)	-27.3, 12.0			24	-10.57 (8.867)	-8.5 (-17.4, -4.3)	-27.3, 6.1						
Day 2 / 0-hr																
Absolute value	30	4.97 (0.521)	4.9 (4.6, 5.2)	4.0, 6.7			24	4.73 (0.463)	4.8 (4.4, 5.0)	3.9, 5.7						
Change from baseline	30	-0.17 (0.425)	-0.2 (-0.3, 0.1)	-1.3, 0.9	-0.16 (0.080)	(-0.32, -0.00)	24	-0.32 (0.482)	-0.3 (-0.8, -0.0)	-1.1, 0.6	-0.33 (0.089)	(-0.51, -0.15)	-0.17 (-0.41, 0.07)	0.1582	-0.33 (-0.87, 0.21)	
Percent change from baseline	30	-3.27 (7.786)	-3.5 (-6.4, 1.4)	-21.6, 15.5			24	-6.10 (9.383)	-5.0 (-14.6, -0.2)	-21.2, 12.2						
Day 2 / 4-hr Post 1st																
Absolute value	29	5.03 (0.441)	5.0 (4.8, 5.2)	3.8, 5.9			24	4.53 (0.411)	4.5 (4.3, 4.7)	3.9, 5.5						
Change from baseline	29	-0.10 (0.399)	-0.1 (-0.4, 0.1)	-0.8, 0.8	-0.10 (0.075)	(-0.25, 0.05)	24	-0.52 (0.487)	-0.5 (-0.9, -0.2)	-1.4, 0.8	-0.53 (0.083)	(-0.70, -0.37)	-0.43 (-0.66, -0.21)	0.0003	-0.94 (-1.51, -0.37)	
Percent change from baseline	29	-1.88 (7.788)	-2.0 (-7.3, 2.1)	-16.5, 15.7			24	-9.99 (9.252)	-11.1 (-15.9, -4.6)	-25.0, 16.2						
Day 2 / 4-hr Post 2nd																
Absolute value	28	5.02 (0.426)	5.1 (4.7, 5.3)	4.2, 5.8			24	4.43 (0.460)	4.4 (4.1, 4.7)	3.6, 5.3						
Change from baseline	28	-0.11 (0.431)	-0.1 (-0.3, 0.2)	-1.1, 0.6	-0.11 (0.075)	(-0.26, 0.05)	24	-0.62 (0.449)	-0.7 (-0.9, -0.4)	-1.3, 0.5	-0.63 (0.083)	(-0.80, -0.47)	-0.53 (-0.75, -0.30)	<.0001	-1.15 (-1.74, -0.57)	
Percent change from baseline	28	-1.97 (8.162)	-1.7 (-7.1, 3.8)	-19.5, 11.1			24	-12.10 (8.902)	-12.9 (-17.8, -8.9)	-25.0, 9.9						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Overall *(contd.)*																
Day 2 / 4-hr Post 3rd																
Absolute value	29	4.87 (0.486)	4.8 (4.5, 5.2)	4.0, 6.1			24	4.13 (0.388)	4.2 (3.9, 4.4)	3.2, 4.8						
Change from baseline	29	-0.26 (0.414)	-0.3 (-0.5, 0.0)	-1.1, 0.8	-0.26 (0.080)	(-0.42, -0.10)	24	-0.92 (0.519)	-0.8 (-1.3, -0.5)	-1.8, -0.1	-0.94 (0.088)	(-1.11, -0.76)	-0.68 (-0.92, -0.44)	<.0001	-1.43 (-2.04, -0.83)	
Percent change from baseline	29	-4.96 (7.839)	-5.9 (-9.8, 0.0)	-21.4, 15.5			24	-17.93 (9.506)	-15.9 (-25.4, -9.9)	-33.8, -2.0						
Day 2 / 20-hr Post 1st																
Absolute value	29	4.80 (0.438)	4.8 (4.6, 5.0)	3.9, 5.6			24	4.19 (0.378)	4.2 (4.0, 4.5)	3.5, 4.8						
Change from baseline	29	-0.34 (0.437)	-0.3 (-0.6, -0.1)	-1.3, 0.6	-0.33 (0.078)	(-0.48, -0.17)	24	-0.86 (0.503)	-0.8 (-1.3, -0.6)	-1.8, -0.0	-0.87 (0.087)	(-1.05, -0.70)	-0.55 (-0.78, -0.31)	<.0001	-1.11 (-1.69, -0.53)	
Percent change from baseline	29	-6.46 (8.240)	-5.5 (-11.7, -2.3)	-25.2, 13.1			24	-16.70 (9.215)	-15.9 (-24.2, -11.5)	-32.7, -0.7						
Day 3 / 0-hr																
Absolute value	30	4.94 (0.549)	5.0 (4.5, 5.1)	4.1, 6.3			24	4.37 (0.448)	4.3 (4.1, 4.7)	3.3, 5.1						
Change from baseline	30	-0.20 (0.439)	-0.3 (-0.5, 0.0)	-1.0, 0.7	-0.19 (0.083)	(-0.36, -0.02)	24	-0.68 (0.502)	-0.7 (-1.1, -0.4)	-1.6, 0.3	-0.69 (0.092)	(-0.88, -0.51)	-0.50 (-0.75, -0.26)	0.0002	-1.03 (-1.60, -0.46)	
Percent change from baseline	30	-3.89 (8.343)	-5.2 (-9.9, 1.1)	-19.5, 13.9			24	-13.24 (9.592)	-13.9 (-21.6, -6.7)	-31.7, 5.6						
Day 4 / 0-hr																
Absolute value	30	4.87 (0.477)	4.8 (4.5, 5.2)	4.0, 6.0			24	4.41 (0.399)	4.4 (4.2, 4.8)	3.6, 5.5						
Change from baseline	30	-0.27 (0.473)	-0.4 (-0.6, 0.0)	-1.0, 0.8	-0.26 (0.078)	(-0.42, -0.10)	24	-0.64 (0.442)	-0.6 (-1.0, -0.4)	-1.5, 0.1	-0.65 (0.088)	(-0.83, -0.48)	-0.39 (-0.63, -0.16)	0.0016	-0.81 (-1.36, -0.25)	
Percent change from baseline	30	-5.07 (9.153)	-7.1 (-12.1, 1.1)	-19.7, 17.0			24	-12.45 (8.197)	-12.2 (-17.0, -7.9)	-27.1, 1.8						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value																
<=5.3 mmol/L																
Baseline																
Absolute value	25	5.02 (0.233)	5.1 (4.9, 5.2)	4.6, 5.3			19	4.90 (0.166)	4.9 (4.8, 5.0)	4.6, 5.2						
Day 1 / 30-min Post 1st																
Absolute value	24	5.10 (0.401)	5.2 (4.7, 5.4)	4.3, 5.7			19	4.85 (0.280)	4.8 (4.6, 5.0)	4.5, 5.4						
Change from baseline	24	0.10 (0.281)	0.1 (-0.1, 0.3)	-0.5, 0.6	0.11 (0.055)	(-0.00, 0.22)	19	-0.05 (0.241)	-0.1 (-0.2, 0.1)	-0.5, 0.5	-0.05 (0.063)	(-0.18, 0.07)	-0.17 (-0.34, 0.00)	0.0557	-0.55 (-1.16, 0.07)	
Percent change from baseline	24	1.90 (5.636)	1.2 (-2.0, 5.2)	-11.3, 11.9			19	-0.94 (4.891)	-2.3 (-4.5, 2.4)	-8.7, 11.2						
Day 1 / 1-hr Post 1st																
Absolute value	25	5.12 (0.367)	5.1 (4.8, 5.4)	4.4, 5.8			19	4.85 (0.426)	4.8 (4.6, 4.9)	4.4, 6.3						
Change from baseline	25	0.10 (0.321)	0.1 (-0.1, 0.3)	-0.5, 0.8	0.11 (0.078)	(-0.05, 0.27)	19	-0.05 (0.469)	-0.1 (-0.2, 0.1)	-0.8, 1.5	-0.06 (0.089)	(-0.24, 0.12)	-0.17 (-0.41, 0.07)	0.1593	-0.40 (-1.00, 0.21)	
Percent change from baseline	25	2.10 (6.336)	2.3 (-2.4, 5.9)	-10.2, 17.2			19	-0.93 (9.618)	-2.4 (-4.6, 1.4)	-14.6, 32.2						
Day 1 / 2-hr Post 1st																
Absolute value	25	4.96 (0.300)	4.9 (4.7, 5.2)	4.5, 5.5			18	4.78 (0.362)	4.7 (4.5, 4.9)	4.2, 5.6						
Change from baseline	25	-0.06 (0.223)	-0.1 (-0.2, 0.2)	-0.5, 0.3	-0.05 (0.059)	(-0.17, 0.07)	18	-0.12 (0.382)	-0.1 (-0.3, 0.1)	-0.7, 0.7	-0.12 (0.069)	(-0.26, 0.01)	-0.07 (-0.26, 0.11)	0.4435	-0.18 (-0.79, 0.42)	
Percent change from baseline	25	-1.19 (4.338)	-1.6 (-4.2, 3.2)	-9.4, 5.3			18	-2.28 (7.745)	-3.1 (-6.6, 2.1)	-12.6, 14.3						
Day 1 / 4-hr Post 1st																
Absolute value	25	4.94 (0.471)	4.9 (4.7, 5.2)	4.0, 6.0			19	4.69 (0.443)	4.7 (4.4, 4.9)	4.0, 5.6						
Change from baseline	25	-0.08 (0.443)	-0.1 (-0.4, 0.2)	-0.6, 1.1	-0.07 (0.088)	(-0.25, 0.10)	19	-0.20 (0.436)	-0.1 (-0.6, 0.1)	-0.8, 0.7	-0.21 (0.101)	(-0.42, -0.01)	-0.14 (-0.41, 0.13)	0.3071	-0.28 (-0.88, 0.32)	
Percent change from baseline	25	-1.55 (9.006)	-2.6 (-7.8, 3.5)	-13.4, 21.2			19	-4.14 (8.816)	-3.1 (-13.1, 2.8)	-17.0, 14.3						
Day 1 / 4-hr Post 2nd																
Absolute value	23	4.83 (0.453)	4.8 (4.5, 5.1)	3.9, 5.8			19	4.59 (0.324)	4.5 (4.4, 4.9)	4.1, 5.1						
Change from baseline	23	-0.19 (0.477)	-0.2 (-0.5, 0.1)	-1.3, 0.7	-0.18 (0.086)	(-0.36, -0.01)	19	-0.30 (0.360)	-0.4 (-0.5, -0.1)	-1.0, 0.3	-0.31 (0.096)	(-0.51, -0.12)	-0.13 (-0.39, 0.13)	0.3185	-0.27 (-0.88, 0.34)	
Percent change from baseline	23	-3.65 (9.351)	-4.2 (-10.2, 1.3)	-25.2, 13.2			19	-6.12 (7.267)	-8.7 (-10.7, -1.7)	-19.2, 6.2						
Day 1 / 4-hr Post 3rd																
Absolute value	25	4.75 (0.457)	4.8 (4.4, 5.1)	4.0, 5.9			19	4.48 (0.344)	4.5 (4.2, 4.7)	3.9, 5.0						
Change from baseline	25	-0.26 (0.409)	-0.3 (-0.4, -0.1)	-1.1, 0.6	-0.26 (0.080)	(-0.42, -0.10)	19	-0.41 (0.397)	-0.3 (-0.8, -0.2)	-1.1, 0.3	-0.42 (0.092)	(-0.61, -0.24)	-0.17 (-0.41, 0.08)	0.1854	-0.37 (-0.97, 0.23)	
Percent change from baseline	25	-5.26 (8.092)	-5.9 (-8.5, -1.6)	-21.4, 12.0			19	-8.35 (7.936)	-7.1 (-16.3, -3.9)	-21.2, 6.1						
Day 2 / 0-hr																
Absolute value	25	4.86 (0.358)	4.9 (4.6, 5.1)	4.0, 5.5			19	4.67 (0.443)	4.8 (4.4, 4.9)	3.9, 5.5						
Change from baseline	25	-0.15 (0.284)	-0.2 (-0.3, 0.1)	-0.8, 0.5	-0.15 (0.075)	(-0.30, 0.01)	19	-0.23 (0.468)	-0.2 (-0.6, 0.0)	-1.1, 0.6	-0.23 (0.086)	(-0.41, -0.06)	-0.09 (-0.32, 0.14)	0.4458	-0.19 (-0.79, 0.40)	
Percent change from baseline	25	-3.04 (5.631)	-3.0 (-6.3, 1.3)	-15.9, 9.1			19	-4.51 (9.439)	-3.7 (-13.4, 0.0)	-21.2, 12.2						
Day 2 / 4-hr Post 1st																
Absolute value	24	4.95 (0.438)	4.9 (4.8, 5.2)	3.8, 5.9			19	4.46 (0.381)	4.5 (4.1, 4.6)	3.9, 5.5						
Change from baseline	24	-0.05 (0.392)	-0.1 (-0.3, 0.2)	-0.8, 0.8	-0.05 (0.085)	(-0.22, 0.12)	19	-0.44 (0.464)	-0.5 (-0.6, -0.2)	-1.3, 0.8	-0.45 (0.096)	(-0.64, -0.26)	-0.40 (-0.66, -0.14)	0.0032	-0.92 (-1.55, -0.29)	
Percent change from baseline	24	-0.99 (7.895)	-1.6 (-6.0, 3.6)	-16.5, 15.7			19	-8.82 (9.271)	-10.2 (-12.5, -3.5)	-25.0, 16.2						
Day 2 / 4-hr Post 2nd																
Absolute value	23	4.95 (0.423)	5.0 (4.6, 5.2)	4.2, 5.8			19	4.34 (0.415)	4.3 (4.1, 4.6)	3.6, 5.2						
Change from baseline	23	-0.05 (0.404)	0.0 (-0.3, 0.2)	-1.0, 0.6	-0.06 (0.087)	(-0.23, 0.12)	19	-0.56 (0.477)	-0.5 (-1.0, -0.4)	-1.3, 0.5	-0.57 (0.098)	(-0.77, -0.37)	-0.52 (-0.78, -0.25)	0.0003	-1.17 (-1.83, -0.51)	
Percent change from baseline	23	-0.94 (7.976)	0.3 (-6.7, 3.9)	-19.5, 11.1			19	-11.33 (9.620)	-10.1 (-20.1, -7.7)	-25.0, 9.9						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value *(contd.)*																
<=5.3 mmol/L *(contd.)*																
Day 2 / 4-hr Post 3rd																
Absolute value	24	4.76 (0.447)	4.7 (4.5, 4.9)	4.0, 6.1			19	4.11 (0.398)	4.2 (3.8, 4.4)	3.2, 4.8						
Change from baseline	24	-0.24 (0.401)	-0.3 (-0.5, -0.0)	-1.1, 0.8	-0.24 (0.088)	(-0.42, -0.07)	19	-0.79 (0.483)	-0.7 (-1.3, -0.4)	-1.7, -0.1	-0.80 (0.099)	(-1.00, -0.60)	-0.55 (-0.82, -0.29)	0.0002	-1.25 (-1.90, -0.59)	
Percent change from baseline	24	-4.82 (7.819)	-5.5 (-9.8, -0.3)	-21.4, 15.5			19	-15.92 (9.435)	-14.9 (-25.3, -9.4)	-33.8, -2.0						
Day 2 / 20-hr Post 1st																
Absolute value	24	4.74 (0.448)	4.7 (4.4, 5.0)	3.9, 5.6			19	4.17 (0.377)	4.1 (4.0, 4.4)	3.5, 4.8						
Change from baseline	24	-0.27 (0.432)	-0.2 (-0.6, -0.0)	-1.3, 0.6	-0.27 (0.087)	(-0.44, -0.09)	19	-0.73 (0.451)	-0.7 (-1.0, -0.3)	-1.6, -0.0	-0.73 (0.099)	(-0.93, -0.53)	-0.47 (-0.73, -0.20)	0.0011	-1.03 (-1.67, -0.39)	
Percent change from baseline	24	-5.35 (8.424)	-4.2 (-11.5, -0.7)	-25.2, 13.1			19	-14.65 (8.885)	-14.9 (-19.9, -5.9)	-30.1, -0.7						
Day 3 / 0-hr																
Absolute value	25	4.84 (0.482)	4.9 (4.5, 5.1)	4.1, 6.0			19	4.33 (0.433)	4.3 (4.1, 4.7)	3.3, 5.1						
Change from baseline	25	-0.18 (0.401)	-0.2 (-0.4, 0.0)	-1.0, 0.7	-0.17 (0.087)	(-0.34, 0.00)	19	-0.57 (0.469)	-0.6 (-0.7, -0.3)	-1.5, 0.3	-0.58 (0.099)	(-0.78, -0.38)	-0.41 (-0.68, -0.14)	0.0033	-0.92 (-1.54, -0.29)	
Percent change from baseline	25	-3.56 (7.881)	-4.9 (-8.8, 1.0)	-19.5, 13.9			19	-11.58 (9.469)	-12.2 (-14.9, -5.1)	-31.7, 5.6						
Day 4 / 0-hr																
Absolute value	25	4.78 (0.447)	4.7 (4.5, 5.0)	4.0, 5.6			19	4.34 (0.309)	4.3 (4.1, 4.5)	3.6, 4.8						
Change from baseline	25	-0.23 (0.460)	-0.2 (-0.6, 0.0)	-1.0, 0.8	-0.23 (0.083)	(-0.39, -0.06)	19	-0.56 (0.367)	-0.6 (-0.8, -0.4)	-1.2, 0.1	-0.57 (0.095)	(-0.76, -0.38)	-0.34 (-0.60, -0.09)	0.0098	-0.78 (-1.40, -0.16)	
Percent change from baseline	25	-4.52 (9.147)	-4.6 (-11.3, 1.1)	-19.7, 17.0			19	-11.36 (7.317)	-11.8 (-15.5, -7.7)	-25.5, 1.8						
5.4-5.5 mmol/L																
Baseline																
Absolute value	2	5.49 (0.012)	5.5 (5.5, 5.5)	5.5, 5.5			3	5.45 (0.087)	5.5 (5.4, 5.5)	5.4, 5.5						
Day 1 / 30-min Post 1st																
Absolute value	2	5.15 (0.354)	5.2 (4.9, 5.4)	4.9, 5.4			3	5.57 (0.208)	5.5 (5.4, 5.8)	5.4, 5.8						
Change from baseline	2	-0.34 (0.365)	-0.3 (-0.6, -0.1)	-0.6, -0.1			3	0.12 (0.161)	0.1 (0.0, 0.3)	0.0, 0.3						
Percent change from baseline	2	-6.21 (6.639)	-6.2 (-10.9, -1.5)	-10.9, -1.5			3	2.13 (2.917)	0.9 (0.0, 5.5)	0.0, 5.5						
Day 1 / 1-hr Post 1st																
Absolute value	2	5.65 (0.354)	5.7 (5.4, 5.9)	5.4, 5.9			3	5.33 (0.321)	5.2 (5.1, 5.7)	5.1, 5.7						
Change from baseline	2	0.16 (0.342)	0.2 (-0.1, 0.4)	-0.1, 0.4			3	-0.12 (0.275)	-0.3 (-0.3, 0.2)	-0.3, 0.2						
Percent change from baseline	2	2.88 (6.217)	2.9 (-1.5, 7.3)	-1.5, 7.3			3	-2.16 (5.038)	-4.7 (-5.5, 3.6)	-5.5, 3.6						
Day 1 / 2-hr Post 1st																
Absolute value	2	5.85 (0.354)	5.9 (5.6, 6.1)	5.6, 6.1			3	5.33 (0.115)	5.4 (5.2, 5.4)	5.2, 5.4						
Change from baseline	2	0.36 (0.342)	0.4 (0.1, 0.6)	0.1, 0.6			3	-0.12 (0.029)	-0.1 (-0.1, -0.1)	-0.1, -0.1						
Percent change from baseline	2	6.52 (6.209)	6.5 (2.1, 10.9)	2.1, 10.9			3	-2.15 (0.569)	-1.8 (-2.8, -1.8)	-2.8, -1.8						
Day 1 / 4-hr Post 1st																
Absolute value	2	4.55 (1.202)	4.6 (3.7, 5.4)	3.7, 5.4			3	5.03 (0.351)	5.0 (4.7, 5.4)	4.7, 5.4						
Change from baseline	2	-0.94 (1.214)	-0.9 (-1.8, -0.1)	-1.8, -0.1			3	-0.42 (0.284)	-0.5 (-0.6, -0.1)	-0.6, -0.1						
Percent change from baseline	2	-17.12 (22.067)	-17.1 (-32.7, -1.5)	-32.7, -1.5			3	-7.69 (5.307)	-9.1 (-12.1, -1.8)	-12.1, -1.8						
Day 1 / 4-hr Post 2nd																
Absolute value	2	5.20 (0.141)	5.2 (5.1, 5.3)	5.1, 5.3			3	4.67 (0.503)	4.6 (4.2, 5.2)	4.2, 5.2						
Change from baseline	2	-0.29 (0.130)	-0.3 (-0.4, -0.2)	-0.4, -0.2			3	-0.78 (0.437)	-0.9 (-1.1, -0.3)	-1.1, -0.3						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value *(contd.)*																
5.4-5.5 mmol/L *(contd.)*																
Day 1 / 4-hr Post 2nd *(contd.)*																
Percent change from baseline	2	-5.31 (2.372)	-5.3 (-7.0, -3.6)	-7.0, -3.6			3	-14.44 (8.192)	-16.4 (-21.5, -5.5)	-21.5, -5.5						
Day 1 / 4-hr Post 3rd																
Absolute value	2	4.90 (1.273)	4.9 (4.0, 5.8)	4.0, 5.8			3	4.20 (0.436)	4.0 (3.9, 4.7)	3.9, 4.7						
Change from baseline	2	-0.59 (1.285)	-0.6 (-1.5, 0.3)	-1.5, 0.3			3	-1.25 (0.391)	-1.5 (-1.5, -0.8)	-1.5, -0.8						
Percent change from baseline	2	-10.75 (23.368)	-10.7 (-27.3, 5.8)	-27.3, 5.8			3	-22.97 (7.300)	-27.1 (-27.3, -14.5)	-27.3, -14.5						
Day 2 / 0-hr																
Absolute value	2	5.25 (0.919)	5.3 (4.6, 5.9)	4.6, 5.9			3	4.70 (0.400)	4.7 (4.3, 5.1)	4.3, 5.1						
Change from baseline	2	-0.24 (0.931)	-0.2 (-0.9, 0.4)	-0.9, 0.4			3	-0.75 (0.328)	-0.8 (-1.1, -0.4)	-1.1, -0.4						
Percent change from baseline	2	-4.38 (16.944)	-4.4 (-16.4, 7.6)	-16.4, 7.6			3	-13.81 (6.209)	-14.5 (-19.6, -7.3)	-19.6, -7.3						
Day 2 / 4-hr Post 1st																
Absolute value	2	5.35 (0.354)	5.4 (5.1, 5.6)	5.1, 5.6			3	4.83 (0.586)	4.6 (4.4, 5.5)	4.4, 5.5						
Change from baseline	2	-0.14 (0.365)	-0.1 (-0.4, 0.1)	-0.4, 0.1			3	-0.62 (0.535)	-0.9 (-0.9, 0.0)	-0.9, 0.0						
Percent change from baseline	2	-2.57 (6.647)	-2.6 (-7.3, 2.1)	-7.3, 2.1			3	-11.37 (9.874)	-16.4 (-17.8, 0.0)	-17.8, 0.0						
Day 2 / 4-hr Post 2nd																
Absolute value	2	5.45 (0.354)	5.5 (5.2, 5.7)	5.2, 5.7			3	4.50 (0.346)	4.7 (4.1, 4.7)	4.1, 4.7						
Change from baseline	2	-0.04 (0.365)	-0.0 (-0.3, 0.2)	-0.3, 0.2			3	-0.95 (0.260)	-0.8 (-1.3, -0.8)	-1.3, -0.8						
Percent change from baseline	2	-0.75 (6.651)	-0.8 (-5.5, 4.0)	-5.5, 4.0			3	-17.49 (5.092)	-14.5 (-23.4, -14.5)	-23.4, -14.5						
Day 2 / 4-hr Post 3rd																
Absolute value	2	5.70 (0.141)	5.7 (5.6, 5.8)	5.6, 5.8			3	4.03 (0.351)	4.0 (3.7, 4.4)	3.7, 4.4						
Change from baseline	2	0.21 (0.130)	0.2 (0.1, 0.3)	0.1, 0.3			3	-1.42 (0.355)	-1.3 (-1.8, -1.1)	-1.8, -1.1						
Percent change from baseline	2	3.79 (2.352)	3.8 (2.1, 5.5)	2.1, 5.5			3	-25.99 (6.397)	-25.2 (-32.7, -20.0)	-32.7, -20.0						
Day 2 / 20-hr Post 1st																
Absolute value	2	4.85 (0.212)	4.9 (4.7, 5.0)	4.7, 5.0			3	4.10 (0.458)	4.0 (3.7, 4.6)	3.7, 4.6						
Change from baseline	2	-0.64 (0.224)	-0.6 (-0.8, -0.5)	-0.8, -0.5			3	-1.35 (0.450)	-1.3 (-1.8, -0.9)	-1.8, -0.9						
Percent change from baseline	2	-11.68 (4.052)	-11.7 (-14.5, -8.8)	-14.5, -8.8			3	-24.77 (8.191)	-25.2 (-32.7, -16.4)	-32.7, -16.4						
Day 3 / 0-hr																
Absolute value	2	5.10 (0.849)	5.1 (4.5, 5.7)	4.5, 5.7			3	4.40 (0.656)	4.3 (3.8, 5.1)	3.8, 5.1						
Change from baseline	2	-0.39 (0.860)	-0.4 (-1.0, 0.2)	-1.0, 0.2			3	-1.05 (0.589)	-1.2 (-1.6, -0.4)	-1.6, -0.4						
Percent change from baseline	2	-7.12 (15.651)	-7.1 (-18.2, 4.0)	-18.2, 4.0			3	-19.35 (11.057)	-21.8 (-29.0, -7.3)	-29.0, -7.3						
Day 4 / 0-hr																
Absolute value	2	5.40 (0.849)	5.4 (4.8, 6.0)	4.8, 6.0			3	4.73 (0.802)	4.8 (3.9, 5.5)	3.9, 5.5						
Change from baseline	2	-0.09 (0.860)	-0.1 (-0.7, 0.5)	-0.7, 0.5			3	-0.72 (0.725)	-0.7 (-1.5, 0.0)	-1.5, 0.0						
Percent change from baseline	2	-1.65 (15.662)	-1.7 (-12.7, 9.4)	-12.7, 9.4			3	-13.28 (13.560)	-12.7 (-27.1, 0.0)	-27.1, 0.0						
>5.5 mmol/L																
Baseline																
Absolute value	3	5.91 (0.129)	5.9 (5.8, 6.1)	5.8, 6.1			2	5.93 (0.082)	5.9 (5.9, 6.0)	5.9, 6.0						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value *(contd.)*																
>5.5 mmol/L *(contd.)*																
Day 1 / 30-min Post 1st																
Absolute value	3	5.67 (0.351)	5.7 (5.3, 6.0)	5.3, 6.0			2	5.95 (0.354)	6.0 (5.7, 6.2)	5.7, 6.2						
Change from baseline	3	-0.24 (0.285)	-0.1 (-0.6, -0.0)	-0.6, -0.0			2	0.02 (0.436)	0.0 (-0.3, 0.3)	-0.3, 0.3						
Percent change from baseline	3	-4.07 (4.861)	-1.7 (-9.7, -0.8)	-9.7, -0.8			2	0.47 (7.366)	0.5 (-4.7, 5.7)	-4.7, 5.7						
Day 1 / 1-hr Post 1st																
Absolute value	3	6.13 (0.874)	5.9 (5.4, 7.1)	5.4, 7.1			2	5.25 (0.354)	5.3 (5.0, 5.5)	5.0, 5.5						
Change from baseline	3	0.23 (0.766)	0.1 (-0.5, 1.1)	-0.5, 1.1			2	-0.68 (0.271)	-0.7 (-0.9, -0.5)	-0.9, -0.5						
Percent change from baseline	3	3.71 (12.771)	1.7 (-8.0, 17.4)	-8.0, 17.4			2	-11.43 (4.734)	-11.4 (-14.8, -8.1)	-14.8, -8.1						
Day 1 / 2-hr Post 1st																
Absolute value	3	6.00 (0.964)	6.4 (4.9, 6.7)	4.9, 6.7			2	5.60 (0.141)	5.6 (5.5, 5.7)	5.5, 5.7						
Change from baseline	3	0.09 (0.919)	0.6 (-1.0, 0.7)	-1.0, 0.7			2	-0.33 (0.224)	-0.3 (-0.5, -0.2)	-0.5, -0.2						
Percent change from baseline	3	1.54 (15.602)	10.3 (-16.5, 10.7)	-16.5, 10.7			2	-5.46 (3.703)	-5.5 (-8.1, -2.8)	-8.1, -2.8						
Day 1 / 4-hr Post 1st																
Absolute value	3	5.57 (0.709)	5.7 (4.8, 6.2)	4.8, 6.2			2	5.45 (0.071)	5.5 (5.4, 5.5)	5.4, 5.5						
Change from baseline	3	-0.34 (0.643)	-0.1 (-1.1, 0.2)	-1.1, 0.2			2	-0.48 (0.153)	-0.5 (-0.6, -0.4)	-0.6, -0.4						
Percent change from baseline	3	-5.81 (10.919)	-1.7 (-18.2, 2.5)	-18.2, 2.5			2	-8.00 (2.474)	-8.0 (-9.7, -6.3)	-9.7, -6.3						
Day 1 / 4-hr Post 2nd																
Absolute value	3	5.33 (0.473)	5.5 (4.8, 5.7)	4.8, 5.7			2	5.55 (0.071)	5.6 (5.5, 5.6)	5.5, 5.6						
Change from baseline	3	-0.57 (0.429)	-0.3 (-1.1, -0.3)	-1.1, -0.3			2	-0.38 (0.012)	-0.4 (-0.4, -0.4)	-0.4, -0.4						
Percent change from baseline	3	-9.71 (7.341)	-5.8 (-18.2, -5.2)	-18.2, -5.2			2	-6.33 (0.111)	-6.3 (-6.4, -6.3)	-6.4, -6.3						
Day 1 / 4-hr Post 3rd																
Absolute value	3	5.30 (0.889)	5.0 (4.6, 6.3)	4.6, 6.3			2	5.15 (0.071)	5.2 (5.1, 5.2)	5.1, 5.2						
Change from baseline	3	-0.61 (0.777)	-0.8 (-1.3, 0.3)	-1.3, 0.3			2	-0.78 (0.012)	-0.8 (-0.8, -0.8)	-0.8, -0.8						
Percent change from baseline	3	-10.42 (13.190)	-13.8 (-21.6, 4.1)	-21.6, 4.1			2	-13.08 (0.017)	-13.1 (-13.1, -13.1)	-13.1, -13.1						
Day 2 / 0-hr																
Absolute value	3	5.63 (1.050)	5.6 (4.6, 6.7)	4.6, 6.7			2	5.35 (0.495)	5.4 (5.0, 5.7)	5.0, 5.7						
Change from baseline	3	-0.27 (1.094)	-0.5 (-1.3, 0.9)	-1.3, 0.9			2	-0.58 (0.577)	-0.6 (-1.0, -0.2)	-1.0, -0.2						
Percent change from baseline	3	-4.50 (18.727)	-7.4 (-21.6, 15.5)	-21.6, 15.5			2	-9.64 (9.612)	-9.6 (-16.4, -2.8)	-16.4, -2.8						
Day 2 / 4-hr Post 1st																
Absolute value	3	5.40 (0.265)	5.3 (5.2, 5.7)	5.2, 5.7			2	4.80 (0.283)	4.8 (4.6, 5.0)	4.6, 5.0						
Change from baseline	3	-0.51 (0.354)	-0.7 (-0.8, -0.1)	-0.8, -0.1			2	-1.13 (0.365)	-1.1 (-1.4, -0.9)	-1.4, -0.9						
Percent change from baseline	3	-8.49 (5.886)	-11.4 (-12.4, -1.7)	-12.4, -1.7			2	-18.95 (5.902)	-18.9 (-23.1, -14.8)	-23.1, -14.8						
Day 2 / 4-hr Post 2nd																
Absolute value	3	5.27 (0.306)	5.2 (5.0, 5.6)	5.0, 5.6			2	5.25 (0.071)	5.3 (5.2, 5.3)	5.2, 5.3						
Change from baseline	3	-0.64 (0.426)	-0.7 (-1.1, -0.2)	-1.1, -0.2			2	-0.68 (0.153)	-0.7 (-0.8, -0.6)	-0.8, -0.6						
Percent change from baseline	3	-10.72 (6.976)	-11.4 (-17.4, -3.4)	-17.4, -3.4			2	-11.38 (2.427)	-11.4 (-13.1, -9.7)	-13.1, -9.7						
Day 2 / 4-hr Post 3rd																
Absolute value	3	5.20 (0.100)	5.2 (5.1, 5.3)	5.1, 5.3			2	4.45 (0.354)	4.5 (4.2, 4.7)	4.2, 4.7						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)								
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value *(contd.)*																
>5.5 mmol/L *(contd.)*																
Day 2 / 4-hr Post 3rd *(contd.)*																
Change from baseline	3	-0.71 (0.142)	-0.7 (-0.8, -0.6)	-0.8, -0.6			2	-1.48 (0.271)	-1.5 (-1.7, -1.3)	-1.7, -1.3						
Percent change from baseline	3	-11.93 (2.199)	-12.1 (-14.0, -9.7)	-14.0, -9.7			2	-24.93 (4.922)	-24.9 (-28.4, -21.4)	-28.4, -21.4						
Day 2 / 20-hr Post 1st																
Absolute value	3	5.20 (0.265)	5.3 (4.9, 5.4)	4.9, 5.4			2	4.50 (0.283)	4.5 (4.3, 4.7)	4.3, 4.7						
Change from baseline	3	-0.71 (0.394)	-0.6 (-1.1, -0.4)	-1.1, -0.4			2	-1.43 (0.200)	-1.4 (-1.6, -1.3)	-1.6, -1.3						
Percent change from baseline	3	-11.85 (6.347)	-9.7 (-19.0, -6.9)	-19.0, -6.9			2	-24.08 (3.717)	-24.1 (-26.7, -21.4)	-26.7, -21.4						
Day 3 / 0-hr																
Absolute value	3	5.63 (0.586)	5.4 (5.2, 6.3)	5.2, 6.3			2	4.75 (0.212)	4.8 (4.6, 4.9)	4.6, 4.9						
Change from baseline	3	-0.27 (0.669)	-0.6 (-0.7, 0.5)	-0.7, 0.5			2	-1.18 (0.130)	-1.2 (-1.3, -1.1)	-1.3, -1.1						
Percent change from baseline	3	-4.50 (11.363)	-10.7 (-11.4, 8.6)	-11.4, 8.6			2	-19.85 (2.464)	-19.8 (-21.6, -18.1)	-21.6, -18.1						
Day 4 / 0-hr																
Absolute value	3	5.20 (0.100)	5.2 (5.1, 5.3)	5.1, 5.3			2	4.65 (0.354)	4.7 (4.4, 4.9)	4.4, 4.9						
Change from baseline	3	-0.71 (0.092)	-0.8 (-0.8, -0.6)	-0.8, -0.6			2	-1.28 (0.271)	-1.3 (-1.5, -1.1)	-1.5, -1.1						
Percent change from baseline	3	-11.94 (1.419)	-12.4 (-13.1, -10.3)	-13.1, -10.3			2	-21.55 (4.875)	-21.6 (-25.0, -18.1)	-25.0, -18.1						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Chronic kidney disease																0.8406
Yes																
Baseline																
Absolute value	6	5.15 (0.406)	5.2 (4.8, 5.3)	4.7, 5.8			7	5.02 (0.445)	4.9 (4.8, 5.0)	4.6, 6.0						
Day 1 / 30-min Post 1st																
Absolute value	6	5.25 (0.455)	5.4 (4.7, 5.7)	4.7, 5.7			7	4.96 (0.391)	4.9 (4.7, 5.2)	4.5, 5.7						
Change from baseline	6	0.10 (0.257)	0.0 (-0.1, 0.2)	-0.1, 0.6			7	-0.06 (0.204)	-0.1 (-0.3, 0.1)	-0.3, 0.3						
Percent change from baseline	6	1.98 (5.003)	0.5 (-1.7, 3.2)	-2.1, 11.4			7	-1.07 (3.995)	-2.6 (-4.7, 1.7)	-5.1, 6.1						
Day 1 / 1-hr Post 1st																
Absolute value	6	4.98 (0.492)	4.9 (4.7, 5.1)	4.5, 5.9			7	4.87 (0.309)	4.8 (4.6, 5.0)	4.6, 5.5						
Change from baseline	6	-0.17 (0.287)	-0.1 (-0.5, 0.1)	-0.5, 0.1			7	-0.15 (0.209)	-0.2 (-0.2, -0.0)	-0.5, 0.2						
Percent change from baseline	6	-3.23 (5.443)	-1.8 (-9.4, 1.7)	-10.2, 2.1			7	-2.69 (3.819)	-3.0 (-4.6, -0.7)	-8.1, 4.2						
Day 1 / 2-hr Post 1st																
Absolute value	6	5.02 (0.700)	4.8 (4.6, 5.0)	4.5, 6.4			6	4.77 (0.437)	4.8 (4.5, 4.9)	4.2, 5.5						
Change from baseline	6	-0.13 (0.392)	-0.2 (-0.4, -0.1)	-0.5, 0.6			6	-0.27 (0.214)	-0.3 (-0.4, -0.2)	-0.5, 0.1						
Percent change from baseline	6	-2.84 (7.059)	-3.7 (-8.3, -2.3)	-9.4, 10.3			6	-5.26 (4.175)	-6.6 (-8.1, -3.0)	-9.4, 2.1						
Day 1 / 4-hr Post 1st																
Absolute value	6	4.93 (0.524)	4.9 (4.6, 5.3)	4.2, 5.7			7	4.70 (0.469)	4.7 (4.2, 5.0)	4.1, 5.4						
Change from baseline	6	-0.22 (0.397)	-0.3 (-0.5, -0.1)	-0.6, 0.5			7	-0.32 (0.352)	-0.5 (-0.6, 0.0)	-0.7, 0.2						
Percent change from baseline	6	-4.14 (8.042)	-5.9 (-9.7, -1.7)	-12.1, 10.4			7	-6.20 (7.007)	-9.7 (-11.5, 1.0)	-14.3, 3.8						
Day 1 / 4-hr Post 2nd																
Absolute value	5	4.96 (0.445)	4.9 (4.7, 5.3)	4.4, 5.5			7	4.70 (0.513)	4.7 (4.3, 5.1)	4.1, 5.6						
Change from baseline	5	-0.29 (0.515)	-0.3 (-0.5, -0.2)	-0.9, 0.5			7	-0.32 (0.292)	-0.4 (-0.5, -0.3)	-0.5, 0.3						
Percent change from baseline	5	-5.23 (10.106)	-5.2 (-10.2, -4.2)	-17.0, 10.4			7	-6.32 (6.071)	-6.6 (-10.7, -5.1)	-11.5, 6.2						
Day 1 / 4-hr Post 3rd																
Absolute value	6	4.63 (0.314)	4.7 (4.4, 4.9)	4.2, 5.0			7	4.53 (0.355)	4.4 (4.3, 4.7)	4.1, 5.2						
Change from baseline	6	-0.52 (0.322)	-0.4 (-0.8, -0.3)	-1.0, -0.3			7	-0.49 (0.210)	-0.4 (-0.8, -0.3)	-0.8, -0.3						
Percent change from baseline	6	-9.82 (5.747)	-6.9 (-13.8, -6.2)	-19.7, -5.4			7	-9.61 (3.674)	-8.3 (-13.1, -7.1)	-16.3, -6.6						
Day 2 / 0-hr																
Absolute value	6	5.15 (0.841)	5.0 (4.5, 5.3)	4.4, 6.7			7	4.84 (0.172)	4.9 (4.8, 5.0)	4.5, 5.0						
Change from baseline	6	0.00 (0.576)	0.0 (-0.3, 0.2)	-0.8, 0.9			7	-0.17 (0.414)	-0.1 (-0.3, 0.0)	-1.0, 0.4						
Percent change from baseline	6	-0.29 (10.580)	0.7 (-6.3, 3.6)	-15.9, 15.5			7	-2.97 (7.422)	-2.6 (-6.6, 0.0)	-16.4, 7.9						
Day 2 / 4-hr Post 1st																
Absolute value	6	5.07 (0.372)	5.0 (4.8, 5.3)	4.7, 5.7			7	4.41 (0.324)	4.5 (4.1, 4.6)	4.0, 4.9						
Change from baseline	6	-0.08 (0.374)	-0.1 (-0.4, 0.1)	-0.5, 0.5			7	-0.60 (0.462)	-0.5 (-1.0, -0.3)	-1.4, -0.0						
Percent change from baseline	6	-1.35 (7.443)	-2.0 (-7.5, 3.2)	-10.2, 10.4			7	-11.62 (7.965)	-11.5 (-20.5, -6.1)	-23.1, -1.0						
Day 2 / 4-hr Post 2nd																
Absolute value	4	5.13 (0.340)	5.1 (4.9, 5.4)	4.8, 5.6			7	4.30 (0.503)	4.3 (3.9, 4.5)	3.6, 5.2						
Change from baseline	4	-0.01 (0.217)	-0.0 (-0.2, 0.2)	-0.2, 0.2			7	-0.72 (0.346)	-0.7 (-1.1, -0.4)	-1.2, -0.3						
Percent change from baseline	4	0.04 (4.238)	-0.1 (-3.6, 3.7)	-3.8, 4.2			7	-14.26 (6.988)	-13.1 (-22.5, -8.7)	-25.0, -7.2						

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Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
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	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Chronic kidney disease *(contd.)*																
Yes *(contd.)*																
Day 2 / 4-hr Post 3rd																
Absolute value	6	4.83 (0.308)	4.8 (4.6, 5.1)	4.5, 5.3			7	4.23 (0.304)	4.2 (4.1, 4.4)	3.7, 4.7						
Change from baseline	6	-0.32 (0.295)	-0.4 (-0.5, 0.0)	-0.7, 0.0			7	-0.79 (0.358)	-0.7 (-1.3, -0.4)	-1.3, -0.4						
Percent change from baseline	6	-5.94 (5.384)	-7.3 (-10.1, 0.0)	-12.1, 1.1			7	-15.44 (6.161)	-14.6 (-21.4, -9.4)	-25.3, -8.7						
Day 2 / 20-hr Post 1st																
Absolute value	6	4.77 (0.446)	4.8 (4.4, 5.0)	4.2, 5.4			7	4.27 (0.236)	4.3 (4.1, 4.4)	4.0, 4.7						
Change from baseline	6	-0.38 (0.322)	-0.3 (-0.6, -0.1)	-0.9, -0.1			7	-0.75 (0.313)	-0.7 (-0.9, -0.7)	-1.3, -0.2						
Percent change from baseline	6	-7.37 (6.212)	-5.7 (-12.5, -2.3)	-17.0, -1.1			7	-14.57 (5.079)	-14.6 (-18.4, -13.1)	-21.4, -5.0						
Day 3 / 0-hr																
Absolute value	6	5.03 (0.668)	4.9 (4.7, 5.1)	4.4, 6.3			7	4.49 (0.285)	4.4 (4.3, 4.7)	4.1, 4.9						
Change from baseline	6	-0.12 (0.376)	-0.2 (-0.4, 0.0)	-0.5, 0.5			7	-0.53 (0.372)	-0.6 (-0.7, -0.3)	-1.1, 0.1						
Percent change from baseline	6	-2.47 (6.991)	-3.0 (-8.3, 1.1)	-10.2, 8.6			7	-10.25 (6.700)	-12.2 (-14.6, -5.1)	-18.1, 1.4						
Day 4 / 0-hr																
Absolute value	6	4.65 (0.327)	4.7 (4.5, 4.7)	4.2, 5.2			7	4.50 (0.337)	4.5 (4.2, 4.8)	4.1, 4.9						
Change from baseline	6	-0.50 (0.377)	-0.6 (-0.6, -0.2)	-1.0, 0.0			7	-0.52 (0.317)	-0.4 (-0.7, -0.2)	-1.1, -0.2						
Percent change from baseline	6	-9.43 (7.152)	-10.8 (-12.1, -4.2)	-19.7, 1.1			7	-10.10 (5.429)	-9.4 (-14.9, -4.6)	-18.1, -3.0						
No																
Baseline																
Absolute value	24	5.13 (0.355)	5.1 (4.9, 5.3)	4.6, 6.1			17	5.07 (0.332)	5.0 (4.8, 5.2)	4.6, 5.9						
Day 1 / 30-min Post 1st																
Absolute value	23	5.14 (0.417)	5.2 (4.9, 5.4)	4.3, 6.0			17	5.06 (0.487)	5.0 (4.7, 5.4)	4.5, 6.2						
Change from baseline	23	0.02 (0.326)	-0.0 (-0.2, 0.2)	-0.6, 0.6	0.03 (0.064)	(-0.10, 0.16)	17	-0.00 (0.261)	-0.0 (-0.1, 0.2)	-0.5, 0.5	-0.01 (0.075)	(-0.16, 0.14)	-0.04 (-0.24, 0.16)	0.6617	-0.06 (-0.69, 0.56)	
Percent change from baseline	23	0.40 (6.337)	-0.4 (-3.3, 5.1)	-11.3, 11.9			17	-0.18 (5.174)	-0.7 (-3.1, 3.8)	-8.7, 11.2						
Day 1 / 1-hr Post 1st																
Absolute value	24	5.33 (0.519)	5.4 (5.1, 5.5)	4.4, 7.1			17	4.97 (0.487)	4.9 (4.7, 5.2)	4.4, 6.3						
Change from baseline	24	0.19 (0.348)	0.2 (-0.0, 0.4)	-0.5, 1.1	0.20 (0.088)	(0.02, 0.38)	17	-0.10 (0.537)	-0.2 (-0.3, 0.1)	-0.9, 1.5	-0.11 (0.104)	(-0.32, 0.10)	-0.30 (-0.58, -0.03)	0.0319	-0.66 (-1.30, -0.03)	
Percent change from baseline	24	3.70 (6.452)	4.6 (-0.2, 7.2)	-9.6, 17.4			17	-1.66 (10.738)	-3.7 (-5.5, 1.4)	-14.8, 32.2						
Day 1 / 2-hr Post 1st																
Absolute value	24	5.15 (0.497)	5.1 (4.8, 5.4)	4.5, 6.7			17	4.98 (0.425)	4.8 (4.6, 5.4)	4.5, 5.7						
Change from baseline	24	0.01 (0.329)	-0.0 (-0.1, 0.2)	-1.0, 0.7	0.02 (0.072)	(-0.13, 0.16)	17	-0.09 (0.374)	-0.1 (-0.3, -0.1)	-0.7, 0.7	-0.09 (0.085)	(-0.27, 0.08)	-0.11 (-0.34, 0.11)	0.3187	-0.28 (-0.91, 0.34)	
Percent change from baseline	24	0.21 (5.919)	-0.4 (-2.8, 4.3)	-16.5, 10.9			17	-1.58 (7.523)	-2.8 (-6.2, -1.7)	-12.6, 14.3						
Day 1 / 4-hr Post 1st																
Absolute value	24	4.98 (0.584)	5.0 (4.8, 5.3)	3.7, 6.2			17	4.84 (0.473)	4.9 (4.5, 5.0)	4.0, 5.6						
Change from baseline	24	-0.15 (0.578)	-0.1 (-0.4, 0.2)	-1.8, 1.1	-0.14 (0.104)	(-0.35, 0.07)	17	-0.23 (0.436)	-0.2 (-0.6, -0.0)	-0.8, 0.7	-0.24 (0.124)	(-0.49, 0.01)	-0.09 (-0.42, 0.24)	0.5744	-0.15 (-0.77, 0.48)	
Percent change from baseline	24	-2.74 (11.061)	-2.1 (-7.9, 3.0)	-32.7, 21.2			17	-4.37 (8.674)	-3.9 (-12.1, -0.4)	-17.0, 14.3						
Day 1 / 4-hr Post 2nd																
Absolute value	23	4.90 (0.478)	4.9 (4.5, 5.2)	3.9, 5.8			17	4.68 (0.393)	4.6 (4.4, 5.0)	4.2, 5.5						
Change from baseline	23	-0.23 (0.463)	-0.2 (-0.5, 0.0)	-1.3, 0.7	-0.22 (0.087)	(-0.40, -0.04)	17	-0.39 (0.416)	-0.4 (-0.5, -0.1)	-1.1, 0.3	-0.40 (0.101)	(-0.61, -0.19)	-0.18 (-0.45, 0.09)	0.1859	-0.37 (-1.00, 0.26)	

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Chronic kidney disease *(contd.)*																
No *(contd.)*																
Day 1 / 4-hr Post 2nd *(contd.)*																
Percent change from baseline	23	-4.24 (8.852)	-4.9 (-9.7, 1.0)	-25.2, 13.2			17	-7.53 (8.052)	-8.7 (-11.3, -2.0)	-21.5, 6.1						
Day 1 / 4-hr Post 3rd																
Absolute value	24	4.86 (0.600)	4.9 (4.5, 5.2)	4.0, 6.3			17	4.49 (0.423)	4.6 (4.1, 4.9)	3.9, 5.1						
Change from baseline	24	-0.27 (0.533)	-0.2 (-0.5, 0.1)	-1.5, 0.6	-0.27 (0.106)	(-0.48, -0.05)	17	-0.57 (0.545)	-0.7 (-1.0, -0.2)	-1.5, 0.3	-0.58 (0.126)	(-0.84, -0.33)	-0.32 (-0.65, 0.02)	0.0609	-0.56 (-1.20, 0.07)	
Percent change from baseline	24	-5.22 (10.034)	-4.2 (-10.5, 2.8)	-27.3, 12.0			17	-10.96 (10.363)	-13.1 (-19.3, -3.9)	-27.3, 6.1						
Day 2 / 0-hr																
Absolute value	24	4.92 (0.422)	4.9 (4.6, 5.2)	4.0, 5.9			17	4.69 (0.538)	4.7 (4.3, 5.0)	3.9, 5.7						
Change from baseline	24	-0.21 (0.383)	-0.2 (-0.4, 0.0)	-1.3, 0.5	-0.21 (0.086)	(-0.38, -0.03)	17	-0.38 (0.506)	-0.4 (-0.8, -0.2)	-1.1, 0.6	-0.39 (0.103)	(-0.60, -0.18)	-0.18 (-0.45, 0.09)	0.1833	-0.38 (-1.01, 0.24)	
Percent change from baseline	24	-4.02 (7.014)	-3.9 (-6.9, 0.3)	-21.6, 9.1			17	-7.39 (9.992)	-7.3 (-14.6, -2.8)	-21.2, 12.2						
Day 2 / 4-hr Post 1st																
Absolute value	23	5.02 (0.464)	5.0 (4.8, 5.2)	3.8, 5.9			17	4.58 (0.442)	4.5 (4.4, 4.7)	3.9, 5.5						
Change from baseline	23	-0.11 (0.414)	-0.1 (-0.4, 0.1)	-0.8, 0.8	-0.11 (0.089)	(-0.29, 0.07)	17	-0.49 (0.507)	-0.5 (-0.9, -0.2)	-1.3, 0.8	-0.49 (0.104)	(-0.71, -0.28)	-0.39 (-0.66, -0.11)	0.0076	-0.83 (-1.48, -0.17)	
Percent change from baseline	23	-2.02 (8.032)	-2.0 (-7.3, 2.1)	-16.5, 15.7			17	-9.31 (9.879)	-10.7 (-15.5, -3.5)	-25.0, 16.2						
Day 2 / 4-hr Post 2nd																
Absolute value	24	5.00 (0.443)	5.1 (4.6, 5.3)	4.2, 5.8			17	4.49 (0.446)	4.6 (4.1, 4.7)	3.9, 5.3						
Change from baseline	24	-0.13 (0.458)	-0.1 (-0.4, 0.2)	-1.1, 0.6	-0.12 (0.091)	(-0.31, 0.06)	17	-0.58 (0.489)	-0.6 (-0.8, -0.5)	-1.3, 0.5	-0.59 (0.108)	(-0.81, -0.37)	-0.47 (-0.75, -0.18)	0.0021	-0.96 (-1.61, -0.30)	
Percent change from baseline	24	-2.31 (8.662)	-1.9 (-7.5, 3.8)	-19.5, 11.1			17	-11.21 (9.630)	-12.8 (-15.5, -9.7)	-24.3, 9.9						
Day 2 / 4-hr Post 3rd																
Absolute value	23	4.88 (0.528)	4.8 (4.5, 5.3)	4.0, 6.1			17	4.09 (0.420)	4.1 (3.8, 4.4)	3.2, 4.8						
Change from baseline	23	-0.24 (0.444)	-0.3 (-0.5, 0.1)	-1.1, 0.8	-0.25 (0.099)	(-0.45, -0.05)	17	-0.98 (0.573)	-0.8 (-1.6, -0.5)	-1.8, -0.1	-0.99 (0.116)	(-1.22, -0.75)	-0.73 (-1.04, -0.43)	<.0001	-1.47 (-2.17, -0.76)	
Percent change from baseline	23	-4.71 (8.444)	-5.1 (-9.8, 1.0)	-21.4, 15.5			17	-18.95 (10.576)	-16.0 (-28.4, -10.1)	-33.8, -2.0						
Day 2 / 20-hr Post 1st																
Absolute value	23	4.80 (0.446)	4.8 (4.6, 5.0)	3.9, 5.6			17	4.16 (0.424)	4.1 (3.7, 4.5)	3.5, 4.8						
Change from baseline	23	-0.33 (0.468)	-0.3 (-0.6, -0.0)	-1.3, 0.6	-0.31 (0.097)	(-0.51, -0.11)	17	-0.91 (0.564)	-0.9 (-1.3, -0.5)	-1.8, -0.0	-0.92 (0.115)	(-1.15, -0.69)	-0.61 (-0.91, -0.30)	0.0003	-1.13 (-1.81, -0.46)	
Percent change from baseline	23	-6.22 (8.795)	-5.5 (-11.7, -0.4)	-25.2, 13.1			17	-17.58 (10.470)	-16.4 (-26.7, -9.8)	-32.7, -0.7						
Day 3 / 0-hr																
Absolute value	24	4.91 (0.529)	5.0 (4.5, 5.2)	4.1, 6.0			17	4.32 (0.499)	4.3 (4.0, 4.6)	3.3, 5.1						
Change from baseline	24	-0.22 (0.458)	-0.3 (-0.6, 0.1)	-1.0, 0.7	-0.22 (0.098)	(-0.41, -0.02)	17	-0.75 (0.544)	-0.7 (-1.2, -0.4)	-1.6, 0.3	-0.75 (0.117)	(-0.99, -0.52)	-0.54 (-0.85, -0.23)	0.0011	-1.06 (-1.72, -0.39)	
Percent change from baseline	24	-4.25 (8.745)	-5.2 (-10.3, 1.2)	-19.5, 13.9			17	-14.48 (10.483)	-14.0 (-21.8, -7.3)	-31.7, 5.6						
Day 4 / 0-hr																
Absolute value	24	4.92 (0.499)	4.9 (4.6, 5.4)	4.0, 6.0			17	4.38 (0.427)	4.4 (4.1, 4.5)	3.6, 5.5						
Change from baseline	24	-0.21 (0.484)	-0.3 (-0.6, 0.2)	-0.9, 0.8	-0.21 (0.094)	(-0.40, -0.02)	17	-0.69 (0.483)	-0.7 (-1.1, -0.4)	-1.5, 0.1	-0.70 (0.112)	(-0.93, -0.47)	-0.49 (-0.79, -0.20)	0.0017	-0.99 (-1.65, -0.33)	
Percent change from baseline	24	-3.98 (9.398)	-5.7 (-11.9, 3.8)	-17.5, 17.0			17	-13.42 (9.062)	-12.7 (-21.2, -8.7)	-27.1, 1.8						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Congestive Heart Disease																0.0054
Yes																
Baseline																
Absolute value	11	5.02 (0.398)	5.0 (4.7, 5.2)	4.6, 5.9			13	5.13 (0.438)	5.0 (4.8, 5.5)	4.6, 6.0						
Day 1 / 30-min Post 1st																
Absolute value	11	4.86 (0.398)	4.7 (4.6, 5.2)	4.3, 5.6			13	5.15 (0.525)	5.0 (4.7, 5.5)	4.5, 6.2						
Change from baseline	11	-0.16 (0.321)	-0.1 (-0.5, -0.0)	-0.6, 0.4	-0.18 (0.097)	(-0.38, 0.02)	13	0.02 (0.282)	0.0 (-0.2, 0.3)	-0.4, 0.5	0.04 (0.089)	(-0.14, 0.23)	0.22 (-0.05, 0.50)	0.1041	0.60 (-0.22, 1.42)	
Percent change from baseline	11	-2.96 (6.071)	-2.1 (-9.7, -0.4)	-11.3, 7.3			13	0.44 (5.551)	0.0 (-4.5, 5.5)	-7.7, 11.2						
Day 1 / 1-hr Post 1st																
Absolute value	11	5.16 (0.478)	5.1 (4.8, 5.6)	4.4, 5.9			13	5.05 (0.516)	4.9 (4.8, 5.2)	4.4, 6.3						
Change from baseline	11	0.14 (0.401)	0.2 (-0.2, 0.4)	-0.5, 0.8	0.12 (0.135)	(-0.16, 0.40)	13	-0.08 (0.547)	-0.2 (-0.2, -0.1)	-0.9, 1.5	-0.06 (0.124)	(-0.32, 0.19)	-0.18 (-0.56, 0.20)	0.3299	-0.47 (-1.28, 0.34)	
Percent change from baseline	11	3.02 (7.780)	4.0 (-3.3, 7.3)	-9.6, 17.2			13	-1.29 (10.927)	-3.7 (-4.7, -2.0)	-14.8, 32.2						
Day 1 / 2-hr Post 1st																
Absolute value	11	4.95 (0.446)	4.9 (4.6, 5.2)	4.5, 6.1			12	4.96 (0.444)	4.8 (4.5, 5.4)	4.5, 5.7						
Change from baseline	11	-0.07 (0.394)	-0.0 (-0.2, 0.2)	-1.0, 0.6	-0.09 (0.094)	(-0.29, 0.11)	12	-0.19 (0.219)	-0.2 (-0.3, -0.1)	-0.5, 0.3	-0.14 (0.088)	(-0.32, 0.04)	-0.05 (-0.32, 0.22)	0.7083	-0.40 (-1.23, 0.42)	
Percent change from baseline	11	-1.13 (7.057)	-1.0 (-4.2, 5.1)	-16.5, 10.9			12	-3.66 (4.325)	-2.9 (-6.6, -1.8)	-9.7, 7.0						
Day 1 / 4-hr Post 1st																
Absolute value	11	4.76 (0.659)	4.8 (4.2, 5.3)	3.7, 6.0			13	4.92 (0.494)	5.0 (4.6, 5.4)	4.0, 5.6						
Change from baseline	11	-0.26 (0.827)	-0.4 (-0.6, 0.5)	-1.8, 1.1	-0.28 (0.172)	(-0.64, 0.08)	13	-0.21 (0.384)	-0.1 (-0.5, 0.0)	-0.8, 0.5	-0.19 (0.158)	(-0.52, 0.14)	0.09 (-0.39, 0.58)	0.6914	0.08 (-0.73, 0.88)	
Percent change from baseline	11	-4.44 (15.952)	-8.0 (-13.4, 10.4)	-32.7, 21.2			13	-3.92 (7.577)	-1.8 (-9.1, 1.0)	-17.0, 9.4						
Day 1 / 4-hr Post 2nd																
Absolute value	11	4.81 (0.464)	4.8 (4.5, 5.3)	3.9, 5.3			13	4.77 (0.429)	4.6 (4.4, 4.9)	4.3, 5.6						
Change from baseline	11	-0.21 (0.565)	-0.2 (-0.4, 0.1)	-1.3, 0.5	-0.24 (0.117)	(-0.48, 0.01)	13	-0.36 (0.273)	-0.4 (-0.5, -0.3)	-0.9, 0.3	-0.34 (0.107)	(-0.56, -0.12)	-0.11 (-0.43, 0.22)	0.5137	-0.35 (-1.16, 0.46)	
Percent change from baseline	11	-3.78 (10.805)	-3.0 (-7.7, 1.9)	-25.2, 10.5			13	-6.94 (5.343)	-6.4 (-10.1, -5.5)	-16.4, 6.1						
Day 1 / 4-hr Post 3rd																
Absolute value	11	4.51 (0.448)	4.5 (4.1, 5.0)	4.0, 5.2			13	4.57 (0.413)	4.6 (4.4, 4.9)	3.9, 5.2						
Change from baseline	11	-0.51 (0.631)	-0.5 (-1.1, -0.0)	-1.5, 0.5	-0.54 (0.139)	(-0.82, -0.25)	13	-0.56 (0.466)	-0.7 (-0.8, -0.3)	-1.5, 0.3	-0.54 (0.127)	(-0.81, -0.28)	-0.01 (-0.40, 0.39)	0.9780	-0.09 (-0.90, 0.71)	
Percent change from baseline	11	-9.62 (11.871)	-11.3 (-21.4, -0.4)	-27.3, 10.5			13	-10.60 (8.753)	-13.1 (-14.5, -5.6)	-27.3, 6.1						
Day 2 / 0-hr																
Absolute value	11	4.67 (0.361)	4.6 (4.5, 4.8)	4.0, 5.4			13	4.77 (0.397)	4.8 (4.6, 4.9)	4.0, 5.7						
Change from baseline	11	-0.35 (0.465)	-0.2 (-0.6, -0.1)	-1.3, 0.5	-0.37 (0.099)	(-0.58, -0.17)	13	-0.36 (0.315)	-0.3 (-0.4, -0.2)	-1.0, 0.0	-0.34 (0.091)	(-0.53, -0.15)	0.03 (-0.25, 0.31)	0.8197	-0.04 (-0.84, 0.77)	
Percent change from baseline	11	-6.56 (8.426)	-4.6 (-12.1, -1.9)	-21.6, 9.1			13	-6.87 (5.729)	-6.2 (-7.7, -3.0)	-17.0, 0.0						
Day 2 / 4-hr Post 1st																
Absolute value	11	4.90 (0.477)	4.9 (4.6, 5.2)	3.8, 5.6			13	4.68 (0.302)	4.6 (4.5, 4.7)	4.3, 5.5						
Change from baseline	11	-0.12 (0.466)	-0.1 (-0.6, 0.2)	-0.8, 0.6	-0.14 (0.110)	(-0.37, 0.08)	13	-0.45 (0.406)	-0.3 (-0.6, -0.2)	-1.4, 0.0	-0.43 (0.101)	(-0.64, -0.22)	-0.28 (-0.59, 0.03)	0.0742	-0.75 (-1.58, 0.08)	
Percent change from baseline	11	-2.17 (9.324)	-1.0 (-11.4, 4.0)	-16.5, 13.1			13	-8.32 (6.888)	-6.6 (-12.1, -3.5)	-23.1, 0.0						
Day 2 / 4-hr Post 2nd																
Absolute value	11	4.88 (0.433)	5.0 (4.4, 5.2)	4.2, 5.5			13	4.57 (0.392)	4.6 (4.3, 4.7)	3.9, 5.3						
Change from baseline	11	-0.14 (0.484)	0.0 (-0.5, 0.2)	-1.0, 0.5	-0.16 (0.103)	(-0.38, 0.05)	13	-0.56 (0.288)	-0.6 (-0.8, -0.5)	-1.0, 0.2	-0.54 (0.095)	(-0.74, -0.34)	-0.38 (-0.67, -0.09)	0.0135	-1.09 (-1.95, -0.23)	
Percent change from baseline	11	-2.41 (9.493)	0.0 (-11.3, 4.2)	-19.5, 11.1			13	-10.80 (5.589)	-10.1 (-14.3, -9.1)	-20.1, 4.0						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Congestive Heart Disease *(contd.)*																
Yes *(contd.)*																
Day 2 / 4-hr Post 3rd																
Absolute value	11	4.86 (0.520)	4.7 (4.5, 5.3)	4.1, 5.8			13	4.24 (0.296)	4.3 (4.1, 4.4)	3.7, 4.7						
Change from baseline	11	-0.16 (0.427)	-0.1 (-0.3, 0.1)	-1.1, 0.5	-0.18 (0.119)	(-0.43, 0.07)	13	-0.89 (0.491)	-0.8 (-1.3, -0.5)	-1.8, -0.2	-0.87 (0.109)	(-1.10, -0.64)	-0.69 (-1.03, -0.36)	0.0003	-1.59 (-2.51, -0.67)	
Percent change from baseline	11	-3.01 (8.141)	-2.5 (-6.3, 1.9)	-21.4, 9.1			13	-16.92 (8.291)	-15.7 (-21.4, -10.1)	-32.7, -4.7						
Day 2 / 20-hr Post 1st																
Absolute value	11	4.64 (0.514)	4.6 (4.2, 5.0)	3.9, 5.6			13	4.20 (0.303)	4.2 (4.1, 4.3)	3.7, 4.7						
Change from baseline	11	-0.38 (0.510)	-0.3 (-0.8, -0.1)	-1.3, 0.6	-0.41 (0.121)	(-0.66, -0.16)	13	-0.93 (0.445)	-0.9 (-1.1, -0.7)	-1.8, -0.1	-0.91 (0.112)	(-1.14, -0.68)	-0.50 (-0.84, -0.16)	0.0061	-1.15 (-2.02, -0.28)	
Percent change from baseline	11	-7.41 (9.913)	-5.5 (-14.5, -2.5)	-25.2, 13.1			13	-17.75 (7.562)	-16.4 (-21.4, -14.9)	-32.7, -2.5						
Day 3 / 0-hr																
Absolute value	11	4.62 (0.462)	4.5 (4.2, 5.0)	4.1, 5.5			13	4.49 (0.307)	4.4 (4.3, 4.7)	4.1, 5.1						
Change from baseline	11	-0.40 (0.455)	-0.4 (-0.7, -0.1)	-1.0, 0.5	-0.43 (0.103)	(-0.64, -0.21)	13	-0.64 (0.360)	-0.6 (-0.7, -0.4)	-1.3, -0.1	-0.62 (0.095)	(-0.81, -0.42)	-0.19 (-0.48, 0.10)	0.1869	-0.58 (-1.40, 0.24)	
Percent change from baseline	11	-7.79 (8.726)	-8.8 (-13.4, -2.5)	-19.5, 11.1			13	-12.15 (6.097)	-12.2 (-14.9, -7.3)	-21.8, -2.5						
Day 4 / 0-hr																
Absolute value	11	4.78 (0.440)	4.8 (4.4, 5.1)	4.0, 5.4			13	4.58 (0.363)	4.4 (4.4, 4.8)	4.1, 5.5						
Change from baseline	11	-0.24 (0.511)	-0.3 (-0.7, 0.0)	-0.8, 0.8	-0.26 (0.118)	(-0.51, -0.02)	13	-0.55 (0.427)	-0.6 (-0.7, -0.4)	-1.5, 0.1	-0.53 (0.108)	(-0.76, -0.31)	-0.27 (-0.60, 0.06)	0.1067	-0.68 (-1.50, 0.15)	
Percent change from baseline	11	-4.37 (10.254)	-6.7 (-12.7, 1.1)	-17.5, 17.0			13	-10.47 (7.415)	-11.7 (-14.9, -7.7)	-25.0, 1.8						
No																
Baseline																
Absolute value	19	5.21 (0.325)	5.2 (5.0, 5.3)	4.7, 6.1			11	4.96 (0.220)	4.9 (4.8, 5.2)	4.6, 5.4						
Day 1 / 30-min Post 1st																
Absolute value	18	5.35 (0.317)	5.4 (5.2, 5.5)	4.7, 6.0			11	4.89 (0.324)	4.8 (4.7, 5.3)	4.5, 5.4						
Change from baseline	18	0.15 (0.248)	0.1 (-0.0, 0.3)	-0.2, 0.6	0.18 (0.055)	(0.07, 0.30)	11	-0.07 (0.188)	-0.1 (-0.1, 0.1)	-0.5, 0.2	-0.10 (0.072)	(-0.25, 0.05)	-0.28 (-0.47, -0.09)	0.0058	-0.96 (-1.75, -0.17)	
Percent change from baseline	18	2.98 (4.916)	1.8 (-0.8, 5.3)	-3.9, 11.9			11	-1.48 (3.692)	-2.0 (-3.1, 0.9)	-8.7, 3.9						
Day 1 / 1-hr Post 1st																
Absolute value	19	5.31 (0.555)	5.4 (5.0, 5.5)	4.5, 7.1			11	4.82 (0.303)	4.8 (4.5, 5.1)	4.4, 5.3						
Change from baseline	19	0.11 (0.349)	0.1 (-0.1, 0.3)	-0.5, 1.1	0.12 (0.084)	(-0.05, 0.29)	11	-0.14 (0.356)	-0.1 (-0.3, 0.2)	-0.8, 0.4	-0.17 (0.111)	(-0.40, 0.06)	-0.29 (-0.58, -0.00)	0.0472	-0.71 (-1.47, 0.06)	
Percent change from baseline	19	1.91 (6.334)	2.2 (-2.4, 5.7)	-10.2, 17.4			11	-2.75 (7.017)	-2.0 (-6.9, 3.9)	-14.6, 7.2						
Day 1 / 2-hr Post 1st																
Absolute value	19	5.22 (0.565)	5.2 (4.8, 5.4)	4.5, 6.7			11	4.89 (0.430)	4.7 (4.6, 5.3)	4.2, 5.6						
Change from baseline	19	0.01 (0.313)	-0.1 (-0.2, 0.2)	-0.5, 0.7	0.03 (0.089)	(-0.16, 0.21)	11	-0.07 (0.447)	-0.1 (-0.4, 0.3)	-0.7, 0.7	-0.10 (0.117)	(-0.34, 0.14)	-0.12 (-0.43, 0.18)	0.4087	-0.22 (-0.97, 0.52)	
Percent change from baseline	19	0.02 (5.736)	-1.6 (-3.7, 4.2)	-9.4, 10.7			11	-1.32 (9.032)	-2.8 (-9.4, 5.9)	-12.6, 14.3						
Day 1 / 4-hr Post 1st																
Absolute value	19	5.09 (0.478)	5.1 (4.8, 5.3)	4.2, 6.2			11	4.65 (0.406)	4.7 (4.4, 4.9)	4.1, 5.6						
Change from baseline	19	-0.11 (0.288)	-0.1 (-0.3, 0.1)	-0.6, 0.6	-0.09 (0.083)	(-0.26, 0.07)	11	-0.31 (0.447)	-0.5 (-0.6, -0.1)	-0.8, 0.7	-0.33 (0.109)	(-0.56, -0.11)	-0.24 (-0.52, 0.04)	0.0945	-0.56 (-1.31, 0.20)	
Percent change from baseline	19	-2.20 (5.613)	-1.7 (-6.5, 2.3)	-12.1, 11.7			11	-6.06 (8.939)	-10.6 (-13.1, -2.1)	-14.6, 14.3						
Day 1 / 4-hr Post 2nd																
Absolute value	17	4.98 (0.467)	4.9 (4.6, 5.2)	4.4, 5.8			11	4.58 (0.405)	4.4 (4.2, 5.0)	4.1, 5.1						
Change from baseline	17	-0.26 (0.402)	-0.3 (-0.5, -0.1)	-0.9, 0.7	-0.23 (0.103)	(-0.44, -0.02)	11	-0.38 (0.491)	-0.5 (-0.8, 0.2)	-1.1, 0.3	-0.41 (0.129)	(-0.67, -0.14)	-0.17 (-0.51, 0.17)	0.3056	-0.28 (-1.05, 0.48)	

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Congestive Heart Disease *(contd.)*																
No *(contd.)*																
Day 1 / 4-hr Post 2nd *(contd.)*																
Percent change from baseline	17	-4.83 (7.752)	-5.2 (-10.2, -2.0)	-17.0, 13.2			11	-7.45 (9.599)	-10.2 (-14.6, 3.4)	-21.5, 6.2						
Day 1 / 4-hr Post 3rd																
Absolute value	19	4.99 (0.546)	4.9 (4.5, 5.2)	4.2, 6.3			11	4.43 (0.382)	4.4 (4.1, 4.7)	3.9, 5.0						
Change from baseline	19	-0.21 (0.390)	-0.3 (-0.4, 0.1)	-1.0, 0.6	-0.19 (0.099)	(-0.40, 0.01)	11	-0.53 (0.494)	-0.3 (-1.0, -0.2)	-1.5, 0.2	-0.56 (0.131)	(-0.83, -0.29)	-0.37 (-0.71, -0.03)	0.0343	-0.75 (-1.52, 0.01)	
Percent change from baseline	19	-4.13 (7.314)	-5.4 (-8.3, 2.2)	-19.7, 12.0			11	-10.54 (9.428)	-7.2 (-19.3, -3.9)	-27.1, 3.1						
Day 2 / 0-hr																
Absolute value	19	5.14 (0.531)	5.0 (4.8, 5.4)	4.4, 6.7			11	4.69 (0.549)	4.8 (4.2, 5.0)	3.9, 5.5						
Change from baseline	19	-0.07 (0.376)	-0.1 (-0.3, 0.1)	-0.8, 0.9	-0.05 (0.112)	(-0.28, 0.18)	11	-0.27 (0.641)	-0.1 (-0.9, 0.4)	-1.1, 0.6	-0.30 (0.147)	(-0.60, 0.00)	-0.25 (-0.63, 0.14)	0.1973	-0.42 (-1.17, 0.33)	
Percent change from baseline	19	-1.37 (6.916)	-1.9 (-6.4, 3.2)	-15.9, 15.5			11	-5.19 (12.704)	-2.6 (-19.3, 7.8)	-21.2, 12.2						
Day 2 / 4-hr Post 1st																
Absolute value	18	5.11 (0.411)	5.0 (4.9, 5.3)	4.3, 5.9			11	4.35 (0.463)	4.2 (4.0, 4.5)	3.9, 5.5						
Change from baseline	18	-0.09 (0.368)	-0.1 (-0.3, 0.1)	-0.8, 0.8	-0.08 (0.102)	(-0.29, 0.13)	11	-0.61 (0.577)	-0.6 (-1.0, -0.5)	-1.3, 0.8	-0.63 (0.132)	(-0.91, -0.36)	-0.55 (-0.90, -0.21)	0.0028	-1.12 (-1.93, -0.32)	
Percent change from baseline	18	-1.70 (6.977)	-2.1 (-6.4, 2.1)	-12.4, 15.7			11	-11.96 (11.491)	-12.5 (-20.5, -10.2)	-25.0, 16.2						
Day 2 / 4-hr Post 2nd																
Absolute value	17	5.11 (0.409)	5.1 (4.8, 5.3)	4.5, 5.8			11	4.27 (0.500)	4.1 (3.9, 4.6)	3.6, 5.2						
Change from baseline	17	-0.10 (0.407)	-0.2 (-0.3, 0.2)	-1.1, 0.6	-0.08 (0.107)	(-0.30, 0.14)	11	-0.69 (0.596)	-0.8 (-1.2, -0.3)	-1.3, 0.5	-0.72 (0.138)	(-1.00, -0.43)	-0.64 (-1.00, -0.28)	0.0012	-1.21 (-2.03, -0.39)	
Percent change from baseline	17	-1.69 (7.474)	-3.4 (-5.9, 3.7)	-17.4, 11.0			11	-13.64 (11.833)	-15.5 (-23.4, -7.2)	-25.0, 9.9						
Day 2 / 4-hr Post 3rd																
Absolute value	18	4.88 (0.480)	4.8 (4.6, 5.1)	4.0, 6.1			11	4.00 (0.456)	4.1 (3.6, 4.2)	3.2, 4.8						
Change from baseline	18	-0.32 (0.405)	-0.5 (-0.5, -0.0)	-0.8, 0.8	-0.32 (0.108)	(-0.54, -0.10)	11	-0.96 (0.573)	-0.8 (-1.6, -0.4)	-1.7, -0.1	-0.99 (0.140)	(-1.28, -0.70)	-0.67 (-1.03, -0.30)	0.0008	-1.35 (-2.18, -0.52)	
Percent change from baseline	18	-6.16 (7.633)	-8.8 (-10.5, -0.6)	-15.5, 15.5			11	-19.11 (11.067)	-16.6 (-30.8, -9.4)	-33.8, -2.0						
Day 2 / 20-hr Post 1st																
Absolute value	18	4.89 (0.365)	4.9 (4.6, 5.0)	4.4, 5.6			11	4.18 (0.467)	4.1 (3.7, 4.7)	3.5, 4.8						
Change from baseline	18	-0.32 (0.400)	-0.3 (-0.6, -0.1)	-1.1, 0.3	-0.30 (0.103)	(-0.51, -0.09)	11	-0.78 (0.575)	-0.7 (-1.3, -0.2)	-1.6, -0.0	-0.81 (0.134)	(-1.08, -0.53)	-0.51 (-0.86, -0.16)	0.0061	-0.98 (-1.77, -0.19)	
Percent change from baseline	18	-5.87 (7.285)	-5.2 (-11.3, -1.1)	-19.0, 6.0			11	-15.46 (11.116)	-14.6 (-27.6, -5.0)	-30.1, -0.7						
Day 3 / 0-hr																
Absolute value	19	5.12 (0.518)	5.0 (4.7, 5.4)	4.3, 6.3			11	4.23 (0.553)	4.1 (3.8, 4.7)	3.3, 5.1						
Change from baseline	19	-0.08 (0.396)	-0.1 (-0.3, 0.2)	-0.7, 0.7	-0.07 (0.114)	(-0.30, 0.17)	11	-0.73 (0.647)	-0.7 (-1.3, 0.0)	-1.6, 0.3	-0.76 (0.150)	(-1.07, -0.45)	-0.69 (-1.08, -0.31)	0.0010	-1.30 (-2.11, -0.49)	
Percent change from baseline	19	-1.64 (7.430)	-2.6 (-5.7, 3.7)	-13.7, 13.9			11	-14.54 (12.791)	-14.6 (-24.3, 0.0)	-31.7, 5.6						
Day 4 / 0-hr																
Absolute value	19	4.92 (0.503)	4.8 (4.5, 5.3)	4.2, 6.0			11	4.22 (0.363)	4.2 (4.0, 4.5)	3.6, 4.8						
Change from baseline	19	-0.29 (0.463)	-0.4 (-0.6, 0.1)	-1.0, 0.5	-0.27 (0.103)	(-0.49, -0.06)	11	-0.74 (0.457)	-0.7 (-1.2, -0.4)	-1.5, 0.1	-0.77 (0.136)	(-1.05, -0.49)	-0.50 (-0.85, -0.14)	0.0075	-0.99 (-1.77, -0.20)	
Percent change from baseline	19	-5.47 (8.723)	-7.4 (-12.1, 1.7)	-19.7, 9.4			11	-14.79 (8.799)	-14.3 (-22.3, -9.4)	-27.1, 1.4						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Diabetes mellitus																0.4906
Yes																
Baseline																
Absolute value	19	5.13 (0.374)	5.1 (4.9, 5.3)	4.6, 6.1			11	5.06 (0.346)	5.0 (4.8, 5.1)	4.8, 6.0						
Day 1 / 30-min Post 1st																
Absolute value	18	5.11 (0.460)	5.2 (4.7, 5.4)	4.3, 6.0			11	4.97 (0.352)	4.9 (4.7, 5.3)	4.6, 5.7						
Change from baseline	18	-0.01 (0.231)	-0.0 (-0.1, 0.1)	-0.5, 0.6	-0.00 (0.052)	(-0.11, 0.10)	11	-0.08 (0.187)	-0.1 (-0.3, 0.1)	-0.4, 0.2	-0.09 (0.066)	(-0.22, 0.05)	-0.08 (-0.26, 0.09)	0.3311	-0.32 (-1.08, 0.43)	
Percent change from baseline	18	-0.30 (4.619)	-0.6 (-2.1, 1.3)	-11.3, 11.4			11	-1.61 (3.675)	-2.0 (-4.7, 1.7)	-7.7, 3.9						
Day 1 / 1-hr Post 1st																
Absolute value	19	5.25 (0.596)	5.1 (4.9, 5.4)	4.4, 7.1			11	4.94 (0.269)	4.8 (4.8, 5.1)	4.6, 5.5						
Change from baseline	19	0.12 (0.381)	0.1 (-0.1, 0.3)	-0.5, 1.1	0.12 (0.076)	(-0.03, 0.28)	11	-0.12 (0.200)	-0.2 (-0.2, 0.0)	-0.5, 0.2	-0.12 (0.100)	(-0.33, 0.08)	-0.25 (-0.50, 0.01)	0.0612	-0.73 (-1.50, 0.03)	
Percent change from baseline	19	2.25 (7.127)	2.1 (-2.5, 5.9)	-9.6, 17.4			11	-2.24 (3.732)	-3.0 (-4.6, 0.3)	-8.1, 4.2						
Day 1 / 2-hr Post 1st																
Absolute value	19	5.16 (0.587)	5.0 (4.8, 5.4)	4.5, 6.7			11	4.95 (0.413)	4.8 (4.5, 5.4)	4.5, 5.6						
Change from baseline	19	0.04 (0.287)	-0.0 (-0.2, 0.2)	-0.5, 0.7	0.04 (0.074)	(-0.11, 0.19)	11	-0.11 (0.359)	-0.2 (-0.3, 0.1)	-0.5, 0.7	-0.11 (0.098)	(-0.32, 0.09)	-0.15 (-0.41, 0.10)	0.2242	-0.47 (-1.22, 0.29)	
Percent change from baseline	19	0.51 (5.223)	-1.0 (-3.2, 4.4)	-9.4, 10.7			11	-2.08 (7.108)	-3.0 (-6.6, 2.1)	-9.7, 14.3						
Day 1 / 4-hr Post 1st																
Absolute value	19	5.05 (0.615)	5.0 (4.7, 5.4)	4.0, 6.2			11	4.84 (0.439)	4.9 (4.5, 5.0)	4.0, 5.6						
Change from baseline	19	-0.08 (0.445)	-0.1 (-0.4, 0.2)	-0.6, 1.1	-0.08 (0.102)	(-0.29, 0.13)	11	-0.22 (0.437)	-0.2 (-0.6, 0.0)	-0.8, 0.7	-0.22 (0.133)	(-0.50, 0.05)	-0.15 (-0.49, 0.20)	0.3906	-0.32 (-1.06, 0.43)	
Percent change from baseline	19	-1.64 (9.005)	-2.5 (-7.8, 2.5)	-13.4, 21.2			11	-4.17 (8.688)	-3.9 (-10.6, 1.0)	-17.0, 14.3						
Day 1 / 4-hr Post 2nd																
Absolute value	18	4.94 (0.463)	5.0 (4.5, 5.3)	4.2, 5.8			11	4.70 (0.422)	4.7 (4.4, 5.0)	4.2, 5.6						
Change from baseline	18	-0.21 (0.369)	-0.3 (-0.4, 0.0)	-0.9, 0.5	-0.20 (0.084)	(-0.38, -0.03)	11	-0.36 (0.358)	-0.4 (-0.5, -0.1)	-1.1, 0.3	-0.36 (0.108)	(-0.58, -0.14)	-0.16 (-0.44, 0.12)	0.2652	-0.40 (-1.16, 0.35)	
Percent change from baseline	18	-3.98 (7.165)	-5.1 (-7.7, 1.0)	-17.0, 10.4			11	-6.95 (6.921)	-6.6 (-10.2, -2.0)	-21.5, 6.2						
Day 1 / 4-hr Post 3rd																
Absolute value	19	4.91 (0.605)	4.8 (4.5, 5.2)	4.0, 6.3			11	4.57 (0.410)	4.6 (4.4, 4.9)	3.9, 5.2						
Change from baseline	19	-0.22 (0.390)	-0.3 (-0.5, 0.1)	-0.9, 0.6	-0.21 (0.093)	(-0.40, -0.02)	11	-0.48 (0.425)	-0.4 (-0.8, -0.2)	-1.5, 0.0	-0.49 (0.122)	(-0.74, -0.24)	-0.27 (-0.59, 0.04)	0.0861	-0.66 (-1.42, 0.10)	
Percent change from baseline	19	-4.38 (7.517)	-5.9 (-9.7, 2.2)	-17.2, 12.0			11	-9.38 (7.964)	-7.1 (-13.1, -4.1)	-27.1, 0.3						
Day 2 / 0-hr																
Absolute value	19	5.11 (0.595)	5.1 (4.8, 5.4)	4.0, 6.7			11	4.80 (0.449)	4.8 (4.5, 5.0)	4.0, 5.5						
Change from baseline	19	-0.02 (0.357)	-0.1 (-0.3, 0.2)	-0.6, 0.9	-0.01 (0.097)	(-0.21, 0.19)	11	-0.26 (0.524)	-0.2 (-0.8, 0.0)	-1.1, 0.6	-0.26 (0.128)	(-0.52, 0.00)	-0.25 (-0.58, 0.08)	0.1381	-0.56 (-1.32, 0.19)	
Percent change from baseline	19	-0.49 (6.751)	-1.9 (-6.3, 3.6)	-12.1, 15.5			11	-4.78 (9.948)	-3.7 (-16.4, 0.0)	-19.6, 12.2						
Day 2 / 4-hr Post 1st																
Absolute value	19	5.05 (0.454)	5.0 (4.8, 5.3)	3.8, 5.7			11	4.45 (0.242)	4.5 (4.3, 4.6)	4.0, 4.9						
Change from baseline	19	-0.07 (0.364)	-0.1 (-0.3, 0.1)	-0.8, 0.6	-0.07 (0.082)	(-0.24, 0.10)	11	-0.60 (0.384)	-0.5 (-0.9, -0.3)	-1.4, -0.0	-0.61 (0.108)	(-0.83, -0.38)	-0.53 (-0.81, -0.25)	0.0006	-1.42 (-2.25, -0.60)	
Percent change from baseline	19	-1.36 (7.184)	-1.7 (-5.7, 2.1)	-16.5, 13.1			11	-11.61 (6.636)	-10.7 (-17.8, -6.6)	-23.1, -1.0						
Day 2 / 4-hr Post 2nd																
Absolute value	18	5.06 (0.468)	5.0 (4.6, 5.5)	4.3, 5.8			11	4.37 (0.498)	4.4 (3.9, 4.6)	3.6, 5.2						
Change from baseline	18	-0.07 (0.431)	0.0 (-0.3, 0.2)	-1.1, 0.6	-0.07 (0.099)	(-0.28, 0.13)	11	-0.68 (0.439)	-0.6 (-1.1, -0.4)	-1.3, 0.2	-0.69 (0.127)	(-0.95, -0.43)	-0.61 (-0.94, -0.28)	0.0007	-1.41 (-2.24, -0.58)	
Percent change from baseline	18	-1.24 (8.071)	0.2 (-6.7, 4.0)	-17.4, 11.1			11	-13.46 (8.689)	-12.8 (-22.5, -8.7)	-25.0, 4.1						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Diabetes mellitus *(contd.)*																
Yes *(contd.)*																
Day 2 / 4-hr Post 3rd																
Absolute value	19	4.96 (0.441)	4.9 (4.6, 5.3)	4.5, 6.1			11	4.19 (0.336)	4.1 (4.0, 4.4)	3.7, 4.8						
Change from baseline	19	-0.16 (0.410)	-0.1 (-0.5, 0.1)	-0.8, 0.8	-0.16 (0.090)	(-0.35, 0.02)	11	-0.87 (0.400)	-0.8 (-1.3, -0.7)	-1.3, -0.1	-0.87 (0.119)	(-1.11, -0.63)	-0.71 (-1.01, -0.40)	<.0001	-1.72 (-2.59, -0.86)	
Percent change from baseline	19	-3.03 (7.631)	-2.5 (-9.7, 1.1)	-14.0, 15.5			11	-16.90 (7.309)	-16.0 (-25.2, -14.6)	-25.5, -2.0						
Day 2 / 20-hr Post 1st																
Absolute value	19	4.82 (0.469)	4.8 (4.4, 5.0)	4.1, 5.6			11	4.28 (0.352)	4.2 (4.1, 4.7)	3.7, 4.8						
Change from baseline	19	-0.31 (0.442)	-0.3 (-0.6, -0.1)	-1.1, 0.6	-0.31 (0.094)	(-0.50, -0.12)	11	-0.77 (0.376)	-0.7 (-1.1, -0.7)	-1.3, -0.1	-0.78 (0.123)	(-1.03, -0.53)	-0.47 (-0.79, -0.15)	0.0054	-1.10 (-1.90, -0.31)	
Percent change from baseline	19	-5.92 (8.326)	-5.5 (-12.5, -2.3)	-19.0, 13.1			11	-15.16 (6.852)	-14.9 (-21.4, -13.1)	-25.2, -2.0						
Day 3 / 0-hr																
Absolute value	19	5.02 (0.636)	5.0 (4.4, 5.5)	4.1, 6.3			11	4.40 (0.379)	4.3 (4.1, 4.7)	3.8, 5.1						
Change from baseline	19	-0.11 (0.442)	-0.2 (-0.5, 0.2)	-0.7, 0.7	-0.11 (0.099)	(-0.31, 0.09)	11	-0.66 (0.414)	-0.7 (-0.7, -0.4)	-1.6, 0.0	-0.66 (0.131)	(-0.93, -0.39)	-0.55 (-0.89, -0.21)	0.0023	-1.26 (-2.07, -0.45)	
Percent change from baseline	19	-2.32 (8.562)	-4.5 (-9.8, 4.0)	-13.7, 13.9			11	-12.79 (7.518)	-14.0 (-14.9, -8.2)	-29.0, 0.0						
Day 4 / 0-hr																
Absolute value	19	4.91 (0.529)	4.7 (4.5, 5.4)	4.0, 6.0			11	4.41 (0.318)	4.4 (4.2, 4.8)	3.9, 4.9						
Change from baseline	19	-0.22 (0.452)	-0.3 (-0.6, 0.3)	-0.8, 0.5	-0.21 (0.095)	(-0.41, -0.02)	11	-0.65 (0.364)	-0.6 (-0.7, -0.4)	-1.5, -0.2	-0.65 (0.125)	(-0.91, -0.39)	-0.44 (-0.76, -0.11)	0.0098	-1.02 (-1.80, -0.23)	
Percent change from baseline	19	-4.14 (8.656)	-6.7 (-11.8, 6.0)	-17.5, 9.4			11	-12.60 (6.490)	-11.9 (-14.9, -8.7)	-27.1, -3.0						
No																
Baseline																
Absolute value	11	5.15 (0.346)	5.2 (4.9, 5.3)	4.6, 5.9			13	5.05 (0.383)	4.9 (4.8, 5.2)	4.6, 5.9						
Day 1 / 30-min Post 1st																
Absolute value	11	5.26 (0.338)	5.3 (4.9, 5.5)	4.6, 5.7			13	5.08 (0.537)	5.0 (4.7, 5.4)	4.5, 6.2						
Change from baseline	11	0.11 (0.412)	0.2 (-0.2, 0.5)	-0.6, 0.6	0.14 (0.109)	(-0.09, 0.36)	13	0.03 (0.278)	-0.0 (-0.1, 0.3)	-0.5, 0.5	0.01 (0.100)	(-0.20, 0.22)	-0.12 (-0.43, 0.19)	0.4160	-0.22 (-1.02, 0.59)	
Percent change from baseline	11	2.40 (7.798)	3.8 (-3.9, 9.9)	-10.9, 11.9			13	0.56 (5.515)	-0.7 (-2.9, 5.5)	-8.7, 11.2						
Day 1 / 1-hr Post 1st																
Absolute value	11	5.27 (0.398)	5.4 (4.8, 5.6)	4.7, 5.9			13	4.95 (0.555)	4.8 (4.5, 5.2)	4.4, 6.3						
Change from baseline	11	0.12 (0.345)	0.3 (-0.1, 0.4)	-0.5, 0.5	0.14 (0.141)	(-0.15, 0.44)	13	-0.11 (0.611)	-0.2 (-0.3, 0.1)	-0.9, 1.5	-0.13 (0.130)	(-0.40, 0.14)	-0.27 (-0.67, 0.13)	0.1728	-0.44 (-1.25, 0.37)	
Percent change from baseline	11	2.43 (6.492)	5.6 (-2.4, 7.3)	-10.2, 9.3			13	-1.72 (12.237)	-4.2 (-6.9, 1.4)	-14.8, 32.2						
Day 1 / 2-hr Post 1st																
Absolute value	11	5.05 (0.437)	4.9 (4.7, 5.3)	4.6, 6.1			12	4.91 (0.460)	4.8 (4.6, 5.4)	4.2, 5.7						
Change from baseline	11	-0.11 (0.417)	-0.1 (-0.4, 0.2)	-1.0, 0.6	-0.08 (0.111)	(-0.31, 0.15)	12	-0.16 (0.346)	-0.1 (-0.4, -0.1)	-0.7, 0.6	-0.16 (0.104)	(-0.37, 0.06)	-0.07 (-0.39, 0.24)	0.6392	-0.12 (-0.94, 0.70)	
Percent change from baseline	11	-1.96 (7.523)	-1.9 (-7.8, 4.2)	-16.5, 10.9			12	-2.97 (7.027)	-2.8 (-7.8, -1.8)	-12.6, 12.0						
Day 1 / 4-hr Post 1st																
Absolute value	11	4.85 (0.461)	4.9 (4.6, 5.3)	3.7, 5.3			13	4.77 (0.504)	4.7 (4.4, 5.0)	4.1, 5.6						
Change from baseline	11	-0.31 (0.675)	-0.1 (-0.6, 0.2)	-1.8, 0.7	-0.28 (0.147)	(-0.59, 0.02)	13	-0.28 (0.397)	-0.4 (-0.6, -0.0)	-0.8, 0.5	-0.30 (0.135)	(-0.58, -0.02)	-0.02 (-0.43, 0.39)	0.9195	0.05 (-0.75, 0.85)	
Percent change from baseline	11	-5.40 (12.604)	-2.6 (-12.1, 3.5)	-32.7, 14.8			13	-5.52 (7.903)	-6.3 (-13.1, -0.4)	-14.6, 9.4						
Day 1 / 4-hr Post 2nd																
Absolute value	10	4.85 (0.486)	4.9 (4.6, 5.1)	3.9, 5.7			13	4.67 (0.435)	4.6 (4.4, 5.0)	4.1, 5.5						
Change from baseline	10	-0.29 (0.618)	-0.2 (-0.6, -0.0)	-1.3, 0.7	-0.27 (0.140)	(-0.56, 0.03)	13	-0.38 (0.411)	-0.5 (-0.5, -0.3)	-1.0, 0.3	-0.40 (0.124)	(-0.66, -0.15)	-0.14 (-0.53, 0.25)	0.4698	-0.18 (-1.01, 0.65)	

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Diabetes mellitus *(contd.)*																
No *(contd.)*																
Day 1 / 4-hr Post 2nd *(contd.)*																
Percent change from baseline	10	-5.20 (11.804)	-4.3 (-11.3, -0.3)	-25.2, 13.2			13	-7.37 (8.091)	-10.1 (-11.5, -5.5)	-19.2, 6.1						
Day 1 / 4-hr Post 3rd																
Absolute value	11	4.65 (0.446)	4.6 (4.2, 5.1)	4.0, 5.2			13	4.45 (0.393)	4.4 (4.1, 4.7)	3.9, 5.1						
Change from baseline	11	-0.50 (0.637)	-0.3 (-1.1, -0.1)	-1.5, 0.5	-0.47 (0.144)	(-0.77, -0.17)	13	-0.61 (0.513)	-0.8 (-0.9, -0.3)	-1.5, 0.3	-0.63 (0.132)	(-0.90, -0.35)	-0.15 (-0.56, 0.26)	0.4447	-0.18 (-0.99, 0.62)	
Percent change from baseline	11	-9.19 (11.849)	-7.0 (-21.4, -1.6)	-27.3, 10.5			13	-11.58 (9.769)	-14.0 (-18.4, -5.6)	-27.3, 6.1						
Day 2 / 0-hr																
Absolute value	11	4.72 (0.209)	4.6 (4.6, 4.9)	4.4, 5.0			13	4.68 (0.485)	4.7 (4.4, 5.0)	3.9, 5.7						
Change from baseline	11	-0.44 (0.415)	-0.3 (-0.8, -0.1)	-1.3, 0.1	-0.41 (0.114)	(-0.65, -0.17)	13	-0.37 (0.458)	-0.4 (-0.8, -0.0)	-1.1, 0.4	-0.40 (0.104)	(-0.61, -0.18)	0.01 (-0.31, 0.34)	0.9258	0.14 (-0.66, 0.95)	
Percent change from baseline	11	-8.09 (7.316)	-5.7 (-15.9, -2.5)	-21.6, 1.4			13	-7.21 (9.129)	-7.3 (-14.5, -0.4)	-21.2, 7.9						
Day 2 / 4-hr Post 1st																
Absolute value	10	4.98 (0.434)	5.0 (4.7, 5.2)	4.3, 5.9			13	4.60 (0.515)	4.6 (4.1, 4.8)	3.9, 5.5						
Change from baseline	10	-0.16 (0.476)	-0.3 (-0.5, 0.2)	-0.7, 0.8	-0.18 (0.148)	(-0.49, 0.13)	13	-0.45 (0.567)	-0.5 (-0.9, -0.0)	-1.3, 0.8	-0.47 (0.132)	(-0.75, -0.20)	-0.29 (-0.71, 0.12)	0.1551	-0.55 (-1.39, 0.29)	
Percent change from baseline	10	-2.85 (9.157)	-6.4 (-10.2, 4.0)	-11.8, 15.7			13	-8.61 (11.086)	-11.5 (-15.5, -0.7)	-25.0, 16.2						
Day 2 / 4-hr Post 2nd																
Absolute value	10	4.96 (0.353)	5.1 (4.8, 5.2)	4.2, 5.3			13	4.48 (0.439)	4.3 (4.1, 4.7)	3.9, 5.3						
Change from baseline	10	-0.19 (0.444)	-0.2 (-0.4, 0.2)	-1.0, 0.5	-0.15 (0.119)	(-0.40, 0.09)	13	-0.57 (0.469)	-0.7 (-0.8, -0.5)	-1.3, 0.5	-0.59 (0.108)	(-0.81, -0.36)	-0.43 (-0.77, -0.10)	0.0133	-0.83 (-1.69, 0.03)	
Percent change from baseline	10	-3.30 (8.589)	-4.4 (-7.4, 3.7)	-19.5, 10.5			13	-10.95 (9.266)	-14.3 (-15.2, -9.7)	-24.3, 9.9						
Day 2 / 4-hr Post 3rd																
Absolute value	10	4.70 (0.544)	4.7 (4.4, 4.9)	4.0, 5.8			13	4.08 (0.434)	4.2 (3.7, 4.4)	3.2, 4.6						
Change from baseline	10	-0.44 (0.375)	-0.5 (-0.6, -0.2)	-1.1, 0.3	-0.41 (0.144)	(-0.71, -0.11)	13	-0.97 (0.615)	-0.8 (-1.6, -0.5)	-1.8, -0.2	-1.00 (0.129)	(-1.26, -0.73)	-0.59 (-0.99, -0.19)	0.0061	-1.02 (-1.89, -0.14)	
Percent change from baseline	10	-8.64 (7.200)	-9.5 (-10.5, -4.7)	-21.4, 5.5			13	-18.79 (11.265)	-15.5 (-30.8, -9.8)	-33.8, -4.7						
Day 2 / 20-hr Post 1st																
Absolute value	10	4.76 (0.392)	4.8 (4.6, 5.0)	3.9, 5.3			13	4.12 (0.395)	4.1 (3.7, 4.4)	3.5, 4.7						
Change from baseline	10	-0.40 (0.445)	-0.4 (-0.6, -0.0)	-1.3, 0.2	-0.31 (0.137)	(-0.60, -0.03)	13	-0.94 (0.594)	-0.9 (-1.5, -0.5)	-1.8, -0.0	-0.96 (0.125)	(-1.22, -0.70)	-0.64 (-1.03, -0.25)	0.0026	-1.00 (-1.87, -0.13)	
Percent change from baseline	10	-7.48 (8.414)	-6.9 (-11.3, -0.4)	-25.2, 3.3			13	-18.01 (10.937)	-18.4 (-27.6, -9.8)	-32.7, -0.7						
Day 3 / 0-hr																
Absolute value	11	4.80 (0.335)	4.9 (4.5, 5.1)	4.2, 5.2			13	4.35 (0.513)	4.3 (4.0, 4.7)	3.3, 5.1						
Change from baseline	11	-0.35 (0.407)	-0.3 (-0.7, 0.0)	-1.0, 0.2	-0.33 (0.135)	(-0.61, -0.05)	13	-0.71 (0.582)	-0.6 (-1.2, -0.3)	-1.5, 0.3	-0.73 (0.124)	(-0.98, -0.47)	-0.40 (-0.78, -0.02)	0.0414	-0.69 (-1.51, 0.14)	
Percent change from baseline	11	-6.61 (7.553)	-5.5 (-11.4, 0.0)	-19.5, 3.7			13	-13.63 (11.353)	-12.2 (-21.8, -6.2)	-31.7, 5.6						
Day 4 / 0-hr																
Absolute value	11	4.79 (0.383)	4.8 (4.4, 5.1)	4.2, 5.4			13	4.42 (0.471)	4.4 (4.1, 4.7)	3.6, 5.5						
Change from baseline	11	-0.36 (0.516)	-0.4 (-0.8, -0.1)	-1.0, 0.8	-0.34 (0.134)	(-0.62, -0.06)	13	-0.64 (0.513)	-0.7 (-1.1, -0.4)	-1.5, 0.1	-0.66 (0.124)	(-0.91, -0.40)	-0.32 (-0.70, 0.06)	0.0954	-0.53 (-1.35, 0.29)	
Percent change from baseline	11	-6.67 (10.181)	-7.4 (-13.1, -2.2)	-19.7, 17.0			13	-12.32 (9.677)	-12.7 (-21.2, -7.7)	-25.5, 1.8						

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RAASi Medications																0.6848
Yes																
Baseline																
Absolute value	19	5.19 (0.414)	5.1 (4.9, 5.5)	4.6, 6.1			20	5.11 (0.365)	5.0 (4.8, 5.3)	4.6, 6.0						
Day 1 / 30-min Post 1st																
Absolute value	18	5.15 (0.453)	5.3 (4.9, 5.4)	4.3, 6.0			20	5.10 (0.472)	5.0 (4.7, 5.4)	4.5, 6.2						
Change from baseline	18	-0.04 (0.305)	-0.0 (-0.2, 0.2)	-0.6, 0.5	-0.02 (0.069)	(-0.16, 0.12)	20	-0.01 (0.264)	-0.1 (-0.2, 0.2)	-0.5, 0.5	-0.03 (0.066)	(-0.16, 0.11)	-0.00 (-0.20, 0.19)	0.9645	0.08 (-0.55, 0.72)	
Percent change from baseline	18	-0.64 (5.870)	-0.6 (-3.3, 3.8)	-11.3, 9.9			20	-0.33 (5.204)	-1.1 (-4.6, 3.9)	-8.7, 11.2						
Day 1 / 1-hr Post 1st																
Absolute value	19	5.38 (0.559)	5.4 (5.0, 5.6)	4.4, 7.1			20	4.99 (0.464)	4.9 (4.8, 5.2)	4.4, 6.3						
Change from baseline	19	0.19 (0.299)	0.1 (0.1, 0.3)	-0.5, 1.1	0.20 (0.094)	(0.01, 0.39)	20	-0.12 (0.504)	-0.2 (-0.3, 0.1)	-0.9, 1.5	-0.13 (0.092)	(-0.32, 0.06)	-0.33 (-0.60, -0.07)	0.0162	-0.75 (-1.39, -0.10)	
Percent change from baseline	19	3.62 (5.229)	2.5 (1.7, 5.9)	-8.0, 17.4			20	-2.06 (10.048)	-4.0 (-6.2, 2.0)	-14.8, 32.2						
Day 1 / 2-hr Post 1st																
Absolute value	19	5.21 (0.618)	5.0 (4.8, 5.5)	4.5, 6.7			19	4.93 (0.390)	4.8 (4.6, 5.4)	4.5, 5.7						
Change from baseline	19	0.02 (0.377)	-0.0 (-0.2, 0.2)	-1.0, 0.7	0.03 (0.079)	(-0.13, 0.19)	19	-0.19 (0.263)	-0.1 (-0.3, -0.1)	-0.7, 0.3	-0.19 (0.077)	(-0.34, -0.03)	-0.21 (-0.44, 0.01)	0.0604	-0.64 (-1.29, 0.01)	
Percent change from baseline	19	0.22 (6.661)	-1.0 (-3.7, 4.4)	-16.5, 10.9			19	-3.62 (5.133)	-2.8 (-6.6, -1.8)	-12.6, 7.0						
Day 1 / 4-hr Post 1st																
Absolute value	19	5.03 (0.617)	5.1 (4.8, 5.3)	3.7, 6.2			20	4.78 (0.448)	4.7 (4.5, 5.0)	4.0, 5.6						
Change from baseline	19	-0.17 (0.590)	-0.1 (-0.4, 0.2)	-1.8, 0.7	-0.16 (0.107)	(-0.37, 0.06)	20	-0.33 (0.352)	-0.4 (-0.6, -0.1)	-0.8, 0.5	-0.34 (0.105)	(-0.55, -0.13)	-0.18 (-0.49, 0.12)	0.2270	-0.34 (-0.97, 0.29)	
Percent change from baseline	19	-2.99 (11.162)	-1.5 (-8.0, 3.5)	-32.7, 14.8			20	-6.39 (6.930)	-7.0 (-12.6, -1.7)	-17.0, 9.4						
Day 1 / 4-hr Post 2nd																
Absolute value	18	4.97 (0.548)	5.1 (4.5, 5.3)	3.9, 5.8			20	4.77 (0.404)	4.7 (4.4, 5.1)	4.2, 5.6						
Change from baseline	18	-0.21 (0.528)	-0.3 (-0.4, 0.1)	-1.3, 0.7	-0.21 (0.102)	(-0.42, -0.01)	20	-0.34 (0.410)	-0.4 (-0.5, -0.1)	-1.1, 0.3	-0.35 (0.098)	(-0.55, -0.15)	-0.14 (-0.42, 0.15)	0.3405	-0.27 (-0.91, 0.37)	
Percent change from baseline	18	-3.89 (10.162)	-5.1 (-7.7, 1.3)	-25.2, 13.2			20	-6.43 (7.937)	-6.3 (-10.2, -1.8)	-21.5, 6.2						
Day 1 / 4-hr Post 3rd																
Absolute value	19	4.88 (0.645)	4.9 (4.4, 5.2)	4.0, 6.3			20	4.51 (0.431)	4.6 (4.1, 4.9)	3.9, 5.2						
Change from baseline	19	-0.31 (0.579)	-0.3 (-0.6, 0.2)	-1.5, 0.6	-0.30 (0.118)	(-0.54, -0.06)	20	-0.61 (0.494)	-0.7 (-0.9, -0.2)	-1.5, 0.3	-0.62 (0.115)	(-0.85, -0.38)	-0.32 (-0.65, 0.02)	0.0613	-0.55 (-1.19, 0.09)	
Percent change from baseline	19	-5.83 (10.741)	-5.9 (-12.1, 3.3)	-27.3, 12.0			20	-11.55 (9.381)	-13.1 (-18.9, -5.0)	-27.3, 6.1						
Day 2 / 0-hr																
Absolute value	19	5.01 (0.612)	4.9 (4.6, 5.4)	4.0, 6.7			20	4.68 (0.464)	4.8 (4.4, 4.9)	3.9, 5.7						
Change from baseline	19	-0.19 (0.478)	-0.2 (-0.5, 0.1)	-1.3, 0.9	-0.18 (0.102)	(-0.38, 0.03)	20	-0.43 (0.425)	-0.3 (-0.8, -0.1)	-1.1, 0.4	-0.44 (0.100)	(-0.64, -0.24)	-0.26 (-0.55, 0.03)	0.0737	-0.54 (-1.18, 0.10)	
Percent change from baseline	19	-3.61 (8.576)	-3.9 (-7.7, 1.4)	-21.6, 15.5			20	-8.28 (8.140)	-6.7 (-15.5, -2.7)	-21.2, 7.8						
Day 2 / 4-hr Post 1st																
Absolute value	18	5.05 (0.529)	5.1 (4.7, 5.3)	3.8, 5.9			20	4.52 (0.380)	4.6 (4.3, 4.7)	3.9, 5.5						
Change from baseline	18	-0.14 (0.438)	-0.1 (-0.4, 0.1)	-0.8, 0.8	-0.13 (0.095)	(-0.32, 0.06)	20	-0.60 (0.439)	-0.6 (-0.9, -0.2)	-1.4, 0.0	-0.61 (0.091)	(-0.79, -0.42)	-0.47 (-0.74, -0.21)	0.0010	-1.04 (-1.72, -0.37)	
Percent change from baseline	18	-2.53 (8.503)	-2.3 (-9.2, 2.1)	-16.5, 15.7			20	-11.38 (8.047)	-11.9 (-17.1, -4.6)	-25.0, 0.0						
Day 2 / 4-hr Post 2nd																
Absolute value	19	5.06 (0.468)	5.1 (4.6, 5.3)	4.2, 5.8			20	4.37 (0.444)	4.3 (4.1, 4.7)	3.6, 5.3						
Change from baseline	19	-0.14 (0.470)	-0.2 (-0.4, 0.2)	-1.1, 0.6	-0.12 (0.090)	(-0.31, 0.06)	20	-0.74 (0.354)	-0.7 (-1.0, -0.5)	-1.3, 0.2	-0.75 (0.088)	(-0.93, -0.57)	-0.63 (-0.88, -0.37)	<.0001	-1.46 (-2.17, -0.75)	
Percent change from baseline	19	-2.33 (8.803)	-3.4 (-7.7, 4.0)	-19.5, 11.0			20	-14.43 (7.014)	-14.4 (-20.6, -9.8)	-25.0, 4.0						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
RAASi Medications *(contd.)*																
Yes *(contd.)*																
Day 2 / 4-hr Post 3rd																
Absolute value	18	4.91 (0.561)	4.9 (4.5, 5.2)	4.0, 6.1			20	4.06 (0.378)	4.1 (3.8, 4.3)	3.2, 4.7						
Change from baseline	18	-0.28 (0.456)	-0.3 (-0.6, -0.0)	-1.1, 0.8	-0.29 (0.102)	(-0.50, -0.08)	20	-1.05 (0.472)	-1.0 (-1.5, -0.7)	-1.8, -0.2	-1.06 (0.097)	(-1.26, -0.86)	-0.77 (-1.06, -0.48)	<.0001	-1.66 (-2.39, -0.92)	
Percent change from baseline	18	-5.35 (8.529)	-6.1 (-9.8, -0.6)	-21.4, 15.5			20	-20.26 (8.548)	-18.3 (-26.9, -14.7)	-33.8, -4.7						
Day 2 / 20-hr Post 1st																
Absolute value	18	4.79 (0.494)	4.8 (4.4, 5.2)	3.9, 5.6			20	4.13 (0.364)	4.1 (3.9, 4.3)	3.5, 4.8						
Change from baseline	18	-0.40 (0.445)	-0.4 (-0.6, -0.1)	-1.3, 0.3	-0.38 (0.094)	(-0.57, -0.19)	20	-0.98 (0.450)	-0.9 (-1.3, -0.7)	-1.8, -0.1	-0.99 (0.091)	(-1.17, -0.81)	-0.61 (-0.87, -0.34)	<.0001	-1.29 (-1.99, -0.59)	
Percent change from baseline	18	-7.59 (8.254)	-7.9 (-12.5, -2.6)	-25.2, 6.0			20	-18.91 (8.097)	-17.4 (-26.0, -14.6)	-32.7, -2.5						
Day 3 / 0-hr																
Absolute value	19	4.94 (0.659)	5.0 (4.4, 5.4)	4.1, 6.3			20	4.31 (0.460)	4.3 (4.1, 4.7)	3.3, 5.1						
Change from baseline	19	-0.25 (0.499)	-0.3 (-0.6, 0.1)	-1.0, 0.7	-0.24 (0.109)	(-0.46, -0.02)	20	-0.80 (0.455)	-0.7 (-1.2, -0.5)	-1.6, 0.0	-0.81 (0.106)	(-1.02, -0.59)	-0.57 (-0.87, -0.26)	0.0006	-1.14 (-1.82, -0.46)	
Percent change from baseline	19	-4.90 (9.372)	-5.7 (-11.4, 1.3)	-19.5, 13.9			20	-15.41 (8.596)	-14.6 (-21.7, -9.6)	-31.7, 0.0						
Day 4 / 0-hr																
Absolute value	19	4.97 (0.524)	4.9 (4.6, 5.4)	4.0, 6.0			20	4.43 (0.418)	4.4 (4.2, 4.8)	3.6, 5.5						
Change from baseline	19	-0.22 (0.508)	-0.2 (-0.7, 0.3)	-0.9, 0.8	-0.21 (0.103)	(-0.42, 0.00)	20	-0.68 (0.453)	-0.6 (-1.1, -0.4)	-1.5, 0.1	-0.69 (0.100)	(-0.89, -0.49)	-0.48 (-0.77, -0.19)	0.0019	-0.96 (-1.62, -0.30)	
Percent change from baseline	19	-3.99 (9.773)	-4.2 (-12.4, 6.0)	-17.5, 17.0			20	-13.08 (8.356)	-12.2 (-19.6, -7.9)	-27.1, 1.8						
No																
Baseline																
Absolute value	11	5.04 (0.220)	5.1 (4.9, 5.2)	4.7, 5.3			4	4.77 (0.114)	4.8 (4.7, 4.9)	4.6, 4.9						
Day 1 / 30-min Post 1st																
Absolute value	11	5.19 (0.375)	5.2 (4.7, 5.5)	4.7, 5.7			4	4.73 (0.171)	4.8 (4.6, 4.9)	4.5, 4.9						
Change from baseline	11	0.15 (0.297)	0.0 (-0.1, 0.5)	-0.3, 0.6			4	-0.05 (0.096)	-0.1 (-0.1, 0.0)	-0.1, 0.1						
Percent change from baseline	11	2.97 (5.880)	1.1 (-1.9, 10.0)	-5.1, 11.9			4	-0.97 (2.012)	-1.4 (-2.5, 0.5)	-2.9, 1.7						
Day 1 / 1-hr Post 1st																
Absolute value	11	5.04 (0.388)	5.1 (4.7, 5.3)	4.5, 5.8			4	4.70 (0.115)	4.7 (4.6, 4.8)	4.6, 4.8						
Change from baseline	11	-0.00 (0.439)	-0.1 (-0.5, 0.3)	-0.5, 0.8			4	-0.07 (0.119)	-0.1 (-0.2, 0.0)	-0.2, 0.1						
Percent change from baseline	11	0.07 (8.696)	-2.4 (-9.4, 7.1)	-10.2, 17.2			4	-1.46 (2.473)	-1.4 (-3.3, 0.3)	-4.5, 1.4						
Day 1 / 2-hr Post 1st																
Absolute value	11	4.96 (0.301)	4.9 (4.7, 5.2)	4.5, 5.4			4	4.90 (0.658)	4.9 (4.4, 5.5)	4.2, 5.6						
Change from baseline	11	-0.08 (0.273)	-0.1 (-0.3, 0.2)	-0.5, 0.3			4	0.13 (0.587)	0.1 (-0.4, 0.6)	-0.4, 0.7						
Percent change from baseline	11	-1.48 (5.296)	-2.3 (-5.8, 4.2)	-9.4, 5.1			4	2.58 (12.267)	2.7 (-8.0, 13.1)	-9.4, 14.3						
Day 1 / 4-hr Post 1st																
Absolute value	11	4.88 (0.471)	4.9 (4.6, 5.1)	4.2, 6.0			4	4.90 (0.616)	5.0 (4.5, 5.3)	4.1, 5.6						
Change from baseline	11	-0.16 (0.472)	-0.3 (-0.5, -0.1)	-0.6, 1.1			4	0.13 (0.506)	0.2 (-0.2, 0.4)	-0.5, 0.7						
Percent change from baseline	11	-3.07 (9.510)	-5.8 (-9.7, -1.6)	-12.1, 21.2			4	2.53 (10.614)	3.7 (-4.0, 9.0)	-11.5, 14.3						
Day 1 / 4-hr Post 2nd																
Absolute value	10	4.80 (0.245)	4.8 (4.7, 4.9)	4.4, 5.3			4	4.25 (0.129)	4.3 (4.2, 4.4)	4.1, 4.4						
Change from baseline	10	-0.28 (0.336)	-0.2 (-0.5, -0.0)	-0.9, 0.1			4	-0.52 (0.016)	-0.5 (-0.5, -0.5)	-0.5, -0.5						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
RAASi Medications *(contd.)*																
No *(contd.)*																
Day 1 / 4-hr Post 2nd *(contd.)*																
Percent change from baseline	10	-5.36 (6.386)	-3.6 (-10.2, -0.3)	-17.0, 1.9			4	-10.93 (0.583)	-11.0 (-11.4, -10.5)	-11.5, -10.2						
Day 1 / 4-hr Post 3rd																
Absolute value	11	4.70 (0.361)	4.8 (4.4, 5.0)	4.1, 5.2			4	4.50 (0.183)	4.5 (4.4, 4.7)	4.3, 4.7						
Change from baseline	11	-0.34 (0.361)	-0.3 (-0.4, -0.1)	-1.0, 0.3			4	-0.27 (0.128)	-0.3 (-0.4, -0.2)	-0.4, -0.1						
Percent change from baseline	11	-6.69 (7.076)	-6.2 (-8.5, -1.6)	-19.7, 5.1			4	-5.69 (2.700)	-5.6 (-7.9, -3.4)	-8.7, -2.8						
Day 2 / 0-hr																
Absolute value	11	4.90 (0.326)	4.9 (4.6, 5.2)	4.4, 5.4			4	5.00 (0.408)	5.0 (4.8, 5.3)	4.5, 5.5						
Change from baseline	11	-0.14 (0.334)	-0.2 (-0.3, 0.1)	-0.8, 0.5			4	0.23 (0.390)	0.3 (-0.0, 0.5)	-0.3, 0.6						
Percent change from baseline	11	-2.70 (6.546)	-3.0 (-6.4, 3.2)	-15.9, 9.1			4	4.80 (8.066)	6.8 (-0.5, 10.1)	-6.6, 12.2						
Day 2 / 4-hr Post 1st																
Absolute value	11	4.99 (0.255)	4.9 (4.8, 5.2)	4.7, 5.6			4	4.63 (0.608)	4.5 (4.3, 5.0)	4.1, 5.5						
Change from baseline	11	-0.05 (0.340)	-0.1 (-0.3, 0.1)	-0.5, 0.6			4	-0.15 (0.616)	-0.4 (-0.5, 0.2)	-0.5, 0.8						
Percent change from baseline	11	-0.82 (6.703)	-1.0 (-6.4, 3.2)	-10.2, 13.1			4	-3.02 (12.983)	-8.4 (-10.9, 4.8)	-11.5, 16.2						
Day 2 / 4-hr Post 2nd																
Absolute value	9	4.94 (0.332)	5.0 (4.8, 5.1)	4.4, 5.5			4	4.75 (0.465)	4.8 (4.4, 5.2)	4.3, 5.2						
Change from baseline	9	-0.07 (0.355)	0.0 (-0.3, 0.1)	-0.6, 0.5			4	-0.02 (0.425)	-0.1 (-0.4, 0.3)	-0.4, 0.5						
Percent change from baseline	9	-1.21 (7.036)	0.0 (-6.7, 3.2)	-12.1, 11.1			4	-0.48 (8.936)	-1.6 (-7.9, 7.0)	-8.7, 9.9						
Day 2 / 4-hr Post 3rd																
Absolute value	11	4.82 (0.349)	4.7 (4.6, 5.3)	4.4, 5.4			4	4.48 (0.250)	4.5 (4.3, 4.7)	4.2, 4.8						
Change from baseline	11	-0.22 (0.352)	-0.3 (-0.5, 0.0)	-0.7, 0.5			4	-0.30 (0.159)	-0.3 (-0.4, -0.2)	-0.4, -0.1						
Percent change from baseline	11	-4.33 (6.906)	-5.1 (-10.1, 1.1)	-14.0, 9.1			4	-6.24 (3.408)	-6.8 (-9.0, -3.5)	-9.4, -2.0						
Day 2 / 20-hr Post 1st																
Absolute value	11	4.80 (0.349)	4.7 (4.6, 5.0)	4.4, 5.6			4	4.50 (0.316)	4.6 (4.3, 4.8)	4.1, 4.8						
Change from baseline	11	-0.24 (0.426)	-0.2 (-0.6, -0.1)	-0.9, 0.6			4	-0.27 (0.309)	-0.2 (-0.5, -0.1)	-0.7, -0.0						
Percent change from baseline	11	-4.60 (8.255)	-3.8 (-11.3, -1.1)	-17.0, 13.1			4	-5.66 (6.404)	-3.5 (-10.0, -1.4)	-14.9, -0.7						
Day 3 / 0-hr																
Absolute value	11	4.93 (0.300)	5.0 (4.7, 5.1)	4.3, 5.5			4	4.65 (0.265)	4.6 (4.5, 4.9)	4.4, 5.0						
Change from baseline	11	-0.11 (0.312)	-0.2 (-0.3, 0.0)	-0.5, 0.5			4	-0.12 (0.342)	-0.2 (-0.4, 0.2)	-0.4, 0.3						
Percent change from baseline	11	-2.16 (6.207)	-4.5 (-5.8, 1.1)	-10.2, 11.1			4	-2.44 (7.108)	-3.4 (-8.4, 3.5)	-8.7, 5.6						
Day 4 / 0-hr																
Absolute value	11	4.68 (0.328)	4.7 (4.4, 4.8)	4.2, 5.4			4	4.33 (0.320)	4.2 (4.2, 4.5)	4.1, 4.8						
Change from baseline	11	-0.36 (0.414)	-0.4 (-0.6, 0.0)	-1.0, 0.5			4	-0.45 (0.365)	-0.6 (-0.7, -0.2)	-0.7, 0.1						
Percent change from baseline	11	-6.93 (8.062)	-7.7 (-12.1, 1.1)	-19.7, 9.1			4	-9.28 (7.542)	-11.8 (-14.6, -4.0)	-14.9, 1.4						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline eGFR																
15-29+																
Baseline																
Absolute value	1	4.95 (NC)	5.0 (5.0, 5.0)	5.0, 5.0			1	5.50 (NC)	5.5 (5.5, 5.5)	5.5, 5.5						
Day 1 / 30-min Post 1st																
Absolute value	1	5.20 (NC)	5.2 (5.2, 5.2)	5.2, 5.2			1	5.50 (NC)	5.5 (5.5, 5.5)	5.5, 5.5						
Change from baseline	1	0.25 (NC)	0.2 (0.2, 0.2)	0.2, 0.2			1	0.00 (NC)	0.0 (0.0, 0.0)	0.0, 0.0						
Percent change from baseline	1	5.05 (NC)	5.1 (5.1, 5.1)	5.1, 5.1			1	0.00 (NC)	0.0 (0.0, 0.0)	0.0, 0.0						
Day 1 / 1-hr Post 1st																
Absolute value	1	5.80 (NC)	5.8 (5.8, 5.8)	5.8, 5.8			1	5.20 (NC)	5.2 (5.2, 5.2)	5.2, 5.2						
Change from baseline	1	0.85 (NC)	0.8 (0.8, 0.8)	0.8, 0.8			1	-0.30 (NC)	-0.3 (-0.3, -0.3)	-0.3, -0.3						
Percent change from baseline	1	17.17 (NC)	17.2 (17.2, 17.2)	17.2, 17.2			1	-5.45 (NC)	-5.5 (-5.5, -5.5)	-5.5, -5.5						
Day 1 / 2-hr Post 1st																
Absolute value	1	5.20 (NC)	5.2 (5.2, 5.2)	5.2, 5.2			1	5.40 (NC)	5.4 (5.4, 5.4)	5.4, 5.4						
Change from baseline	1	0.25 (NC)	0.2 (0.2, 0.2)	0.2, 0.2			1	-0.10 (NC)	-0.1 (-0.1, -0.1)	-0.1, -0.1						
Percent change from baseline	1	5.05 (NC)	5.1 (5.1, 5.1)	5.1, 5.1			1	-1.82 (NC)	-1.8 (-1.8, -1.8)	-1.8, -1.8						
Day 1 / 4-hr Post 1st																
Absolute value	1	4.40 (NC)	4.4 (4.4, 4.4)	4.4, 4.4			1	5.00 (NC)	5.0 (5.0, 5.0)	5.0, 5.0						
Change from baseline	1	-0.55 (NC)	-0.6 (-0.6, -0.6)	-0.6, -0.6			1	-0.50 (NC)	-0.5 (-0.5, -0.5)	-0.5, -0.5						
Percent change from baseline	1	-11.11 (NC)	-11.1 (-11.1, -11.1)	-11.1, -11.1			1	-9.09 (NC)	-9.1 (-9.1, -9.1)	-9.1, -9.1						
Day 1 / 4-hr Post 2nd																
Absolute value	1	4.80 (NC)	4.8 (4.8, 4.8)	4.8, 4.8			1	4.60 (NC)	4.6 (4.6, 4.6)	4.6, 4.6						
Change from baseline	1	-0.15 (NC)	-0.2 (-0.2, -0.2)	-0.2, -0.2			1	-0.90 (NC)	-0.9 (-0.9, -0.9)	-0.9, -0.9						
Percent change from baseline	1	-3.03 (NC)	-3.0 (-3.0, -3.0)	-3.0, -3.0			1	-16.36 (NC)	-16.4 (-16.4, -16.4)	-16.4, -16.4						
Day 1 / 4-hr Post 3rd																
Absolute value	1	4.10 (NC)	4.1 (4.1, 4.1)	4.1, 4.1			1	4.00 (NC)	4.0 (4.0, 4.0)	4.0, 4.0						
Change from baseline	1	-0.85 (NC)	-0.9 (-0.9, -0.9)	-0.9, -0.9			1	-1.50 (NC)	-1.5 (-1.5, -1.5)	-1.5, -1.5						
Percent change from baseline	1	-17.17 (NC)	-17.2 (-17.2, -17.2)	-17.2, -17.2			1	-27.27 (NC)	-27.3 (-27.3, -27.3)	-27.3, -27.3						
Day 2 / 0-hr																
Absolute value	1	4.80 (NC)	4.8 (4.8, 4.8)	4.8, 4.8			1	4.70 (NC)	4.7 (4.7, 4.7)	4.7, 4.7						
Change from baseline	1	-0.15 (NC)	-0.2 (-0.2, -0.2)	-0.2, -0.2			1	-0.80 (NC)	-0.8 (-0.8, -0.8)	-0.8, -0.8						
Percent change from baseline	1	-3.03 (NC)	-3.0 (-3.0, -3.0)	-3.0, -3.0			1	-14.55 (NC)	-14.5 (-14.5, -14.5)	-14.5, -14.5						
Day 2 / 4-hr Post 1st																
Absolute value	1	4.90 (NC)	4.9 (4.9, 4.9)	4.9, 4.9			1	4.60 (NC)	4.6 (4.6, 4.6)	4.6, 4.6						
Change from baseline	1	-0.05 (NC)	-0.1 (-0.1, -0.1)	-0.1, -0.1			1	-0.90 (NC)	-0.9 (-0.9, -0.9)	-0.9, -0.9						
Percent change from baseline	1	-1.01 (NC)	-1.0 (-1.0, -1.0)	-1.0, -1.0			1	-16.36 (NC)	-16.4 (-16.4, -16.4)	-16.4, -16.4						
Day 2 / 4-hr Post 2nd																
Absolute value	1	5.00 (NC)	5.0 (5.0, 5.0)	5.0, 5.0			1	4.70 (NC)	4.7 (4.7, 4.7)	4.7, 4.7						
Change from baseline	1	0.05 (NC)	0.0 (0.0, 0.0)	0.0, 0.0			1	-0.80 (NC)	-0.8 (-0.8, -0.8)	-0.8, -0.8						
Percent change from baseline	1	1.01 (NC)	1.0 (1.0, 1.0)	1.0, 1.0			1	-14.55 (NC)	-14.5 (-14.5, -14.5)	-14.5, -14.5						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline eGFR *(contd.)*																
15-29+ *(contd.)*																
Day 2 / 4-hr Post 3rd																
Absolute value	1	4.70 (NC)	4.7 (4.7, 4.7)	4.7, 4.7			1	3.70 (NC)	3.7 (3.7, 3.7)	3.7, 3.7						
Change from baseline	1	-0.25 (NC)	-0.3 (-0.3, -0.3)	-0.3, -0.3			1	-1.80 (NC)	-1.8 (-1.8, -1.8)	-1.8, -1.8						
Percent change from baseline	1	-5.05 (NC)	-5.1 (-5.1, -5.1)	-5.1, -5.1			1	-32.73 (NC)	-32.7 (-32.7, -32.7)	-32.7, -32.7						
Day 2 / 20-hr Post 1st																
Absolute value	1	4.70 (NC)	4.7 (4.7, 4.7)	4.7, 4.7			1	3.70 (NC)	3.7 (3.7, 3.7)	3.7, 3.7						
Change from baseline	1	-0.25 (NC)	-0.3 (-0.3, -0.3)	-0.3, -0.3			1	-1.80 (NC)	-1.8 (-1.8, -1.8)	-1.8, -1.8						
Percent change from baseline	1	-5.05 (NC)	-5.1 (-5.1, -5.1)	-5.1, -5.1			1	-32.73 (NC)	-32.7 (-32.7, -32.7)	-32.7, -32.7						
Day 3 / 0-hr																
Absolute value	1	5.00 (NC)	5.0 (5.0, 5.0)	5.0, 5.0			1	4.30 (NC)	4.3 (4.3, 4.3)	4.3, 4.3						
Change from baseline	1	0.05 (NC)	0.0 (0.0, 0.0)	0.0, 0.0			1	-1.20 (NC)	-1.2 (-1.2, -1.2)	-1.2, -1.2						
Percent change from baseline	1	1.01 (NC)	1.0 (1.0, 1.0)	1.0, 1.0			1	-21.82 (NC)	-21.8 (-21.8, -21.8)	-21.8, -21.8						
Day 4 / 0-hr																
Absolute value	1	4.40 (NC)	4.4 (4.4, 4.4)	4.4, 4.4			1	4.80 (NC)	4.8 (4.8, 4.8)	4.8, 4.8						
Change from baseline	1	-0.55 (NC)	-0.6 (-0.6, -0.6)	-0.6, -0.6			1	-0.70 (NC)	-0.7 (-0.7, -0.7)	-0.7, -0.7						
Percent change from baseline	1	-11.11 (NC)	-11.1 (-11.1, -11.1)	-11.1, -11.1			1	-12.73 (NC)	-12.7 (-12.7, -12.7)	-12.7, -12.7						
30-59+																
Baseline																
Absolute value	28	5.16 (0.360)	5.2 (4.9, 5.3)	4.6, 6.1			22	5.03 (0.362)	4.9 (4.8, 5.2)	4.6, 6.0						
Day 1 / 30-min Post 1st																
Absolute value	27	5.18 (0.424)	5.3 (4.9, 5.5)	4.3, 6.0			22	5.01 (0.465)	4.9 (4.7, 5.3)	4.5, 6.2						
Change from baseline	27	0.03 (0.320)	0.0 (-0.1, 0.2)	-0.6, 0.6	0.05 (0.058)	(-0.07, 0.16)	22	-0.02 (0.253)	-0.1 (-0.2, 0.2)	-0.5, 0.5	-0.04 (0.064)	(-0.16, 0.09)	-0.08 (-0.26, 0.09)	0.3474	-0.15 (-0.71, 0.42)	
Percent change from baseline	27	0.61 (6.203)	0.0 (-2.5, 3.9)	-11.3, 11.9			22	-0.37 (4.997)	-1.4 (-4.5, 3.8)	-8.7, 11.2						
Day 1 / 1-hr Post 1st																
Absolute value	28	5.24 (0.532)	5.3 (4.9, 5.5)	4.4, 7.1			22	4.93 (0.455)	4.8 (4.6, 5.1)	4.4, 6.3						
Change from baseline	28	0.08 (0.343)	0.1 (-0.1, 0.3)	-0.5, 1.1	0.10 (0.077)	(-0.06, 0.25)	22	-0.10 (0.480)	-0.1 (-0.3, 0.1)	-0.9, 1.5	-0.12 (0.087)	(-0.29, 0.06)	-0.22 (-0.45, 0.02)	0.0687	-0.45 (-1.01, 0.12)	
Percent change from baseline	28	1.58 (6.284)	2.1 (-2.5, 5.8)	-10.2, 17.4			22	-1.70 (9.559)	-2.7 (-4.7, 1.4)	-14.8, 32.2						
Day 1 / 2-hr Post 1st																
Absolute value	28	5.13 (0.545)	5.0 (4.8, 5.4)	4.5, 6.7			21	4.91 (0.436)	4.8 (4.5, 5.3)	4.2, 5.7						
Change from baseline	28	-0.03 (0.349)	-0.1 (-0.2, 0.2)	-1.0, 0.7	-0.01 (0.069)	(-0.15, 0.13)	21	-0.13 (0.359)	-0.1 (-0.3, -0.1)	-0.7, 0.7	-0.14 (0.079)	(-0.30, 0.02)	-0.13 (-0.34, 0.08)	0.2250	-0.28 (-0.85, 0.28)	
Percent change from baseline	28	-0.60 (6.291)	-1.3 (-4.2, 3.7)	-16.5, 10.9			21	-2.40 (7.206)	-2.8 (-6.6, -1.7)	-12.6, 14.3						
Day 1 / 4-hr Post 1st																
Absolute value	28	4.99 (0.573)	4.9 (4.8, 5.3)	3.7, 6.2			22	4.75 (0.451)	4.7 (4.5, 5.0)	4.0, 5.6						
Change from baseline	28	-0.17 (0.549)	-0.1 (-0.4, 0.1)	-1.8, 1.1	-0.15 (0.089)	(-0.33, 0.03)	22	-0.28 (0.391)	-0.3 (-0.6, -0.0)	-0.8, 0.7	-0.29 (0.101)	(-0.50, -0.09)	-0.14 (-0.41, 0.13)	0.2929	-0.23 (-0.79, 0.33)	
Percent change from baseline	28	-3.05 (10.541)	-2.6 (-7.9, 2.4)	-32.7, 21.2			22	-5.36 (7.829)	-5.1 (-12.1, -0.4)	-17.0, 14.3						
Day 1 / 4-hr Post 2nd																
Absolute value	26	4.92 (0.480)	5.0 (4.5, 5.3)	3.9, 5.8			22	4.69 (0.439)	4.6 (4.4, 5.0)	4.1, 5.6						
Change from baseline	26	-0.25 (0.479)	-0.3 (-0.5, 0.0)	-1.3, 0.7	-0.23 (0.080)	(-0.39, -0.07)	22	-0.34 (0.377)	-0.4 (-0.5, -0.1)	-1.1, 0.3	-0.36 (0.088)	(-0.53, -0.18)	-0.13 (-0.37, 0.11)	0.2884	-0.21 (-0.77, 0.36)	

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline eGFR *(contd.)*																
30-59+ *(contd.)*																
Day 1 / 4-hr Post 2nd *(contd.)*																
Percent change from baseline	26	-4.63 (9.202)	-5.1 (-10.2, 1.0)	-25.2, 13.2			22	-6.63 (7.451)	-6.5 (-10.7, -2.0)	-21.5, 6.2						
Day 1 / 4-hr Post 3rd																
Absolute value	28	4.85 (0.560)	4.9 (4.5, 5.1)	4.0, 6.3			22	4.53 (0.399)	4.6 (4.2, 4.9)	3.9, 5.2						
Change from baseline	28	-0.31 (0.508)	-0.3 (-0.5, 0.0)	-1.5, 0.6	-0.30 (0.087)	(-0.47, -0.12)	22	-0.50 (0.440)	-0.4 (-0.8, -0.2)	-1.5, 0.3	-0.52 (0.098)	(-0.71, -0.32)	-0.22 (-0.48, 0.04)	0.1003	-0.39 (-0.95, 0.18)	
Percent change from baseline	28	-5.95 (9.479)	-6.0 (-10.5, 0.3)	-27.3, 12.0			22	-9.65 (8.449)	-7.8 (-16.3, -4.1)	-27.1, 6.1						
Day 2 / 0-hr																
Absolute value	28	4.99 (0.531)	4.9 (4.6, 5.3)	4.0, 6.7			22	4.73 (0.484)	4.8 (4.4, 5.0)	3.9, 5.7						
Change from baseline	28	-0.17 (0.441)	-0.2 (-0.4, 0.1)	-1.3, 0.9	-0.15 (0.085)	(-0.33, 0.02)	22	-0.30 (0.493)	-0.2 (-0.8, 0.0)	-1.1, 0.6	-0.32 (0.096)	(-0.51, -0.12)	-0.16 (-0.42, 0.10)	0.2138	-0.28 (-0.84, 0.28)	
Percent change from baseline	28	-3.24 (8.065)	-3.2 (-6.9, 1.8)	-21.6, 15.5			22	-5.71 (9.637)	-3.7 (-14.6, 0.0)	-21.2, 12.2						
Day 2 / 4-hr Post 1st																
Absolute value	27	5.04 (0.454)	5.0 (4.8, 5.3)	3.8, 5.9			22	4.53 (0.430)	4.5 (4.2, 4.7)	3.9, 5.5						
Change from baseline	27	-0.11 (0.413)	-0.1 (-0.4, 0.1)	-0.8, 0.8	-0.10 (0.081)	(-0.26, 0.06)	22	-0.50 (0.502)	-0.5 (-0.9, -0.2)	-1.4, 0.8	-0.52 (0.090)	(-0.70, -0.34)	-0.42 (-0.66, -0.17)	0.0012	-0.85 (-1.43, -0.26)	
Percent change from baseline	27	-2.04 (8.047)	-2.3 (-7.5, 3.2)	-16.5, 15.7			22	-9.60 (9.563)	-10.5 (-15.5, -3.5)	-25.0, 16.2						
Day 2 / 4-hr Post 2nd																
Absolute value	26	5.05 (0.424)	5.1 (4.8, 5.3)	4.2, 5.8			22	4.41 (0.476)	4.3 (4.1, 4.7)	3.6, 5.3						
Change from baseline	26	-0.11 (0.445)	-0.1 (-0.4, 0.2)	-1.1, 0.6	-0.10 (0.080)	(-0.26, 0.06)	22	-0.62 (0.468)	-0.7 (-1.0, -0.4)	-1.3, 0.5	-0.64 (0.089)	(-0.82, -0.46)	-0.54 (-0.78, -0.29)	<.0001	-1.11 (-1.72, -0.50)	
Percent change from baseline	26	-1.90 (8.407)	-1.7 (-7.4, 3.9)	-19.5, 11.1			22	-12.08 (9.291)	-12.9 (-20.1, -8.7)	-25.0, 9.9						
Day 2 / 4-hr Post 3rd																
Absolute value	27	4.89 (0.500)	4.8 (4.5, 5.3)	4.0, 6.1			22	4.13 (0.382)	4.2 (4.0, 4.4)	3.2, 4.8						
Change from baseline	27	-0.26 (0.428)	-0.3 (-0.5, 0.0)	-1.1, 0.8	-0.26 (0.083)	(-0.43, -0.09)	22	-0.90 (0.500)	-0.8 (-1.3, -0.5)	-1.7, -0.1	-0.92 (0.092)	(-1.11, -0.74)	-0.66 (-0.91, -0.41)	<.0001	-1.38 (-2.01, -0.76)	
Percent change from baseline	27	-5.05 (8.120)	-6.3 (-10.1, 1.0)	-21.4, 15.5			22	-17.61 (9.247)	-15.9 (-25.3, -9.8)	-33.8, -2.0						
Day 2 / 20-hr Post 1st																
Absolute value	27	4.81 (0.452)	4.8 (4.4, 5.0)	3.9, 5.6			22	4.22 (0.379)	4.3 (4.0, 4.5)	3.5, 4.8						
Change from baseline	27	-0.35 (0.451)	-0.3 (-0.6, -0.1)	-1.3, 0.6	-0.33 (0.080)	(-0.50, -0.17)	22	-0.81 (0.481)	-0.8 (-1.3, -0.5)	-1.6, -0.0	-0.83 (0.090)	(-1.01, -0.65)	-0.50 (-0.74, -0.25)	0.0002	-0.99 (-1.58, -0.39)	
Percent change from baseline	27	-6.66 (8.508)	-5.9 (-12.5, -1.1)	-25.2, 13.1			22	-15.83 (8.917)	-15.6 (-23.2, -9.8)	-30.1, -0.7						
Day 3 / 0-hr																
Absolute value	28	4.96 (0.555)	5.0 (4.5, 5.2)	4.1, 6.3			22	4.35 (0.458)	4.3 (4.1, 4.7)	3.3, 5.1						
Change from baseline	28	-0.20 (0.451)	-0.3 (-0.5, 0.1)	-1.0, 0.7	-0.19 (0.087)	(-0.36, -0.01)	22	-0.68 (0.507)	-0.7 (-1.1, -0.4)	-1.6, 0.3	-0.69 (0.098)	(-0.89, -0.50)	-0.51 (-0.77, -0.24)	0.0003	-1.00 (-1.59, -0.40)	
Percent change from baseline	28	-3.89 (8.542)	-5.2 (-10.0, 1.2)	-19.5, 13.9			22	-13.18 (9.741)	-13.9 (-21.6, -7.3)	-31.7, 5.6						
Day 4 / 0-hr																
Absolute value	28	4.90 (0.477)	4.8 (4.6, 5.3)	4.0, 6.0			22	4.40 (0.408)	4.4 (4.1, 4.7)	3.6, 5.5						
Change from baseline	28	-0.26 (0.487)	-0.3 (-0.6, 0.1)	-1.0, 0.8	-0.24 (0.084)	(-0.41, -0.08)	22	-0.63 (0.460)	-0.6 (-1.1, -0.4)	-1.5, 0.1	-0.65 (0.094)	(-0.84, -0.46)	-0.41 (-0.66, -0.15)	0.0025	-0.78 (-1.36, -0.20)	
Percent change from baseline	28	-4.79 (9.405)	-6.0 (-12.1, 1.4)	-19.7, 17.0			22	-12.28 (8.542)	-11.9 (-18.1, -7.7)	-27.1, 1.8						
>=60																
Baseline																
Absolute value	1	4.72 (NC)	4.7 (4.7, 4.7)	4.7, 4.7			1	5.12 (NC)	5.1 (5.1, 5.1)	5.1, 5.1						

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	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline eGFR *(contd.)*																
>=60 *(contd.)*																
Day 1 / 30-min Post 1st																
Absolute value	1	4.70 (NC)	4.7 (4.7, 4.7)	4.7, 4.7			1	5.00 (NC)	5.0 (5.0, 5.0)	5.0, 5.0						
Change from baseline	1	-0.02 (NC)	-0.0 (-0.0, -0.0)	-0.0, -0.0			1	-0.12 (NC)	-0.1 (-0.1, -0.1)	-0.1, -0.1						
Percent change from baseline	1	-0.35 (NC)	-0.4 (-0.4, -0.4)	-0.4, -0.4			1	-2.28 (NC)	-2.3 (-2.3, -2.3)	-2.3, -2.3						
Day 1 / 1-hr Post 1st																
Absolute value	1	5.10 (NC)	5.1 (5.1, 5.1)	5.1, 5.1			1	4.90 (NC)	4.9 (4.9, 4.9)	4.9, 4.9						
Change from baseline	1	0.38 (NC)	0.4 (0.4, 0.4)	0.4, 0.4			1	-0.22 (NC)	-0.2 (-0.2, -0.2)	-0.2, -0.2						
Percent change from baseline	1	8.13 (NC)	8.1 (8.1, 8.1)	8.1, 8.1			1	-4.23 (NC)	-4.2 (-4.2, -4.2)	-4.2, -4.2						
Day 1 / 2-hr Post 1st																
Absolute value	1	4.70 (NC)	4.7 (4.7, 4.7)	4.7, 4.7			1	4.80 (NC)	4.8 (4.8, 4.8)	4.8, 4.8						
Change from baseline	1	-0.02 (NC)	-0.0 (-0.0, -0.0)	-0.0, -0.0			1	-0.32 (NC)	-0.3 (-0.3, -0.3)	-0.3, -0.3						
Percent change from baseline	1	-0.35 (NC)	-0.4 (-0.4, -0.4)	-0.4, -0.4			1	-6.19 (NC)	-6.2 (-6.2, -6.2)	-6.2, -6.2						
Day 1 / 4-hr Post 1st																
Absolute value	1	5.00 (NC)	5.0 (5.0, 5.0)	5.0, 5.0			1	5.60 (NC)	5.6 (5.6, 5.6)	5.6, 5.6						
Change from baseline	1	0.28 (NC)	0.3 (0.3, 0.3)	0.3, 0.3			1	0.48 (NC)	0.5 (0.5, 0.5)	0.5, 0.5						
Percent change from baseline	1	6.01 (NC)	6.0 (6.0, 6.0)	6.0, 6.0			1	9.45 (NC)	9.4 (9.4, 9.4)	9.4, 9.4						
Day 1 / 4-hr Post 2nd																
Absolute value	1	4.70 (NC)	4.7 (4.7, 4.7)	4.7, 4.7			1	4.60 (NC)	4.6 (4.6, 4.6)	4.6, 4.6						
Change from baseline	1	-0.02 (NC)	-0.0 (-0.0, -0.0)	-0.0, -0.0			1	-0.52 (NC)	-0.5 (-0.5, -0.5)	-0.5, -0.5						
Percent change from baseline	1	-0.35 (NC)	-0.4 (-0.4, -0.4)	-0.4, -0.4			1	-10.10 (NC)	-10.1 (-10.1, -10.1)	-10.1, -10.1						
Day 1 / 4-hr Post 3rd																
Absolute value	1	4.70 (NC)	4.7 (4.7, 4.7)	4.7, 4.7			1	4.40 (NC)	4.4 (4.4, 4.4)	4.4, 4.4						
Change from baseline	1	-0.02 (NC)	-0.0 (-0.0, -0.0)	-0.0, -0.0			1	-0.72 (NC)	-0.7 (-0.7, -0.7)	-0.7, -0.7						
Percent change from baseline	1	-0.35 (NC)	-0.4 (-0.4, -0.4)	-0.4, -0.4			1	-14.01 (NC)	-14.0 (-14.0, -14.0)	-14.0, -14.0						
Day 2 / 0-hr																
Absolute value	1	4.50 (NC)	4.5 (4.5, 4.5)	4.5, 4.5			1	4.80 (NC)	4.8 (4.8, 4.8)	4.8, 4.8						
Change from baseline	1	-0.22 (NC)	-0.2 (-0.2, -0.2)	-0.2, -0.2			1	-0.32 (NC)	-0.3 (-0.3, -0.3)	-0.3, -0.3						
Percent change from baseline	1	-4.59 (NC)	-4.6 (-4.6, -4.6)	-4.6, -4.6			1	-6.19 (NC)	-6.2 (-6.2, -6.2)	-6.2, -6.2						
Day 2 / 4-hr Post 1st																
Absolute value	1	4.80 (NC)	4.8 (4.8, 4.8)	4.8, 4.8			1	4.50 (NC)	4.5 (4.5, 4.5)	4.5, 4.5						
Change from baseline	1	0.08 (NC)	0.1 (0.1, 0.1)	0.1, 0.1			1	-0.62 (NC)	-0.6 (-0.6, -0.6)	-0.6, -0.6						
Percent change from baseline	1	1.77 (NC)	1.8 (1.8, 1.8)	1.8, 1.8			1	-12.05 (NC)	-12.1 (-12.1, -12.1)	-12.1, -12.1						
Day 2 / 4-hr Post 2nd																
Absolute value	1	4.40 (NC)	4.4 (4.4, 4.4)	4.4, 4.4			1	4.60 (NC)	4.6 (4.6, 4.6)	4.6, 4.6						
Change from baseline	1	-0.32 (NC)	-0.3 (-0.3, -0.3)	-0.3, -0.3			1	-0.52 (NC)	-0.5 (-0.5, -0.5)	-0.5, -0.5						
Percent change from baseline	1	-6.71 (NC)	-6.7 (-6.7, -6.7)	-6.7, -6.7			1	-10.10 (NC)	-10.1 (-10.1, -10.1)	-10.1, -10.1						
Day 2 / 4-hr Post 3rd																
Absolute value	1	4.60 (NC)	4.6 (4.6, 4.6)	4.6, 4.6			1	4.60 (NC)	4.6 (4.6, 4.6)	4.6, 4.6						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline eGFR *(contd.)*																
>=60 *(contd.)*																
Day 2 / 4-hr Post 3rd *(contd.)*																
Change from baseline	1	-0.12 (NC)	-0.1 (-0.1, -0.1)	-0.1, -0.1			1	-0.52 (NC)	-0.5 (-0.5, -0.5)	-0.5, -0.5						
Percent change from baseline	1	-2.47 (NC)	-2.5 (-2.5, -2.5)	-2.5, -2.5			1	-10.10 (NC)	-10.1 (-10.1, -10.1)	-10.1, -10.1						
Day 2 / 20-hr Post 1st																
Absolute value	1	4.60 (NC)	4.6 (4.6, 4.6)	4.6, 4.6			1	4.10 (NC)	4.1 (4.1, 4.1)	4.1, 4.1						
Change from baseline	1	-0.12 (NC)	-0.1 (-0.1, -0.1)	-0.1, -0.1			1	-1.02 (NC)	-1.0 (-1.0, -1.0)	-1.0, -1.0						
Percent change from baseline	1	-2.47 (NC)	-2.5 (-2.5, -2.5)	-2.5, -2.5			1	-19.87 (NC)	-19.9 (-19.9, -19.9)	-19.9, -19.9						
Day 3 / 0-hr																
Absolute value	1	4.30 (NC)	4.3 (4.3, 4.3)	4.3, 4.3			1	4.80 (NC)	4.8 (4.8, 4.8)	4.8, 4.8						
Change from baseline	1	-0.42 (NC)	-0.4 (-0.4, -0.4)	-0.4, -0.4			1	-0.32 (NC)	-0.3 (-0.3, -0.3)	-0.3, -0.3						
Percent change from baseline	1	-8.83 (NC)	-8.8 (-8.8, -8.8)	-8.8, -8.8			1	-6.19 (NC)	-6.2 (-6.2, -6.2)	-6.2, -6.2						
Day 4 / 0-hr																
Absolute value	1	4.40 (NC)	4.4 (4.4, 4.4)	4.4, 4.4			1	4.30 (NC)	4.3 (4.3, 4.3)	4.3, 4.3						
Change from baseline	1	-0.32 (NC)	-0.3 (-0.3, -0.3)	-0.3, -0.3			1	-0.82 (NC)	-0.8 (-0.8, -0.8)	-0.8, -0.8						
Percent change from baseline	1	-6.71 (NC)	-6.7 (-6.7, -6.7)	-6.7, -6.7			1	-15.96 (NC)	-16.0 (-16.0, -16.0)	-16.0, -16.0						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Sex																0.4490
Male																
Baseline																
Absolute value	23	5.17 (0.385)	5.1 (4.9, 5.3)	4.6, 6.1			9	5.01 (0.405)	4.9 (4.8, 5.0)	4.6, 6.0						
Day 1 / 30-min Post 1st																
Absolute value	22	5.16 (0.468)	5.3 (4.7, 5.5)	4.3, 6.0			9	4.98 (0.402)	4.9 (4.7, 5.3)	4.5, 5.7						
Change from baseline	22	0.00 (0.339)	-0.0 (-0.2, 0.2)	-0.6, 0.6	0.03 (0.070)	(-0.11, 0.18)	9	-0.03 (0.273)	-0.1 (-0.1, 0.1)	-0.4, 0.5	-0.07 (0.111)	(-0.30, 0.16)	-0.10 (-0.37, 0.17)	0.4353	-0.09 (-0.87, 0.68)	
Percent change from baseline	22	0.10 (6.524)	-0.6 (-3.3, 3.9)	-11.3, 11.9			9	-0.44 (5.509)	-2.0 (-2.9, 1.7)	-7.7, 11.2						
Day 1 / 1-hr Post 1st																
Absolute value	23	5.35 (0.532)	5.4 (5.1, 5.6)	4.4, 7.1			9	4.97 (0.577)	4.8 (4.6, 4.8)	4.5, 6.3						
Change from baseline	23	0.19 (0.322)	0.1 (-0.0, 0.3)	-0.5, 1.1	0.20 (0.091)	(0.02, 0.39)	9	-0.04 (0.634)	-0.2 (-0.2, -0.0)	-0.7, 1.5	-0.08 (0.146)	(-0.38, 0.22)	-0.28 (-0.64, 0.07)	0.1113	-0.52 (-1.31, 0.26)	
Percent change from baseline	23	3.56 (5.898)	2.3 (-0.3, 7.1)	-8.0, 17.4			9	-0.39 (12.951)	-3.7 (-4.6, -0.7)	-13.5, 32.2						
Day 1 / 2-hr Post 1st																
Absolute value	23	5.18 (0.577)	5.0 (4.7, 5.4)	4.5, 6.7			9	4.89 (0.499)	4.7 (4.5, 5.3)	4.2, 5.6						
Change from baseline	23	0.02 (0.351)	-0.0 (-0.2, 0.2)	-1.0, 0.7	0.03 (0.088)	(-0.15, 0.21)	9	-0.12 (0.503)	-0.3 (-0.5, 0.3)	-0.6, 0.7	-0.16 (0.142)	(-0.45, 0.13)	-0.19 (-0.53, 0.15)	0.2632	-0.33 (-1.11, 0.44)	
Percent change from baseline	23	0.21 (6.258)	-1.0 (-3.7, 4.4)	-16.5, 10.9			9	-2.07 (10.154)	-6.6 (-9.4, 7.0)	-11.5, 14.3						
Day 1 / 4-hr Post 1st																
Absolute value	23	5.04 (0.615)	5.1 (4.7, 5.3)	3.7, 6.2			9	4.87 (0.461)	4.9 (4.5, 5.0)	4.1, 5.6						
Change from baseline	23	-0.12 (0.601)	-0.1 (-0.4, 0.2)	-1.8, 1.1	-0.11 (0.113)	(-0.34, 0.12)	9	-0.14 (0.475)	-0.1 (-0.5, 0.2)	-0.7, 0.7	-0.18 (0.181)	(-0.55, 0.19)	-0.07 (-0.51, 0.36)	0.7310	-0.03 (-0.80, 0.74)	
Percent change from baseline	23	-2.17 (11.522)	-1.6 (-8.0, 3.9)	-32.7, 21.2			9	-2.51 (9.394)	-1.7 (-10.6, 3.5)	-13.5, 14.3						
Day 1 / 4-hr Post 2nd																
Absolute value	22	4.90 (0.462)	4.9 (4.6, 5.1)	3.9, 5.8			9	4.54 (0.472)	4.4 (4.2, 4.7)	4.1, 5.6						
Change from baseline	22	-0.27 (0.448)	-0.3 (-0.5, -0.0)	-1.3, 0.5	-0.25 (0.082)	(-0.41, -0.08)	9	-0.46 (0.252)	-0.5 (-0.5, -0.3)	-1.0, -0.1	-0.50 (0.128)	(-0.76, -0.24)	-0.26 (-0.57, 0.05)	0.1030	-0.49 (-1.27, 0.30)	
Percent change from baseline	22	-4.91 (8.604)	-5.1 (-9.7, -0.4)	-25.2, 10.5			9	-9.25 (4.971)	-10.2 (-11.3, -6.4)	-19.2, -1.7						
Day 1 / 4-hr Post 3rd																
Absolute value	23	4.85 (0.606)	4.8 (4.5, 5.1)	4.0, 6.3			9	4.61 (0.341)	4.6 (4.4, 4.7)	4.1, 5.2						
Change from baseline	23	-0.32 (0.546)	-0.3 (-0.6, 0.1)	-1.5, 0.6	-0.30 (0.101)	(-0.51, -0.10)	9	-0.39 (0.344)	-0.3 (-0.4, -0.2)	-1.1, 0.0	-0.44 (0.162)	(-0.77, -0.11)	-0.13 (-0.52, 0.26)	0.4885	-0.15 (-0.92, 0.62)	
Percent change from baseline	23	-6.06 (10.217)	-6.2 (-12.1, 2.2)	-27.3, 12.0			9	-7.65 (6.308)	-6.6 (-8.7, -4.1)	-21.2, 0.3						
Day 2 / 0-hr																
Absolute value	23	4.98 (0.579)	4.9 (4.6, 5.4)	4.0, 6.7			9	4.80 (0.412)	4.9 (4.5, 5.0)	4.1, 5.5						
Change from baseline	23	-0.19 (0.455)	-0.2 (-0.4, 0.1)	-1.3, 0.9	-0.17 (0.099)	(-0.37, 0.03)	9	-0.21 (0.575)	-0.2 (-0.4, 0.3)	-1.1, 0.6	-0.25 (0.159)	(-0.57, 0.08)	-0.08 (-0.46, 0.31)	0.6889	-0.03 (-0.81, 0.74)	
Percent change from baseline	23	-3.64 (8.255)	-4.6 (-7.4, 2.2)	-21.6, 15.5			9	-3.60 (11.001)	-3.7 (-7.7, 5.6)	-21.2, 12.2						
Day 2 / 4-hr Post 1st																
Absolute value	22	5.08 (0.470)	5.1 (4.8, 5.3)	3.8, 5.9			9	4.48 (0.479)	4.5 (4.1, 4.6)	3.9, 5.5						
Change from baseline	22	-0.08 (0.435)	-0.1 (-0.3, 0.2)	-0.8, 0.8	-0.06 (0.096)	(-0.26, 0.13)	9	-0.53 (0.661)	-0.5 (-1.0, -0.3)	-1.4, 0.8	-0.57 (0.152)	(-0.88, -0.26)	-0.51 (-0.87, -0.14)	0.0083	-0.89 (-1.69, -0.08)	
Percent change from baseline	22	-1.34 (8.444)	-1.8 (-6.4, 4.0)	-16.5, 15.7			9	-9.99 (12.596)	-10.2 (-20.5, -5.7)	-25.0, 16.2						
Day 2 / 4-hr Post 2nd																
Absolute value	22	5.01 (0.441)	5.1 (4.6, 5.3)	4.2, 5.8			9	4.57 (0.490)	4.4 (4.3, 5.1)	3.9, 5.2						
Change from baseline	22	-0.16 (0.456)	-0.2 (-0.4, 0.2)	-1.1, 0.5	-0.14 (0.090)	(-0.32, 0.04)	9	-0.44 (0.534)	-0.4 (-0.8, -0.3)	-1.1, 0.5	-0.48 (0.142)	(-0.77, -0.19)	-0.34 (-0.69, 0.00)	0.0527	-0.58 (-1.37, 0.21)	
Percent change from baseline	22	-2.82 (8.617)	-3.6 (-7.7, 3.9)	-19.5, 11.1			9	-8.46 (10.471)	-8.7 (-13.1, -7.2)	-22.5, 9.9						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
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	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Sex *(contd.)*																
Male *(contd.)*																
Day 2 / 4-hr Post 3rd																
Absolute value	22	4.87 (0.507)	4.7 (4.5, 5.2)	4.1, 6.1			9	4.32 (0.349)	4.3 (4.2, 4.5)	3.6, 4.8						
Change from baseline	22	-0.29 (0.445)	-0.3 (-0.5, -0.1)	-1.1, 0.8	-0.28 (0.089)	(-0.47, -0.10)	9	-0.68 (0.494)	-0.5 (-0.8, -0.4)	-1.6, -0.1	-0.72 (0.141)	(-1.01, -0.44)	-0.44 (-0.78, -0.10)	0.0134	-0.86 (-1.67, -0.06)	
Percent change from baseline	22	-5.45 (8.341)	-6.6 (-10.1, -1.1)	-21.4, 15.5			9	-13.25 (8.905)	-9.8 (-16.6, -8.7)	-30.8, -2.0						
Day 2 / 20-hr Post 1st																
Absolute value	22	4.79 (0.480)	4.8 (4.4, 5.0)	3.9, 5.6			9	4.36 (0.347)	4.3 (4.2, 4.7)	3.7, 4.8						
Change from baseline	22	-0.38 (0.465)	-0.4 (-0.6, -0.1)	-1.3, 0.6	-0.36 (0.089)	(-0.54, -0.18)	9	-0.65 (0.505)	-0.7 (-0.8, -0.2)	-1.5, -0.0	-0.69 (0.141)	(-0.98, -0.40)	-0.33 (-0.67, 0.01)	0.0562	-0.56 (-1.35, 0.23)	
Percent change from baseline	22	-7.22 (8.767)	-7.9 (-12.5, -2.3)	-25.2, 13.1			9	-12.56 (9.214)	-14.6 (-15.7, -5.0)	-28.8, -0.7						
Day 3 / 0-hr																
Absolute value	23	4.97 (0.617)	5.0 (4.4, 5.4)	4.1, 6.3			9	4.48 (0.331)	4.4 (4.3, 4.7)	4.0, 5.0						
Change from baseline	23	-0.20 (0.492)	-0.3 (-0.6, 0.2)	-1.0, 0.7	-0.18 (0.100)	(-0.39, 0.02)	9	-0.53 (0.480)	-0.6 (-0.7, -0.4)	-1.2, 0.3	-0.57 (0.160)	(-0.90, -0.24)	-0.38 (-0.77, 0.00)	0.0511	-0.67 (-1.46, 0.12)	
Percent change from baseline	23	-3.92 (9.336)	-5.5 (-10.7, 3.7)	-19.5, 13.9			9	-10.12 (9.050)	-11.9 (-14.6, -8.2)	-23.1, 5.6						
Day 4 / 0-hr																
Absolute value	23	4.92 (0.486)	4.9 (4.5, 5.3)	4.0, 6.0			9	4.43 (0.320)	4.4 (4.2, 4.8)	4.1, 4.9						
Change from baseline	23	-0.25 (0.486)	-0.3 (-0.6, 0.1)	-0.9, 0.8	-0.23 (0.087)	(-0.41, -0.05)	9	-0.57 (0.381)	-0.6 (-0.7, -0.4)	-1.1, 0.1	-0.61 (0.140)	(-0.90, -0.33)	-0.38 (-0.72, -0.04)	0.0278	-0.70 (-1.49, 0.09)	
Percent change from baseline	23	-4.59 (9.385)	-6.7 (-12.1, 1.7)	-17.5, 17.0			9	-11.16 (6.963)	-11.7 (-14.9, -7.7)	-21.2, 1.4						
Female																
Baseline																
Absolute value	7	5.04 (0.253)	5.1 (4.7, 5.2)	4.7, 5.3			15	5.08 (0.340)	5.0 (4.8, 5.4)	4.6, 5.9						
Day 1 / 30-min Post 1st																
Absolute value	7	5.17 (0.229)	5.2 (5.1, 5.3)	4.7, 5.4			15	5.07 (0.495)	5.0 (4.7, 5.4)	4.5, 6.2						
Change from baseline	7	0.13 (0.189)	0.1 (0.0, 0.3)	-0.1, 0.5	0.13 (0.082)	(-0.04, 0.31)	15	-0.02 (0.233)	0.0 (-0.2, 0.2)	-0.5, 0.3	-0.02 (0.056)	(-0.13, 0.10)	-0.15 (-0.36, 0.06)	0.1454	-0.66 (-1.58, 0.25)	
Percent change from baseline	7	2.68 (3.905)	1.3 (0.0, 5.3)	-1.9, 9.9			15	-0.43 (4.513)	0.0 (-4.5, 3.9)	-8.7, 6.1						
Day 1 / 1-hr Post 1st																
Absolute value	7	4.94 (0.378)	4.8 (4.7, 5.4)	4.5, 5.5			15	4.93 (0.353)	4.9 (4.7, 5.2)	4.4, 5.7						
Change from baseline	7	-0.10 (0.428)	-0.2 (-0.5, 0.3)	-0.5, 0.5	-0.09 (0.145)	(-0.40, 0.21)	15	-0.16 (0.338)	-0.2 (-0.3, 0.2)	-0.9, 0.4	-0.16 (0.099)	(-0.37, 0.05)	-0.06 (-0.43, 0.31)	0.7284	-0.16 (-1.06, 0.74)	
Percent change from baseline	7	-1.77 (8.352)	-3.2 (-9.6, 5.6)	-10.2, 9.3			15	-2.90 (6.328)	-3.0 (-5.5, 3.6)	-14.8, 7.2						
Day 1 / 2-hr Post 1st																
Absolute value	7	4.91 (0.291)	4.8 (4.8, 5.3)	4.5, 5.3			14	4.95 (0.396)	4.8 (4.7, 5.4)	4.5, 5.7						
Change from baseline	7	-0.13 (0.301)	-0.2 (-0.4, 0.2)	-0.5, 0.3	-0.12 (0.095)	(-0.32, 0.08)	14	-0.15 (0.211)	-0.1 (-0.2, -0.1)	-0.7, 0.3	-0.13 (0.065)	(-0.27, 0.00)	-0.01 (-0.25, 0.23)	0.9289	-0.08 (-0.99, 0.83)	
Percent change from baseline	7	-2.39 (5.799)	-3.2 (-8.3, 3.2)	-9.4, 5.3			14	-2.84 (4.158)	-2.8 (-3.1, -1.8)	-12.6, 5.9						
Day 1 / 4-hr Post 1st																
Absolute value	7	4.74 (0.264)	4.9 (4.6, 4.9)	4.2, 4.9			15	4.76 (0.481)	4.7 (4.4, 5.0)	4.0, 5.6						
Change from baseline	7	-0.30 (0.255)	-0.3 (-0.5, -0.1)	-0.6, 0.2	-0.29 (0.129)	(-0.56, -0.03)	15	-0.32 (0.362)	-0.4 (-0.6, -0.1)	-0.8, 0.5	-0.32 (0.088)	(-0.51, -0.14)	-0.03 (-0.36, 0.30)	0.8562	-0.07 (-0.97, 0.82)	
Percent change from baseline	7	-5.82 (5.084)	-6.5 (-9.7, -2.6)	-12.1, 3.5			15	-6.34 (7.205)	-6.3 (-13.1, -1.8)	-17.0, 9.4						
Day 1 / 4-hr Post 2nd																
Absolute value	6	4.97 (0.513)	5.0 (4.5, 5.3)	4.4, 5.7			15	4.77 (0.377)	4.7 (4.4, 5.1)	4.2, 5.5						
Change from baseline	6	-0.14 (0.546)	-0.1 (-0.5, 0.1)	-0.9, 0.7	-0.13 (0.184)	(-0.52, 0.25)	15	-0.32 (0.438)	-0.4 (-0.5, 0.2)	-1.1, 0.3	-0.32 (0.123)	(-0.57, -0.06)	-0.18 (-0.65, 0.28)	0.4159	-0.38 (-1.33, 0.58)	

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Sex *(contd.)*																
Female *(contd.)*																
Day 1 / 4-hr Post 2nd *(contd.)*																
Percent change from baseline	6	-2.61 (10.551)	-1.8 (-10.2, 1.9)	-17.0, 13.2			15	-5.93 (8.477)	-6.3 (-10.2, 3.4)	-21.5, 6.2						
Day 1 / 4-hr Post 3rd																
Absolute value	7	4.71 (0.376)	4.9 (4.4, 5.0)	4.2, 5.2			15	4.44 (0.426)	4.4 (4.0, 4.9)	3.9, 5.1						
Change from baseline	7	-0.33 (0.360)	-0.3 (-0.4, -0.2)	-1.0, 0.2	-0.32 (0.187)	(-0.72, 0.07)	15	-0.64 (0.518)	-0.8 (-1.0, -0.2)	-1.5, 0.3	-0.64 (0.128)	(-0.91, -0.37)	-0.32 (-0.80, 0.16)	0.1747	-0.66 (-1.58, 0.25)	
Percent change from baseline	7	-6.40 (6.894)	-5.4 (-7.5, -3.8)	-19.7, 3.3			15	-12.32 (9.883)	-14.0 (-19.3, -4.5)	-27.3, 6.1						
Day 2 / 0-hr																
Absolute value	7	4.93 (0.287)	5.0 (4.8, 5.2)	4.4, 5.2			15	4.69 (0.501)	4.7 (4.3, 4.9)	3.9, 5.7						
Change from baseline	7	-0.11 (0.331)	-0.0 (-0.1, 0.1)	-0.8, 0.1	-0.11 (0.154)	(-0.43, 0.21)	15	-0.39 (0.423)	-0.3 (-0.8, -0.0)	-1.1, 0.4	-0.39 (0.105)	(-0.61, -0.17)	-0.28 (-0.67, 0.11)	0.1480	-0.70 (-1.62, 0.22)	
Percent change from baseline	7	-2.07 (6.396)	-0.7 (-1.9, 1.4)	-15.9, 3.2			15	-7.60 (8.309)	-6.2 (-14.6, -0.4)	-19.6, 7.8						
Day 2 / 4-hr Post 1st																
Absolute value	7	4.86 (0.299)	4.9 (4.7, 5.1)	4.3, 5.2			15	4.57 (0.379)	4.5 (4.3, 4.8)	4.0, 5.5						
Change from baseline	7	-0.18 (0.271)	-0.1 (-0.4, 0.1)	-0.5, 0.1	-0.18 (0.137)	(-0.47, 0.11)	15	-0.52 (0.375)	-0.6 (-0.9, -0.0)	-1.2, 0.0	-0.52 (0.094)	(-0.71, -0.32)	-0.34 (-0.69, 0.01)	0.0592	-0.96 (-1.90, -0.02)	
Percent change from baseline	7	-3.56 (5.396)	-2.6 (-9.2, 1.3)	-10.2, 3.2			15	-9.98 (7.069)	-11.8 (-15.5, -1.0)	-22.3, 0.0						
Day 2 / 4-hr Post 2nd																
Absolute value	6	5.07 (0.403)	5.1 (4.8, 5.2)	4.5, 5.7			15	4.35 (0.439)	4.2 (4.1, 4.7)	3.6, 5.3						
Change from baseline	6	0.06 (0.291)	0.0 (-0.2, 0.1)	-0.2, 0.6	-0.03 (0.147)	(-0.35, 0.28)	15	-0.73 (0.367)	-0.7 (-1.0, -0.5)	-1.3, 0.2	-0.73 (0.098)	(-0.94, -0.52)	-0.70 (-1.07, -0.32)	0.0011	-2.26 (-3.43, -1.09)	
Percent change from baseline	6	1.15 (5.739)	0.7 (-3.8, 3.2)	-4.9, 11.0			15	-14.28 (7.344)	-14.5 (-20.1, -9.8)	-25.0, 4.0						
Day 2 / 4-hr Post 3rd																
Absolute value	7	4.87 (0.450)	4.9 (4.7, 5.3)	4.0, 5.3			15	4.01 (0.374)	4.1 (3.7, 4.3)	3.2, 4.6						
Change from baseline	7	-0.17 (0.305)	-0.0 (-0.4, 0.0)	-0.7, 0.1	-0.17 (0.175)	(-0.53, 0.20)	15	-1.07 (0.493)	-1.1 (-1.6, -0.7)	-1.8, -0.2	-1.07 (0.119)	(-1.32, -0.82)	-0.90 (-1.35, -0.46)	0.0005	-2.02 (-3.10, -0.94)	
Percent change from baseline	7	-3.44 (6.299)	-0.6 (-8.3, 1.1)	-15.5, 1.9			15	-20.73 (8.981)	-20.0 (-28.4, -14.6)	-33.8, -4.7						
Day 2 / 20-hr Post 1st																
Absolute value	7	4.83 (0.293)	5.0 (4.6, 5.0)	4.4, 5.2			15	4.09 (0.371)	4.1 (3.7, 4.3)	3.5, 4.8						
Change from baseline	7	-0.21 (0.331)	-0.1 (-0.2, -0.1)	-0.9, 0.2	-0.21 (0.172)	(-0.57, 0.15)	15	-0.99 (0.472)	-0.9 (-1.3, -0.7)	-1.8, -0.1	-0.99 (0.117)	(-1.24, -0.74)	-0.78 (-1.22, -0.34)	0.0017	-1.79 (-2.83, -0.75)	
Percent change from baseline	7	-4.07 (6.246)	-2.8 (-4.5, -1.1)	-17.0, 3.3			15	-19.18 (8.566)	-18.4 (-26.7, -14.6)	-32.7, -2.5						
Day 3 / 0-hr																
Absolute value	7	4.84 (0.215)	4.9 (4.7, 5.0)	4.5, 5.1			15	4.31 (0.505)	4.3 (3.9, 4.7)	3.3, 5.1						
Change from baseline	7	-0.20 (0.212)	-0.2 (-0.3, 0.0)	-0.5, 0.1	-0.19 (0.171)	(-0.55, 0.17)	15	-0.78 (0.508)	-0.7 (-1.3, -0.3)	-1.6, 0.0	-0.78 (0.117)	(-1.02, -0.53)	-0.58 (-1.02, -0.15)	0.0117	-1.31 (-2.29, -0.34)	
Percent change from baseline	7	-3.82 (4.101)	-4.9 (-5.8, 1.1)	-10.2, 1.3			15	-15.12 (9.712)	-14.6 (-21.8, -6.2)	-31.7, 0.0						
Day 4 / 0-hr																
Absolute value	7	4.70 (0.440)	4.7 (4.2, 4.8)	4.2, 5.5			15	4.40 (0.450)	4.4 (4.1, 4.7)	3.6, 5.5						
Change from baseline	7	-0.34 (0.457)	-0.4 (-0.6, 0.0)	-1.0, 0.4	-0.34 (0.185)	(-0.73, 0.05)	15	-0.68 (0.482)	-0.6 (-1.2, -0.4)	-1.5, 0.1	-0.68 (0.126)	(-0.95, -0.42)	-0.35 (-0.82, 0.12)	0.1401	-0.72 (-1.64, 0.20)	
Percent change from baseline	7	-6.63 (8.848)	-7.7 (-11.3, 1.1)	-19.7, 7.1			15	-13.22 (8.998)	-12.5 (-22.3, -8.2)	-27.1, 1.8						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Age																0.0625
<65 years																
Baseline																
Absolute value	9	5.03 (0.389)	5.0 (4.7, 5.3)	4.6, 5.8			7	5.05 (0.441)	5.0 (4.8, 5.1)	4.6, 6.0						
Day 1 / 30-min Post 1st																
Absolute value	9	5.19 (0.420)	5.3 (5.0, 5.5)	4.4, 5.7			7	4.90 (0.396)	4.9 (4.6, 5.0)	4.5, 5.7						
Change from baseline	9	0.16 (0.246)	0.1 (0.0, 0.3)	-0.2, 0.6			7	-0.15 (0.121)	-0.1 (-0.3, -0.1)	-0.3, 0.1						
Percent change from baseline	9	3.27 (5.053)	2.2 (0.3, 5.3)	-3.3, 11.9			7	-2.91 (2.325)	-2.9 (-4.7, -2.3)	-5.1, 1.7						
Day 1 / 1-hr Post 1st																
Absolute value	9	5.13 (0.510)	5.1 (4.8, 5.5)	4.4, 5.9			7	4.84 (0.310)	4.8 (4.6, 4.9)	4.6, 5.5						
Change from baseline	9	0.11 (0.216)	0.1 (-0.1, 0.3)	-0.2, 0.5			7	-0.21 (0.141)	-0.2 (-0.2, -0.1)	-0.5, -0.0						
Percent change from baseline	9	1.99 (4.390)	2.2 (-2.4, 5.6)	-3.3, 9.3			7	-3.95 (2.292)	-4.2 (-4.6, -2.4)	-8.1, -0.7						
Day 1 / 2-hr Post 1st																
Absolute value	9	5.04 (0.590)	4.8 (4.7, 5.2)	4.5, 6.4			7	4.71 (0.406)	4.7 (4.5, 4.8)	4.2, 5.5						
Change from baseline	9	0.02 (0.264)	-0.1 (-0.2, 0.1)	-0.2, 0.6			7	-0.34 (0.106)	-0.3 (-0.4, -0.3)	-0.5, -0.2						
Percent change from baseline	9	0.13 (4.842)	-1.6 (-3.2, 1.4)	-4.4, 10.3			7	-6.63 (1.944)	-6.6 (-8.1, -6.2)	-9.4, -3.0						
Day 1 / 4-hr Post 1st																
Absolute value	9	4.96 (0.633)	4.9 (4.6, 5.3)	4.0, 5.9			7	4.80 (0.619)	5.0 (4.1, 5.4)	4.0, 5.6						
Change from baseline	9	-0.07 (0.355)	-0.1 (-0.3, 0.1)	-0.6, 0.6			7	-0.25 (0.484)	-0.5 (-0.6, 0.2)	-0.8, 0.5						
Percent change from baseline	9	-1.67 (7.247)	-1.7 (-6.4, 2.3)	-12.1, 11.7			7	-4.94 (9.674)	-9.7 (-11.5, 3.8)	-17.0, 9.4						
Day 1 / 4-hr Post 2nd																
Absolute value	7	5.01 (0.649)	4.9 (4.5, 5.7)	4.2, 5.8			7	4.63 (0.482)	4.6 (4.3, 4.7)	4.1, 5.6						
Change from baseline	7	-0.03 (0.448)	-0.2 (-0.4, 0.5)	-0.5, 0.7			7	-0.42 (0.107)	-0.4 (-0.5, -0.3)	-0.5, -0.3						
Percent change from baseline	7	-0.69 (8.871)	-4.9 (-7.7, 9.8)	-9.7, 13.2			7	-8.44 (2.462)	-8.7 (-10.7, -6.4)	-11.5, -5.1						
Day 1 / 4-hr Post 3rd																
Absolute value	9	4.72 (0.466)	4.5 (4.4, 5.1)	4.0, 5.4			7	4.60 (0.300)	4.6 (4.4, 4.7)	4.3, 5.2						
Change from baseline	9	-0.31 (0.309)	-0.3 (-0.5, -0.2)	-0.8, 0.2			7	-0.45 (0.214)	-0.4 (-0.7, -0.3)	-0.8, -0.2						
Percent change from baseline	9	-6.08 (5.895)	-7.0 (-9.7, -3.8)	-13.8, 3.3			7	-8.73 (3.520)	-7.2 (-13.1, -6.6)	-14.0, -4.5						
Day 2 / 0-hr																
Absolute value	9	4.99 (0.746)	4.8 (4.6, 5.0)	4.0, 6.7			7	4.71 (0.358)	4.8 (4.5, 5.0)	4.0, 5.0						
Change from baseline	9	-0.04 (0.430)	-0.0 (-0.3, 0.1)	-0.6, 0.9			7	-0.34 (0.451)	-0.3 (-0.8, -0.1)	-1.0, 0.4						
Percent change from baseline	9	-1.13 (8.107)	-0.7 (-6.4, 2.2)	-12.1, 15.5			7	-6.27 (8.587)	-6.2 (-16.4, -2.6)	-17.0, 7.9						
Day 2 / 4-hr Post 1st																
Absolute value	8	4.91 (0.658)	5.0 (4.5, 5.5)	3.8, 5.7			7	4.41 (0.308)	4.5 (4.1, 4.6)	4.0, 4.9						
Change from baseline	8	-0.08 (0.391)	-0.0 (-0.4, 0.2)	-0.8, 0.4			7	-0.64 (0.445)	-0.5 (-1.0, -0.3)	-1.4, -0.0						
Percent change from baseline	8	-1.86 (8.201)	-0.2 (-7.4, 4.5)	-16.5, 7.9			7	-12.22 (7.617)	-11.5 (-20.5, -6.6)	-23.1, -1.0						
Day 2 / 4-hr Post 2nd																
Absolute value	9	4.97 (0.367)	5.1 (4.6, 5.1)	4.5, 5.6			7	4.44 (0.404)	4.4 (4.2, 4.6)	3.9, 5.2						
Change from baseline	9	-0.06 (0.197)	0.0 (-0.2, 0.1)	-0.4, 0.2			7	-0.61 (0.275)	-0.5 (-0.8, -0.4)	-1.1, -0.3						
Percent change from baseline	9	-1.13 (3.961)	0.3 (-3.8, 1.3)	-7.7, 3.7			7	-11.92 (5.144)	-10.1 (-13.1, -8.7)	-22.5, -7.2						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Age *(contd.)*																
<65 years *(contd.)*																
Day 2 / 4-hr Post 3rd																
Absolute value	8	4.78 (0.630)	4.6 (4.5, 5.0)	4.0, 6.1			7	4.27 (0.335)	4.2 (4.1, 4.6)	3.7, 4.7						
Change from baseline	8	-0.22 (0.512)	-0.3 (-0.6, -0.0)	-0.7, 0.8			7	-0.78 (0.366)	-0.7 (-1.3, -0.4)	-1.3, -0.4						
Percent change from baseline	8	-4.37 (9.896)	-6.2 (-11.3, -0.0)	-15.5, 15.5			7	-15.18 (6.392)	-14.9 (-21.4, -9.4)	-25.3, -8.7						
Day 2 / 20-hr Post 1st																
Absolute value	9	4.87 (0.450)	4.8 (4.6, 5.2)	4.3, 5.6			7	4.23 (0.309)	4.3 (4.1, 4.4)	3.7, 4.7						
Change from baseline	9	-0.16 (0.302)	-0.1 (-0.4, -0.0)	-0.6, 0.3			7	-0.82 (0.349)	-0.7 (-1.1, -0.7)	-1.3, -0.2						
Percent change from baseline	9	-3.16 (5.808)	-2.8 (-6.9, -0.3)	-11.7, 6.0			7	-16.02 (6.164)	-14.9 (-21.4, -13.1)	-23.2, -5.0						
Day 3 / 0-hr																
Absolute value	9	4.99 (0.706)	5.0 (4.5, 5.1)	4.1, 6.3			7	4.56 (0.294)	4.7 (4.3, 4.8)	4.1, 4.9						
Change from baseline	9	-0.04 (0.412)	0.0 (-0.3, 0.2)	-0.7, 0.5			7	-0.49 (0.380)	-0.4 (-0.7, -0.3)	-1.1, 0.1						
Percent change from baseline	9	-1.07 (8.051)	1.1 (-5.7, 3.7)	-13.7, 9.8			7	-9.43 (6.829)	-8.7 (-14.9, -5.1)	-18.1, 1.4						
Day 4 / 0-hr																
Absolute value	9	4.82 (0.421)	4.8 (4.6, 5.0)	4.2, 5.6			7	4.50 (0.327)	4.4 (4.2, 4.8)	4.1, 4.9						
Change from baseline	9	-0.21 (0.395)	-0.1 (-0.5, 0.0)	-0.9, 0.3			7	-0.55 (0.335)	-0.4 (-0.8, -0.2)	-1.1, -0.2						
Percent change from baseline	9	-3.89 (7.511)	-1.7 (-10.3, 1.1)	-17.0, 6.0			7	-10.66 (5.796)	-9.4 (-16.0, -4.6)	-18.1, -3.0						
>= 65 years																
Baseline																
Absolute value	21	5.18 (0.344)	5.2 (5.0, 5.3)	4.6, 6.1			17	5.05 (0.335)	4.9 (4.8, 5.2)	4.6, 5.9						
Day 1 / 30-min Post 1st																
Absolute value	20	5.16 (0.429)	5.2 (4.8, 5.4)	4.3, 6.0			17	5.09 (0.478)	5.0 (4.7, 5.4)	4.5, 6.2						
Change from baseline	20	-0.03 (0.325)	-0.0 (-0.2, 0.2)	-0.6, 0.6	0.01 (0.072)	(-0.14, 0.16)	17	0.03 (0.263)	0.0 (-0.1, 0.2)	-0.5, 0.5	0.01 (0.078)	(-0.15, 0.17)	0.00 (-0.22, 0.22)	0.9911	0.20 (-0.45, 0.84)	
Percent change from baseline	20	-0.42 (6.208)	-0.6 (-3.2, 3.6)	-11.3, 11.4			17	0.58 (5.215)	0.0 (-2.5, 3.9)	-8.7, 11.2						
Day 1 / 1-hr Post 1st																
Absolute value	21	5.31 (0.534)	5.3 (4.9, 5.4)	4.7, 7.1			17	4.98 (0.484)	4.9 (4.8, 5.2)	4.4, 6.3						
Change from baseline	21	0.13 (0.414)	0.1 (-0.1, 0.3)	-0.5, 1.1	0.14 (0.101)	(-0.06, 0.35)	17	-0.07 (0.541)	-0.1 (-0.3, 0.2)	-0.9, 1.5	-0.10 (0.112)	(-0.32, 0.13)	-0.24 (-0.55, 0.07)	0.1201	-0.42 (-1.06, 0.23)	
Percent change from baseline	21	2.45 (7.683)	2.5 (-1.5, 7.1)	-10.2, 17.4			17	-1.14 (10.803)	-2.0 (-5.5, 3.6)	-14.8, 32.2						
Day 1 / 2-hr Post 1st																
Absolute value	21	5.15 (0.517)	5.0 (4.8, 5.4)	4.6, 6.7			16	5.02 (0.417)	5.0 (4.7, 5.4)	4.5, 5.7						
Change from baseline	21	-0.03 (0.374)	-0.0 (-0.2, 0.2)	-1.0, 0.7	-0.01 (0.082)	(-0.18, 0.15)	16	-0.05 (0.377)	-0.1 (-0.2, 0.2)	-0.7, 0.7	-0.06 (0.093)	(-0.25, 0.13)	-0.05 (-0.30, 0.20)	0.6895	-0.04 (-0.69, 0.61)	
Percent change from baseline	21	-0.63 (6.739)	-0.4 (-4.2, 4.2)	-16.5, 10.9			16	-0.75 (7.580)	-2.2 (-3.0, 4.0)	-12.6, 14.3						
Day 1 / 4-hr Post 1st																
Absolute value	21	4.98 (0.548)	4.9 (4.8, 5.3)	3.7, 6.2			17	4.80 (0.411)	4.7 (4.5, 4.9)	4.2, 5.6						
Change from baseline	21	-0.20 (0.607)	-0.2 (-0.4, 0.2)	-1.8, 1.1	-0.18 (0.107)	(-0.40, 0.03)	17	-0.25 (0.389)	-0.2 (-0.6, -0.1)	-0.8, 0.7	-0.28 (0.118)	(-0.52, -0.04)	-0.09 (-0.42, 0.23)	0.5576	-0.10 (-0.74, 0.54)	
Percent change from baseline	21	-3.60 (11.627)	-4.2 (-8.0, 2.5)	-32.7, 21.2			17	-4.89 (7.720)	-3.9 (-12.1, -1.7)	-14.6, 14.3						
Day 1 / 4-hr Post 2nd																
Absolute value	21	4.88 (0.400)	4.9 (4.7, 5.1)	3.9, 5.7			17	4.71 (0.405)	4.6 (4.4, 5.0)	4.2, 5.5						
Change from baseline	21	-0.31 (0.457)	-0.3 (-0.5, -0.0)	-1.3, 0.5	-0.29 (0.089)	(-0.47, -0.11)	17	-0.35 (0.448)	-0.4 (-0.5, -0.1)	-1.1, 0.3	-0.37 (0.099)	(-0.57, -0.17)	-0.08 (-0.36, 0.19)	0.5350	-0.09 (-0.73, 0.55)	

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
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Table 1.1.2.1 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)						Lokelma 10g QD (N=24)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Age *(contd.)*																
>= 65 years *(contd.)*																
Day 1 / 4-hr Post 2nd *(contd.)*																
Percent change from baseline	21	-5.66 (8.758)	-5.1 (-10.2, -0.4)	-25.2, 10.5			17	-6.66 (8.709)	-6.3 (-11.3, -1.7)	-21.5, 6.2						
Day 1 / 4-hr Post 3rd																
Absolute value	21	4.86 (0.599)	4.8 (4.5, 5.1)	4.0, 6.3			17	4.46 (0.433)	4.5 (4.1, 4.9)	3.9, 5.1						
Change from baseline	21	-0.33 (0.574)	-0.3 (-0.5, -0.0)	-1.5, 0.6	-0.31 (0.115)	(-0.54, -0.07)	17	-0.59 (0.541)	-0.8 (-1.0, -0.2)	-1.5, 0.3	-0.61 (0.128)	(-0.87, -0.35)	-0.31 (-0.66, 0.04)	0.0849	-0.47 (-1.12, 0.18)	
Percent change from baseline	21	-6.17 (10.733)	-5.9 (-11.3, -0.4)	-27.3, 12.0			17	-11.33 (10.310)	-13.1 (-19.3, -3.9)	-27.3, 6.1						
Day 2 / 0-hr																
Absolute value	21	4.96 (0.414)	4.9 (4.6, 5.2)	4.4, 5.9			17	4.74 (0.510)	4.7 (4.4, 5.0)	3.9, 5.7						
Change from baseline	21	-0.23 (0.421)	-0.2 (-0.3, -0.0)	-1.3, 0.5	-0.21 (0.095)	(-0.40, -0.02)	17	-0.31 (0.507)	-0.2 (-0.8, 0.0)	-1.1, 0.6	-0.34 (0.105)	(-0.55, -0.12)	-0.13 (-0.42, 0.16)	0.3679	-0.19 (-0.83, 0.45)	
Percent change from baseline	21	-4.19 (7.659)	-3.9 (-6.4, -1.0)	-21.6, 9.1			17	-6.03 (9.944)	-3.8 (-14.5, 0.0)	-21.2, 12.2						
Day 2 / 4-hr Post 1st																
Absolute value	21	5.07 (0.336)	5.0 (4.9, 5.2)	4.6, 5.9			17	4.58 (0.446)	4.6 (4.4, 4.7)	3.9, 5.5						
Change from baseline	21	-0.11 (0.412)	-0.1 (-0.4, 0.1)	-0.8, 0.8	-0.09 (0.089)	(-0.27, 0.09)	17	-0.47 (0.509)	-0.5 (-0.9, -0.2)	-1.3, 0.8	-0.50 (0.099)	(-0.70, -0.29)	-0.40 (-0.67, -0.13)	0.0049	-0.79 (-1.45, -0.12)	
Percent change from baseline	21	-1.89 (7.834)	-2.3 (-7.3, 1.8)	-12.4, 15.7			17	-9.07 (9.910)	-10.2 (-15.5, -3.5)	-25.0, 16.2						
Day 2 / 4-hr Post 2nd																
Absolute value	19	5.05 (0.459)	5.1 (4.8, 5.3)	4.2, 5.8			17	4.43 (0.493)	4.3 (4.1, 4.7)	3.6, 5.3						
Change from baseline	19	-0.14 (0.509)	-0.2 (-0.5, 0.2)	-1.1, 0.6	-0.11 (0.103)	(-0.32, 0.10)	17	-0.63 (0.512)	-0.7 (-1.0, -0.5)	-1.3, 0.5	-0.65 (0.112)	(-0.88, -0.42)	-0.54 (-0.85, -0.22)	0.0013	-0.96 (-1.65, -0.27)	
Percent change from baseline	19	-2.37 (9.613)	-3.8 (-11.3, 4.2)	-19.5, 11.1			17	-12.17 (10.197)	-14.5 (-20.1, -9.7)	-25.0, 9.9						
Day 2 / 4-hr Post 3rd																
Absolute value	21	4.91 (0.432)	4.8 (4.6, 5.3)	4.1, 5.8			17	4.07 (0.403)	4.1 (3.8, 4.3)	3.2, 4.8						
Change from baseline	21	-0.27 (0.383)	-0.3 (-0.5, 0.0)	-1.1, 0.5	-0.26 (0.094)	(-0.45, -0.06)	17	-0.98 (0.569)	-0.8 (-1.6, -0.6)	-1.8, -0.1	-1.01 (0.105)	(-1.22, -0.80)	-0.75 (-1.04, -0.47)	<.0001	-1.49 (-2.22, -0.77)	
Percent change from baseline	21	-5.19 (7.181)	-5.9 (-9.7, 0.0)	-21.4, 9.1			17	-19.06 (10.484)	-16.0 (-28.4, -12.2)	-33.8, -2.0						
Day 2 / 20-hr Post 1st																
Absolute value	20	4.77 (0.440)	4.8 (4.5, 5.0)	3.9, 5.6			17	4.18 (0.410)	4.1 (4.0, 4.5)	3.5, 4.8						
Change from baseline	20	-0.42 (0.470)	-0.4 (-0.8, -0.1)	-1.3, 0.6	-0.39 (0.101)	(-0.60, -0.19)	17	-0.88 (0.562)	-0.8 (-1.3, -0.5)	-1.8, -0.0	-0.90 (0.111)	(-1.13, -0.68)	-0.51 (-0.82, -0.21)	0.0018	-0.88 (-1.56, -0.21)	
Percent change from baseline	20	-7.94 (8.854)	-7.3 (-15.0, -2.5)	-25.2, 13.1			17	-16.98 (10.370)	-16.0 (-26.7, -9.8)	-32.7, -0.7						
Day 3 / 0-hr																
Absolute value	21	4.91 (0.485)	5.0 (4.5, 5.1)	4.2, 6.0			17	4.29 (0.484)	4.3 (4.0, 4.5)	3.3, 5.1						
Change from baseline	21	-0.27 (0.441)	-0.3 (-0.5, -0.0)	-1.0, 0.7	-0.25 (0.100)	(-0.45, -0.05)	17	-0.76 (0.535)	-0.7 (-1.2, -0.4)	-1.6, 0.3	-0.78 (0.112)	(-1.01, -0.56)	-0.53 (-0.84, -0.23)	0.0011	-1.01 (-1.69, -0.33)	
Percent change from baseline	21	-5.10 (8.359)	-5.7 (-10.2, -0.3)	-19.5, 13.9			17	-14.81 (10.285)	-14.0 (-21.8, -8.2)	-31.7, 5.6						
Day 4 / 0-hr																
Absolute value	21	4.89 (0.508)	4.8 (4.5, 5.3)	4.0, 6.0			17	4.38 (0.429)	4.4 (4.1, 4.5)	3.6, 5.5						
Change from baseline	21	-0.30 (0.510)	-0.4 (-0.6, -0.1)	-1.0, 0.8	-0.28 (0.102)	(-0.49, -0.07)	17	-0.68 (0.483)	-0.6 (-1.1, -0.4)	-1.5, 0.1	-0.70 (0.113)	(-0.93, -0.47)	-0.42 (-0.73, -0.11)	0.0087	-0.76 (-1.43, -0.10)	
Percent change from baseline	21	-5.57 (9.901)	-7.7 (-12.1, -2.2)	-19.7, 17.0			17	-13.18 (9.056)	-12.5 (-21.2, -8.2)	-27.1, 1.8						

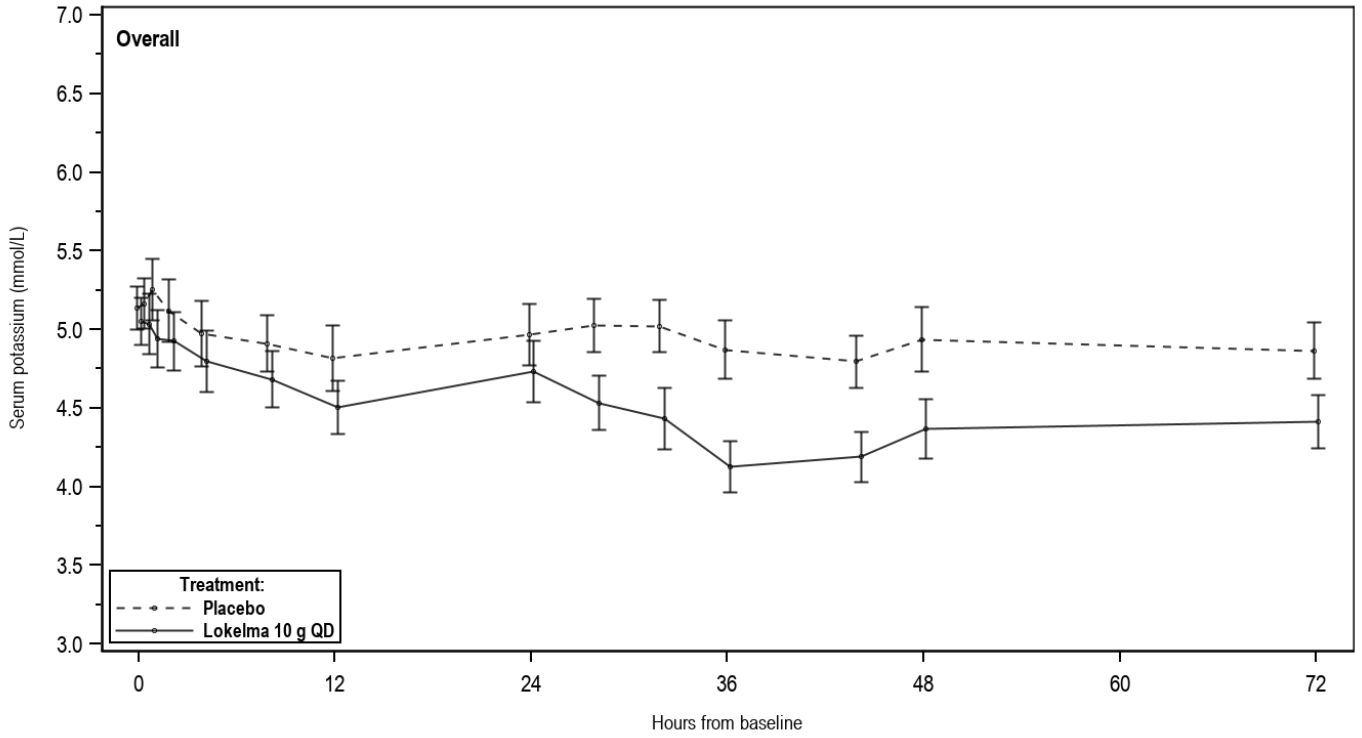
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Figure 1.1.2.2 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint): absolute values, ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)



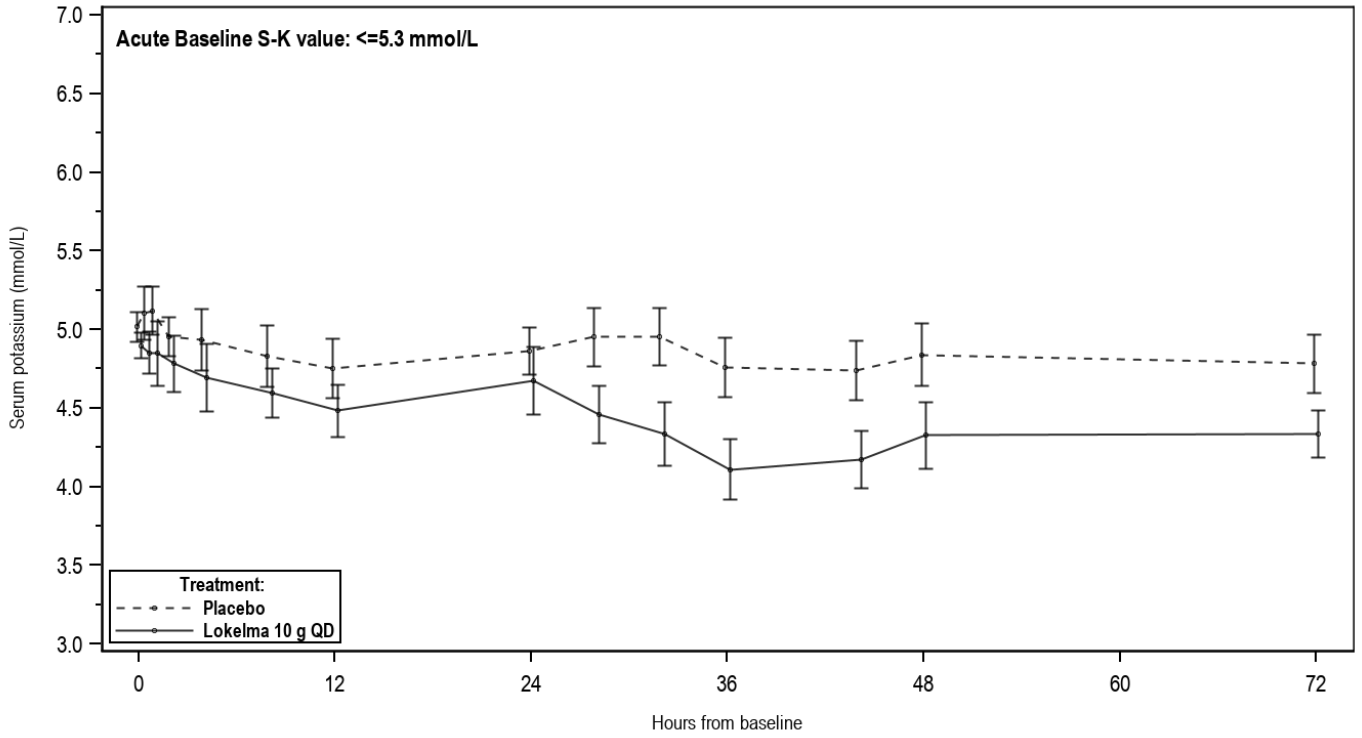
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.

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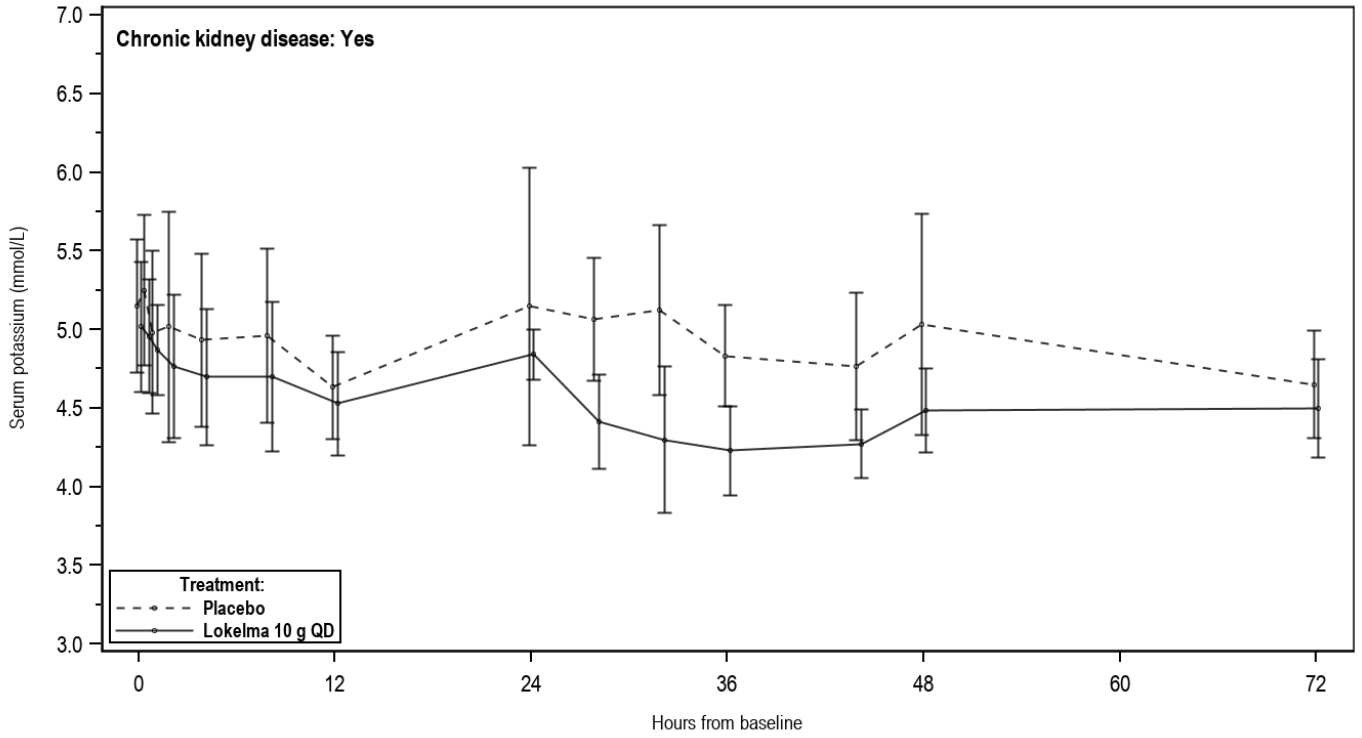
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.

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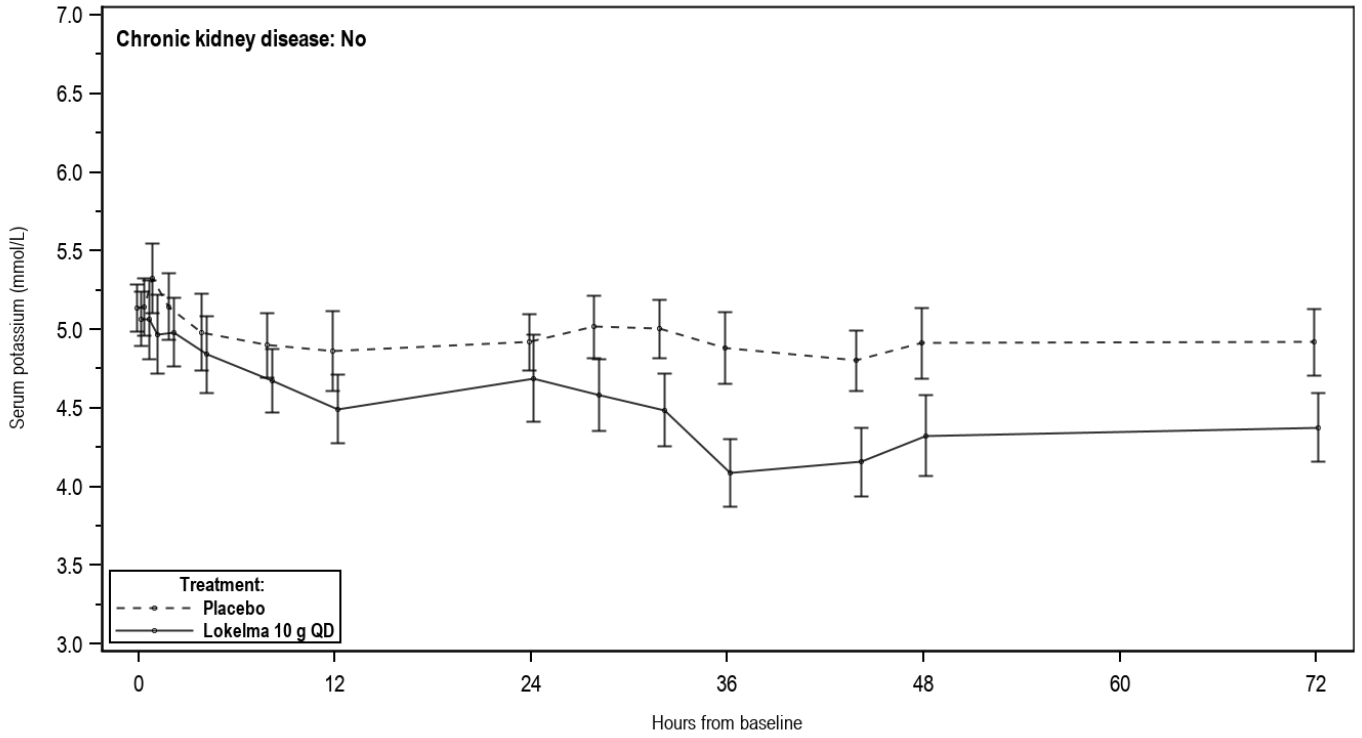
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.

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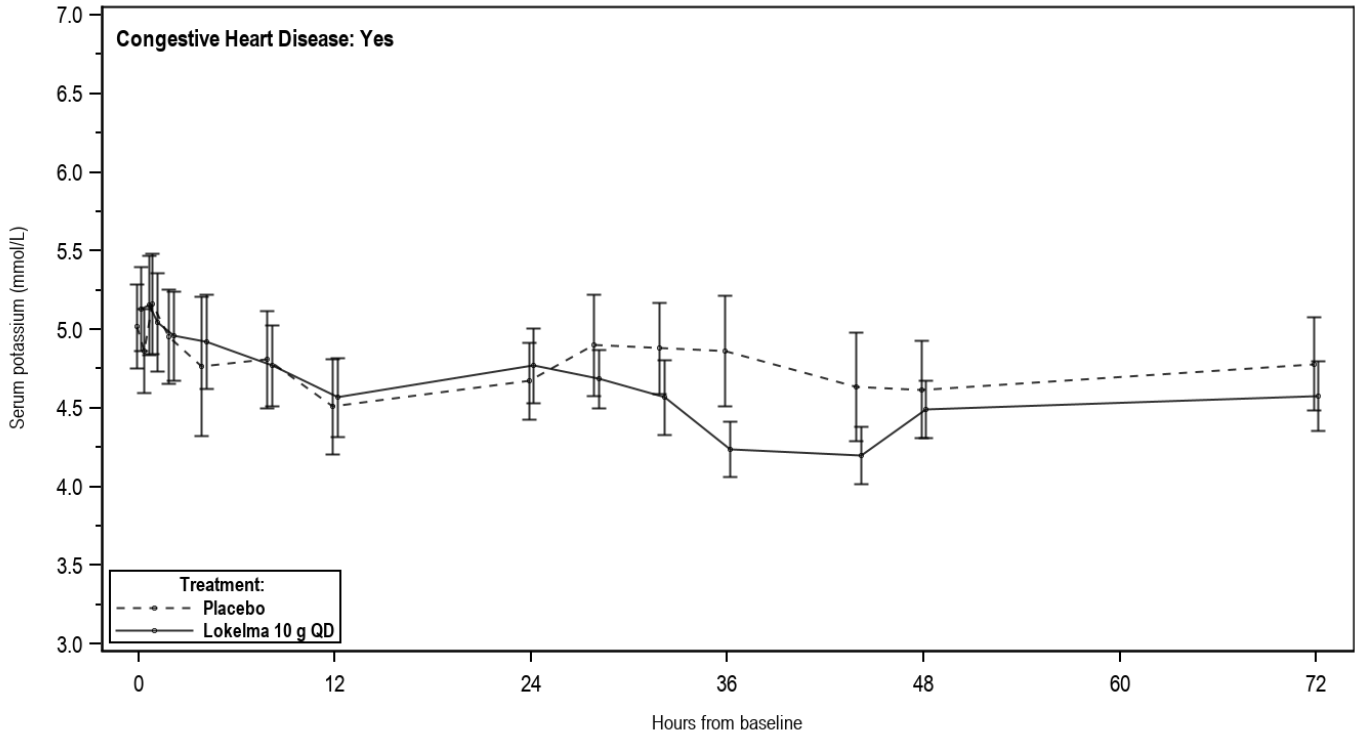
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.

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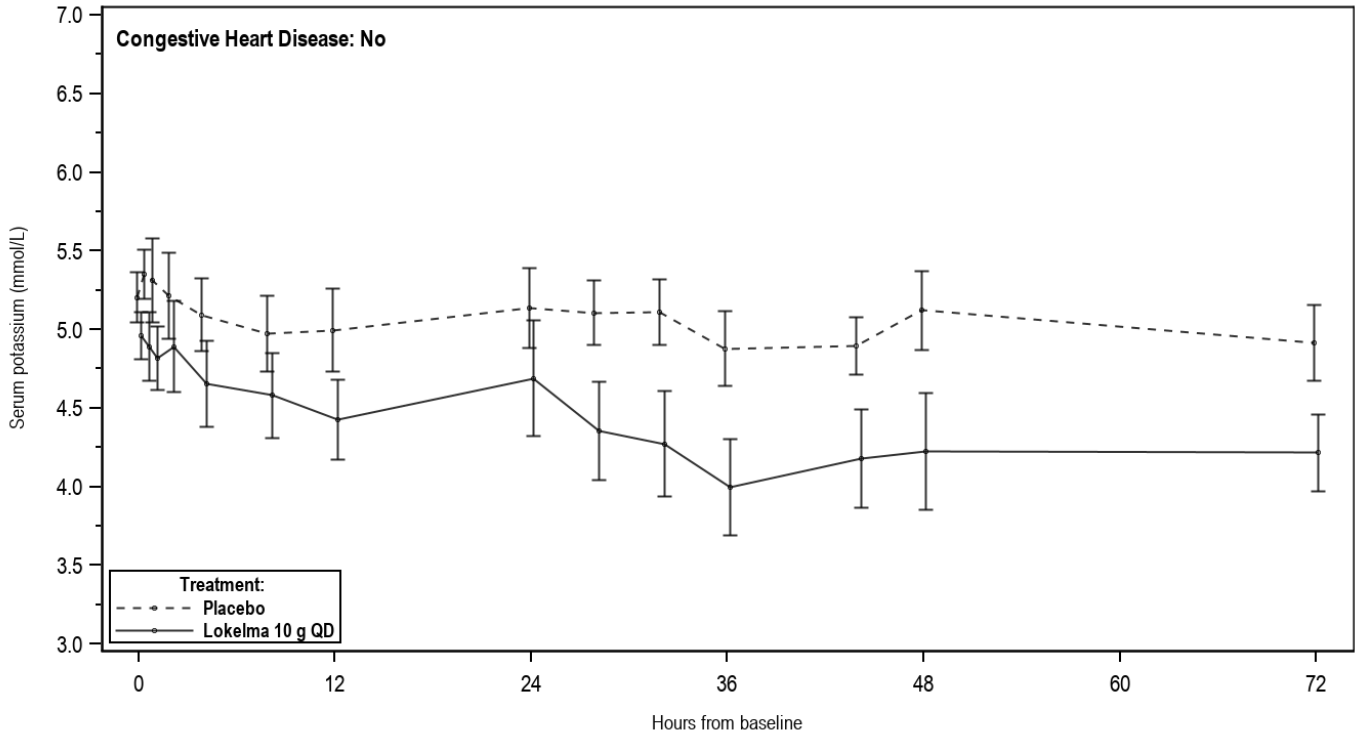
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.

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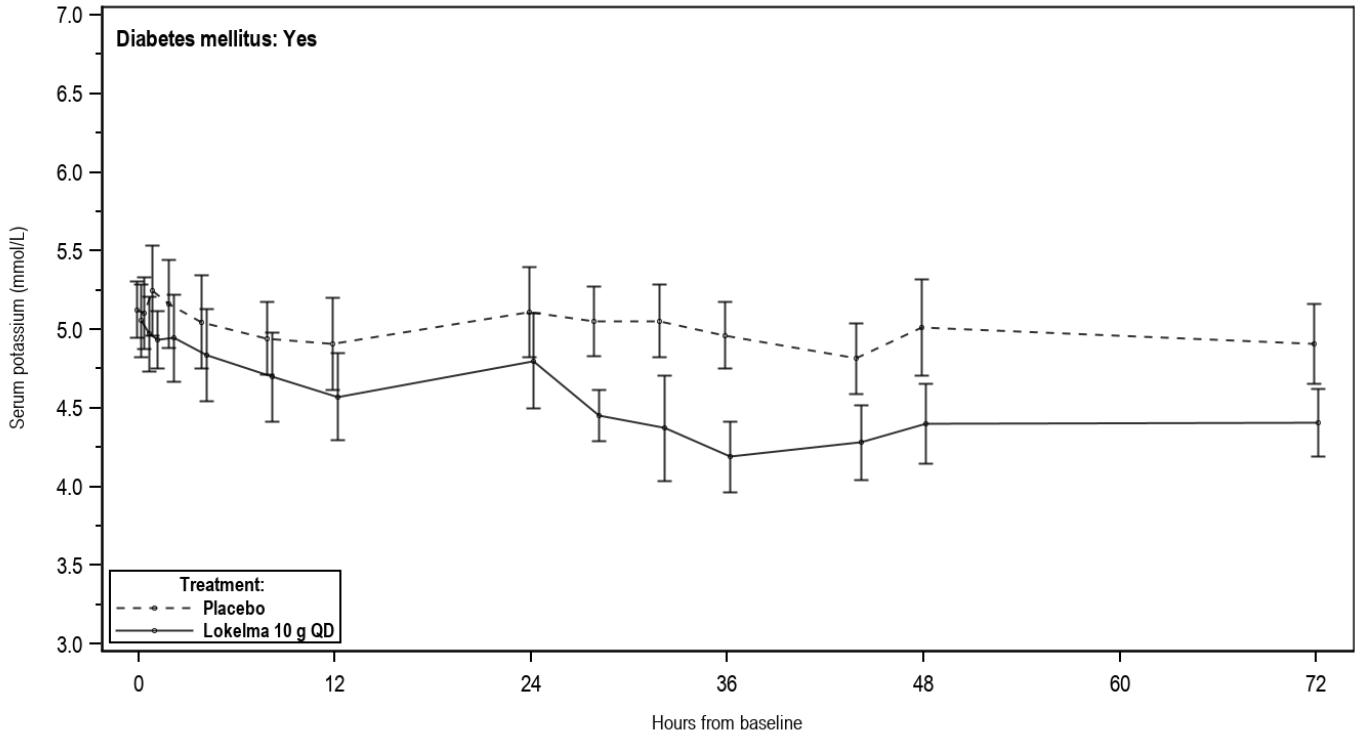
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
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Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.

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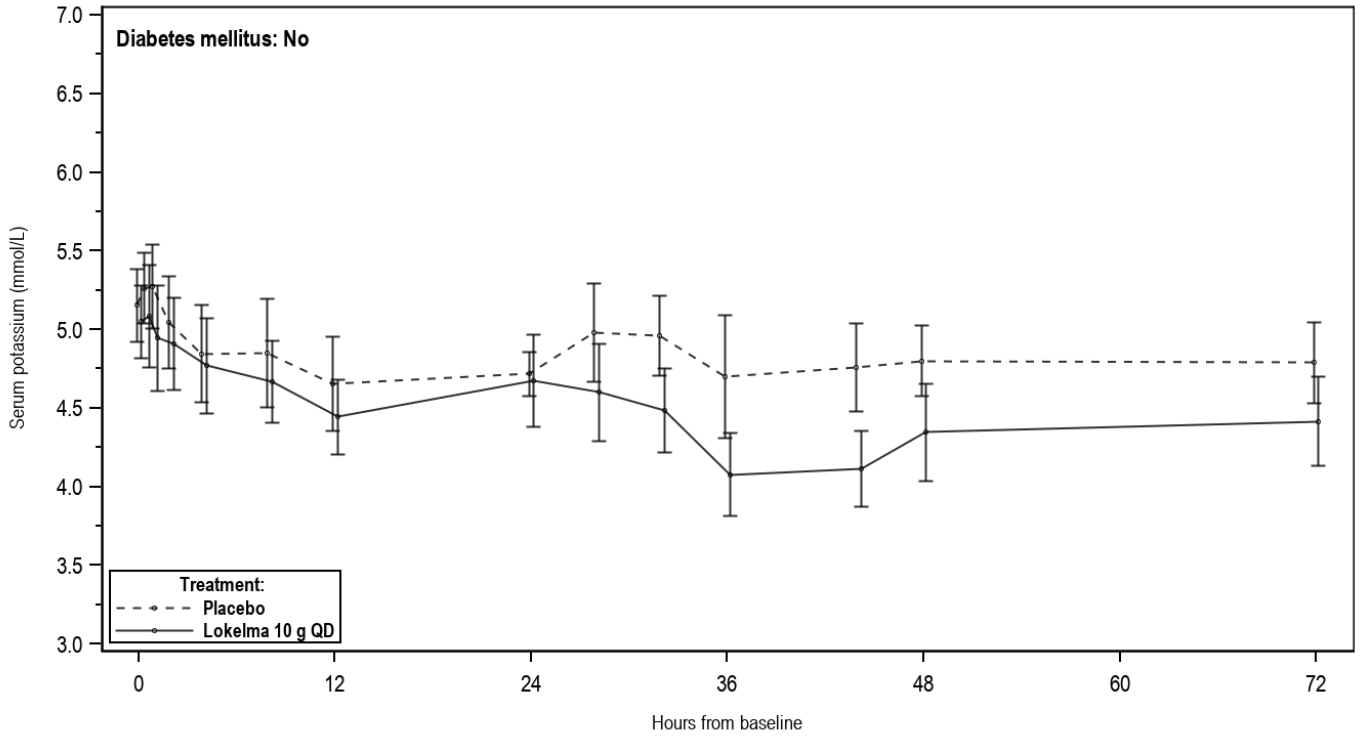
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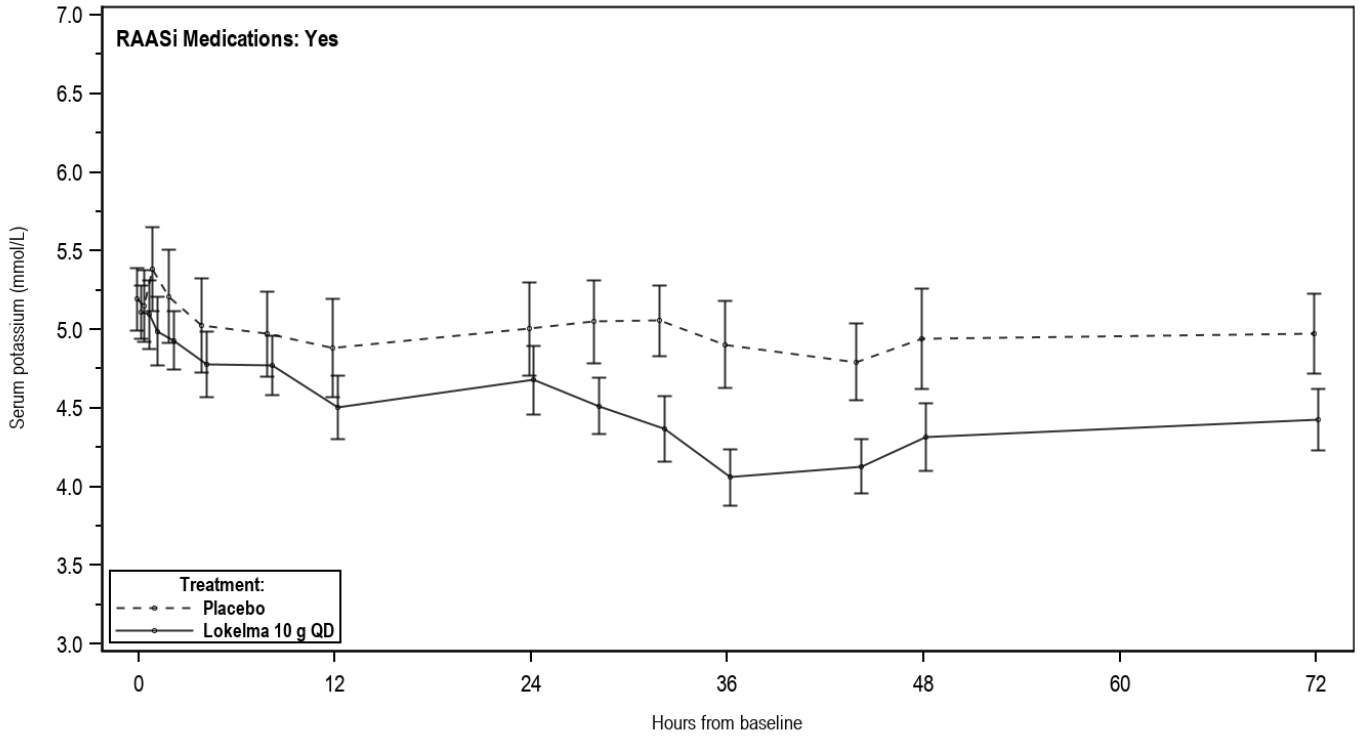
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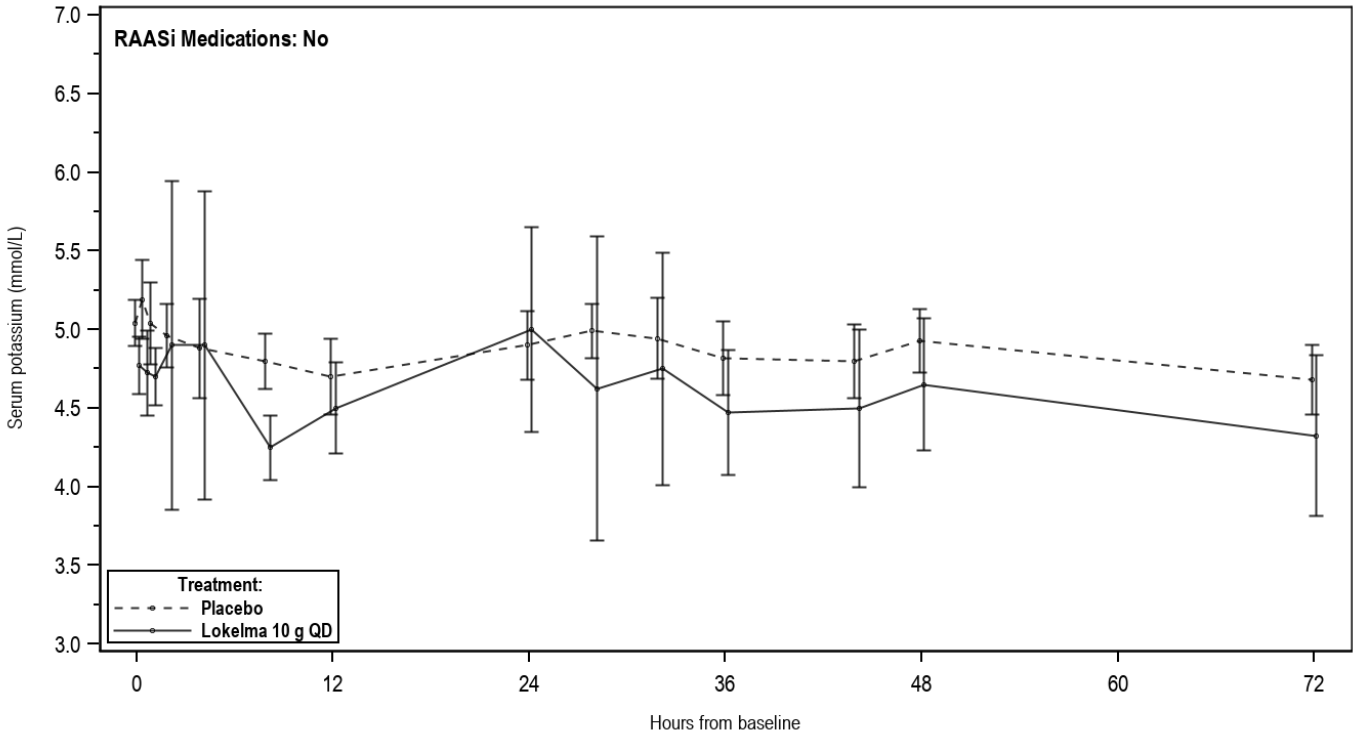
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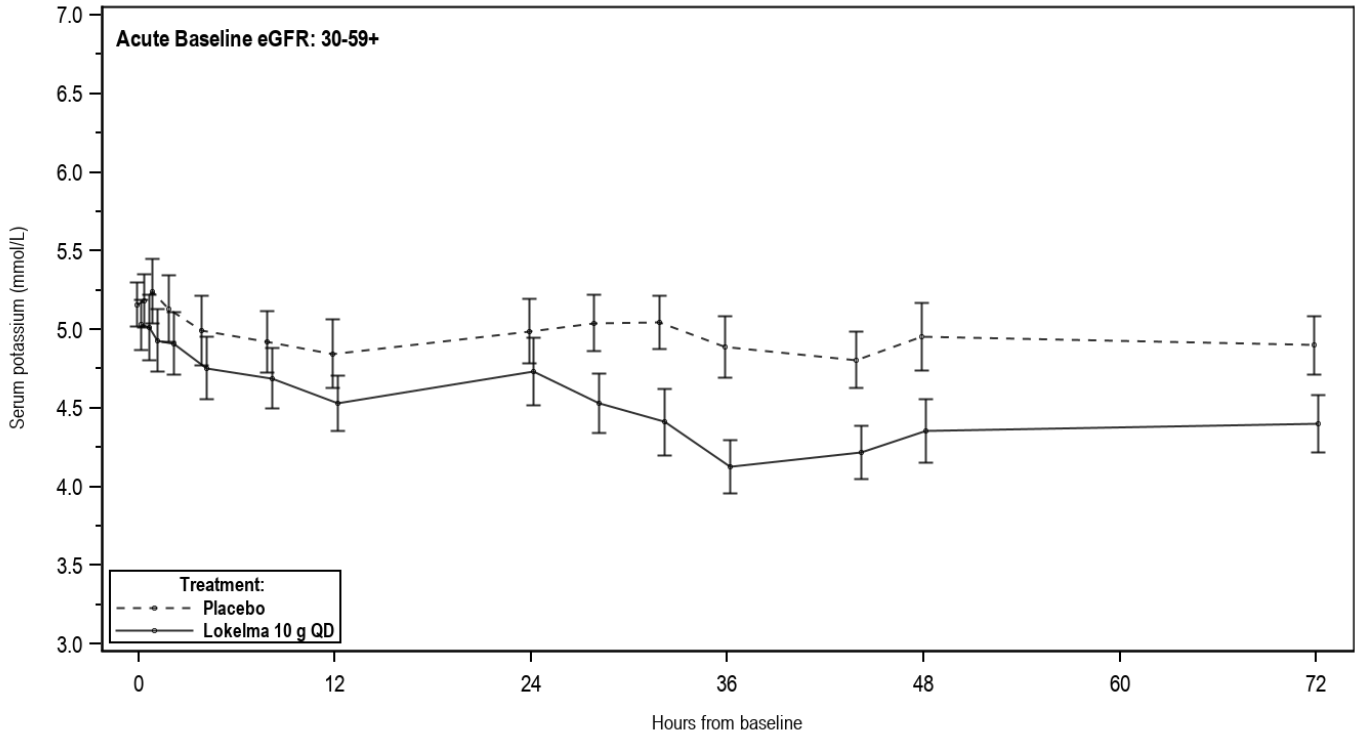
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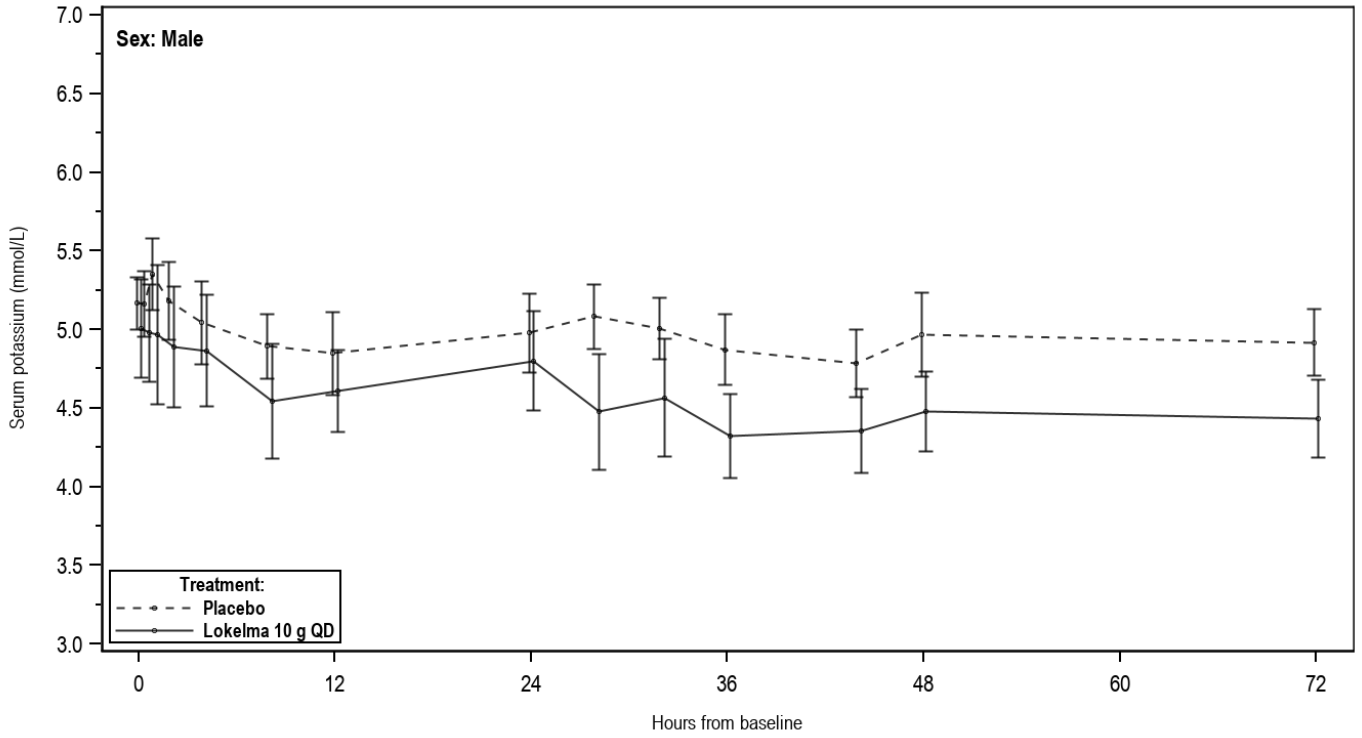
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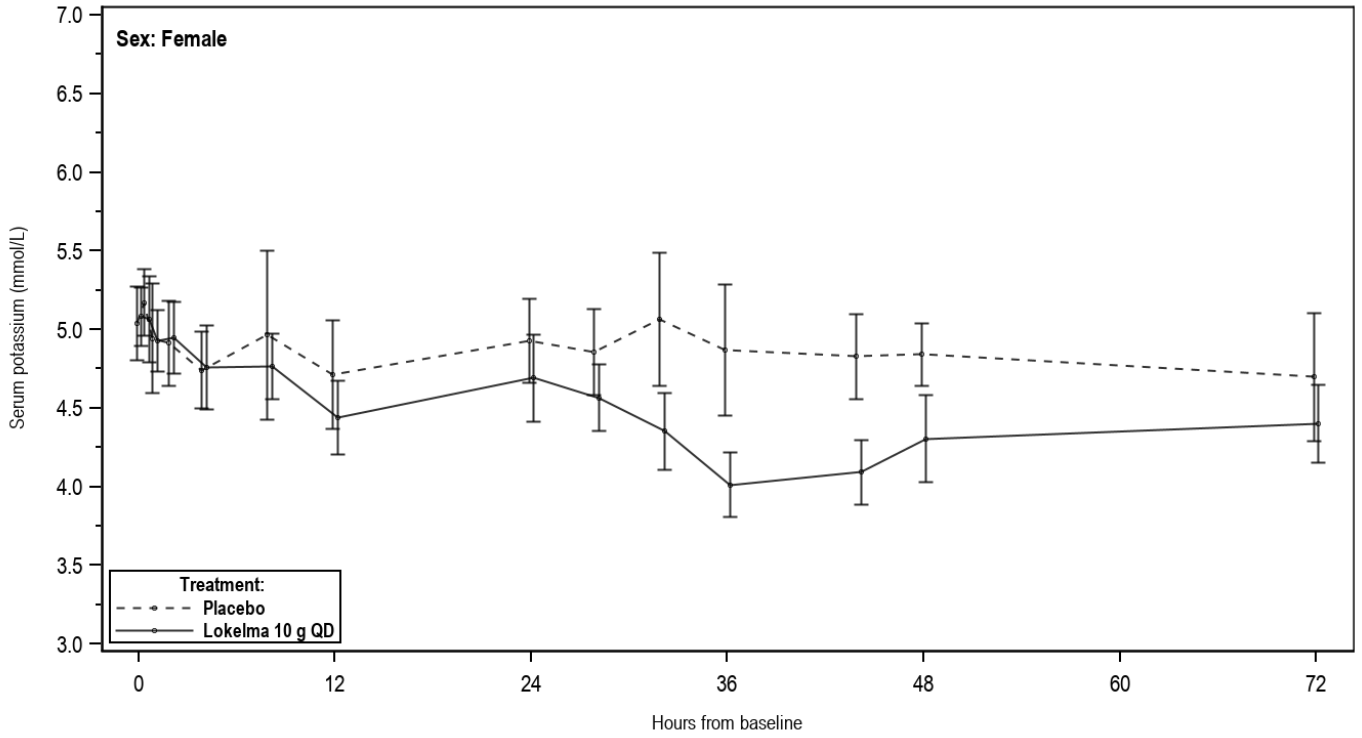
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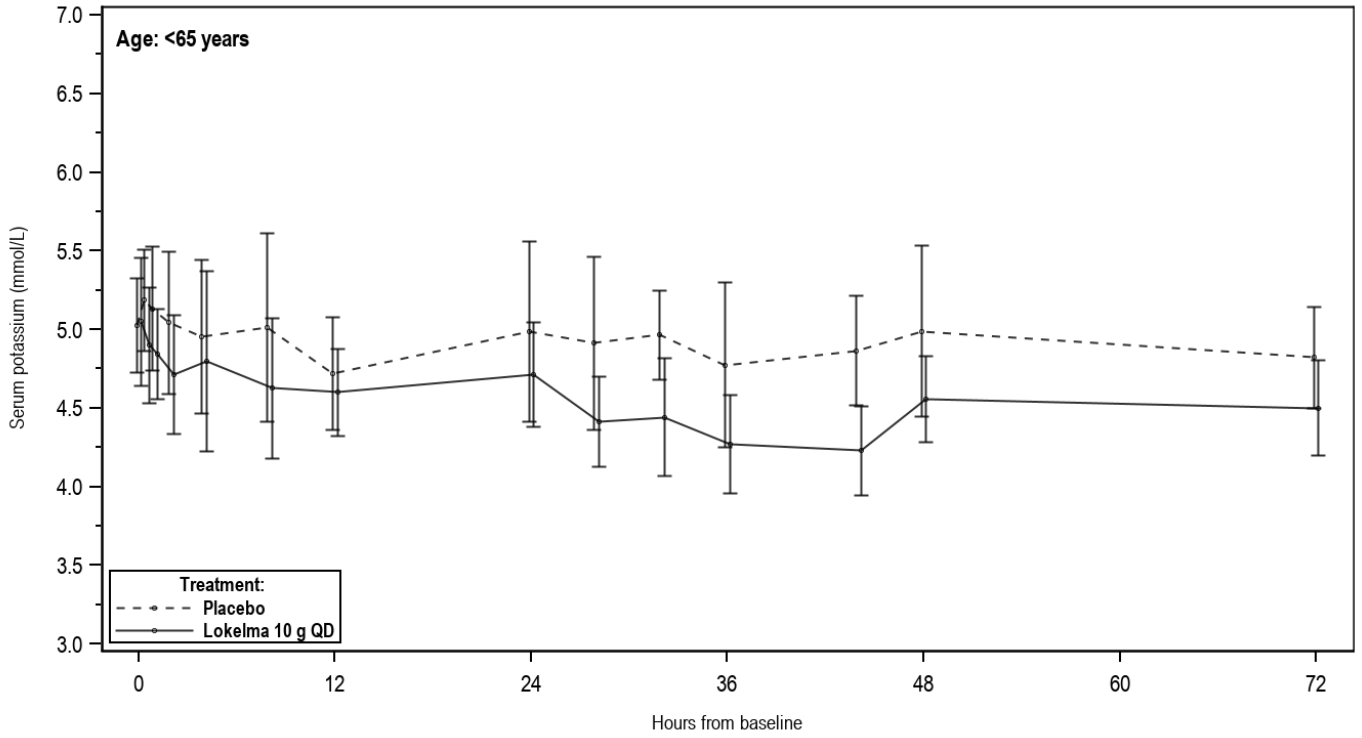
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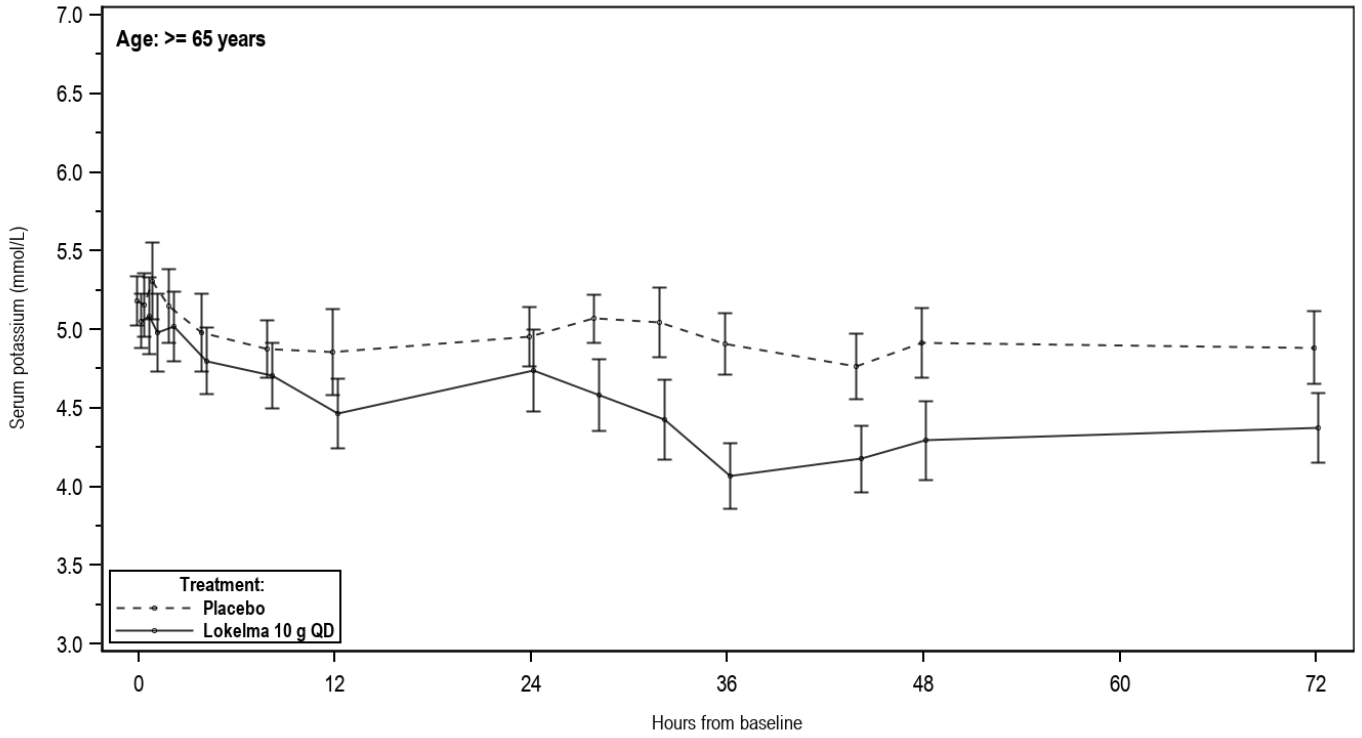
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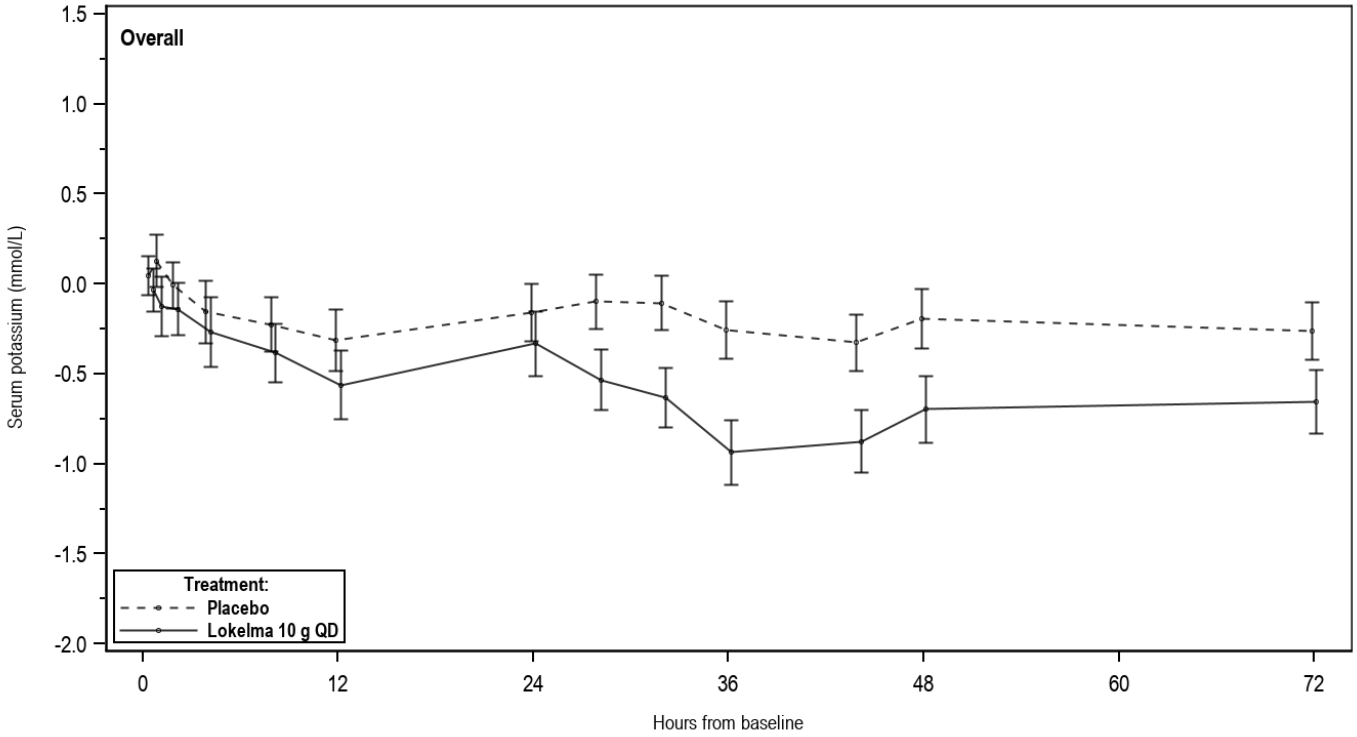
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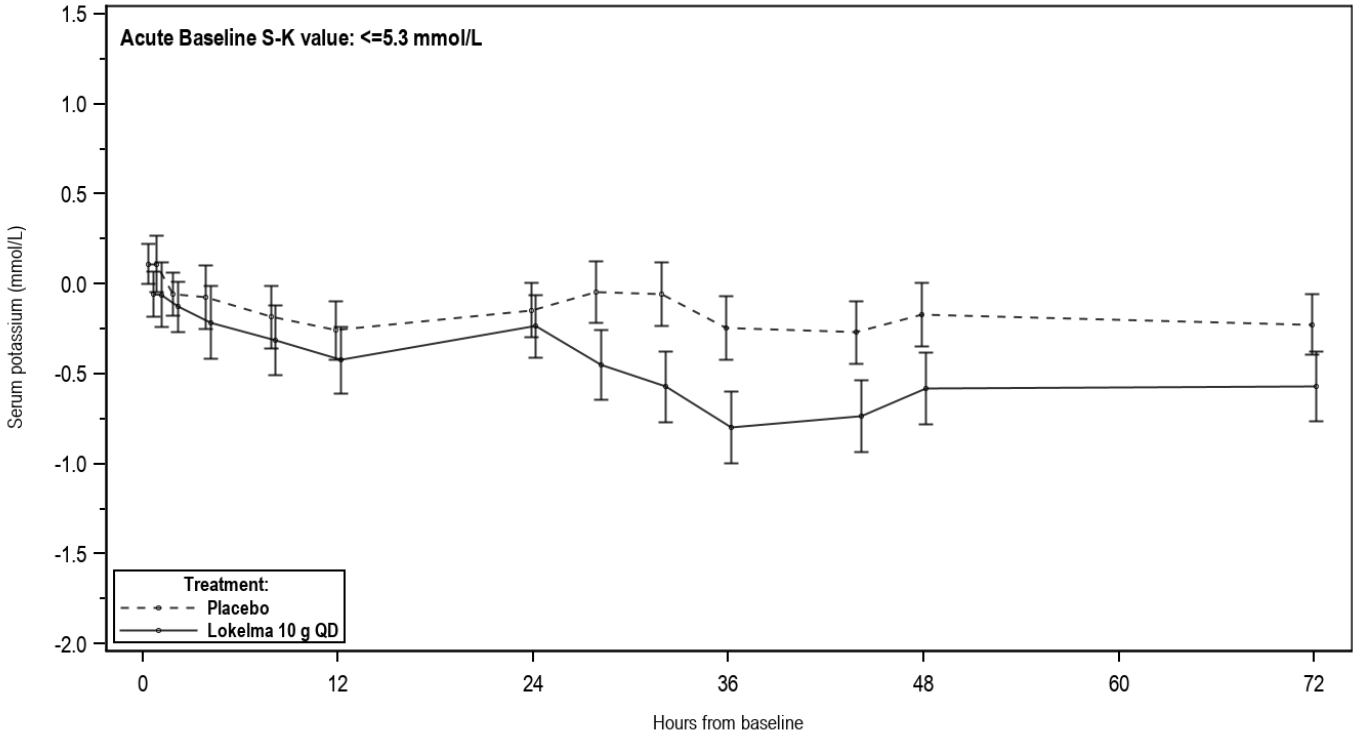
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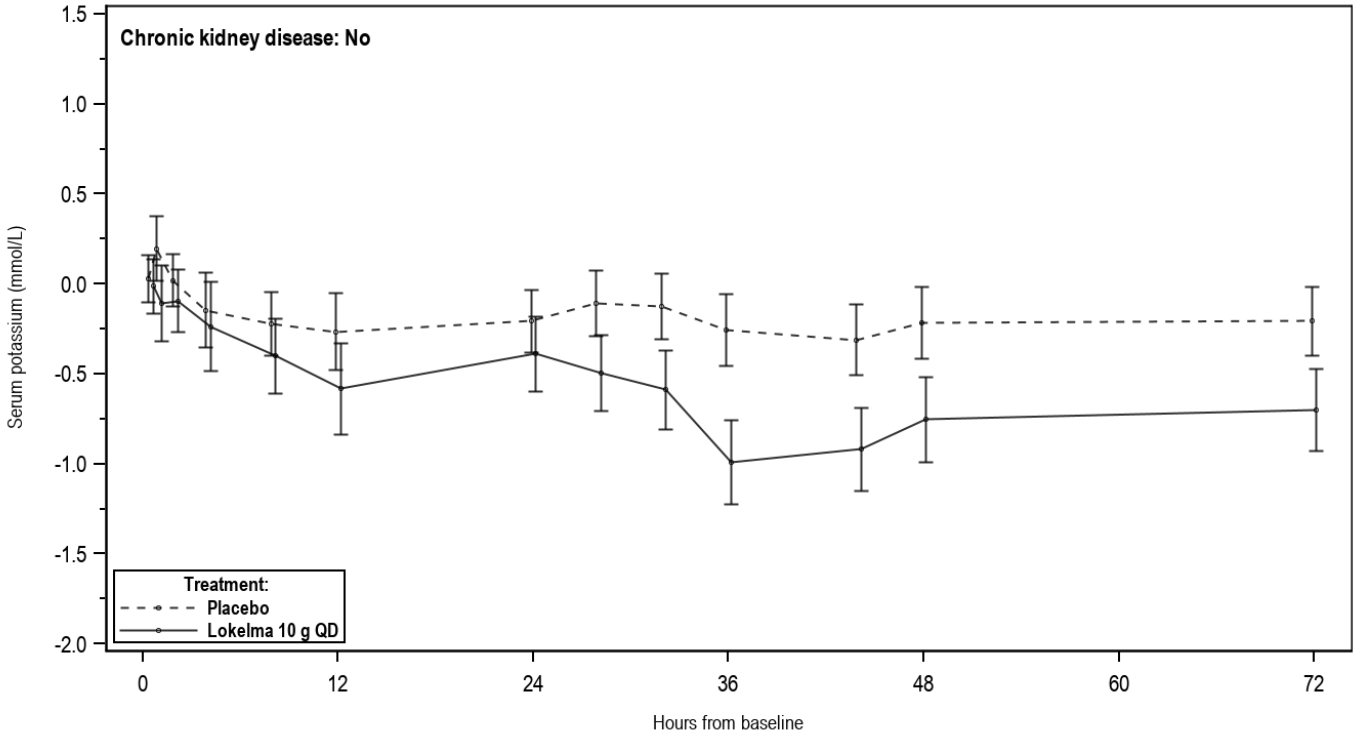
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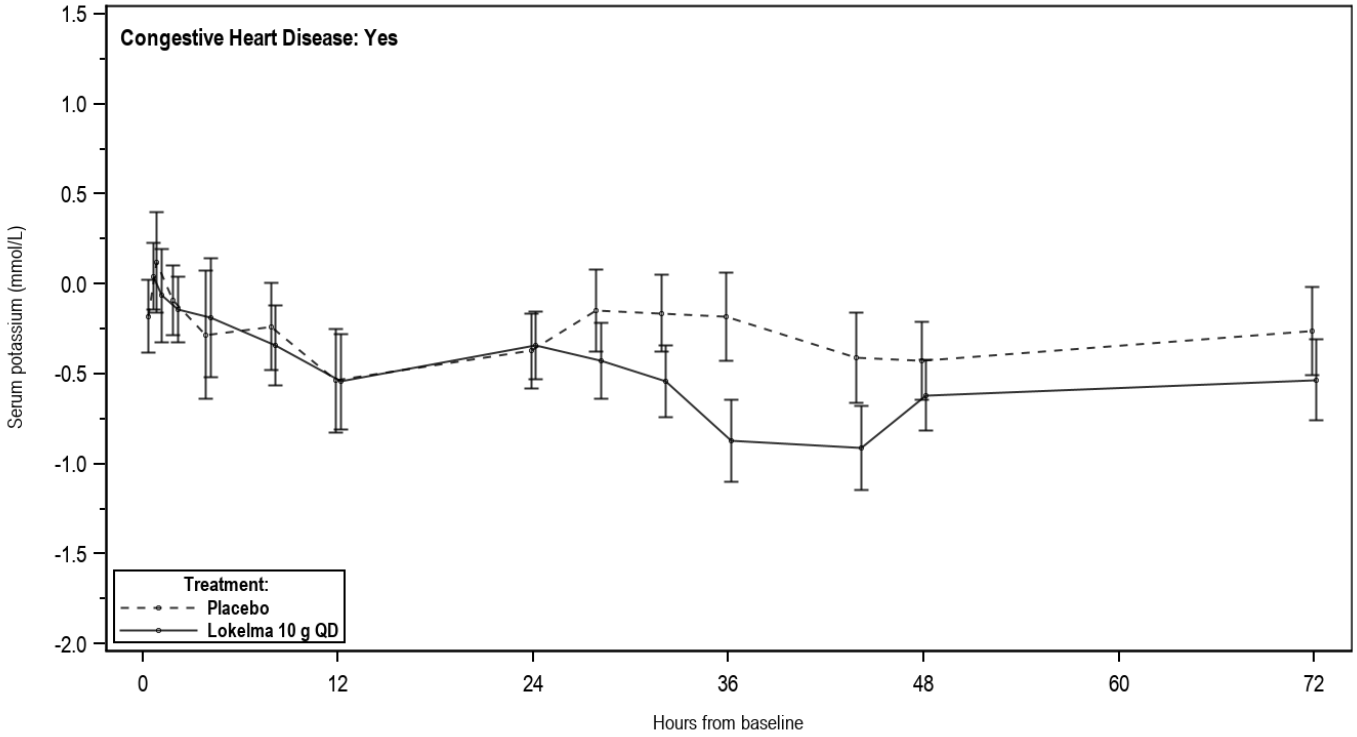
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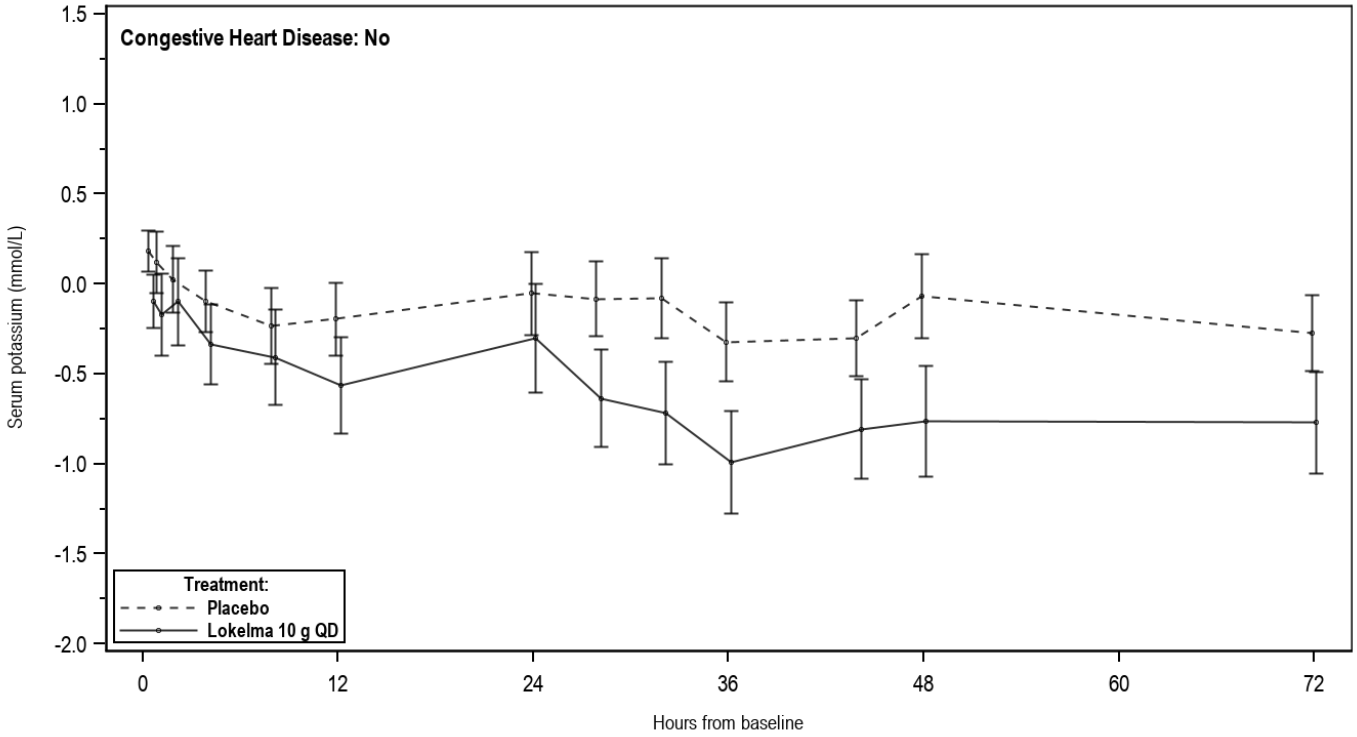
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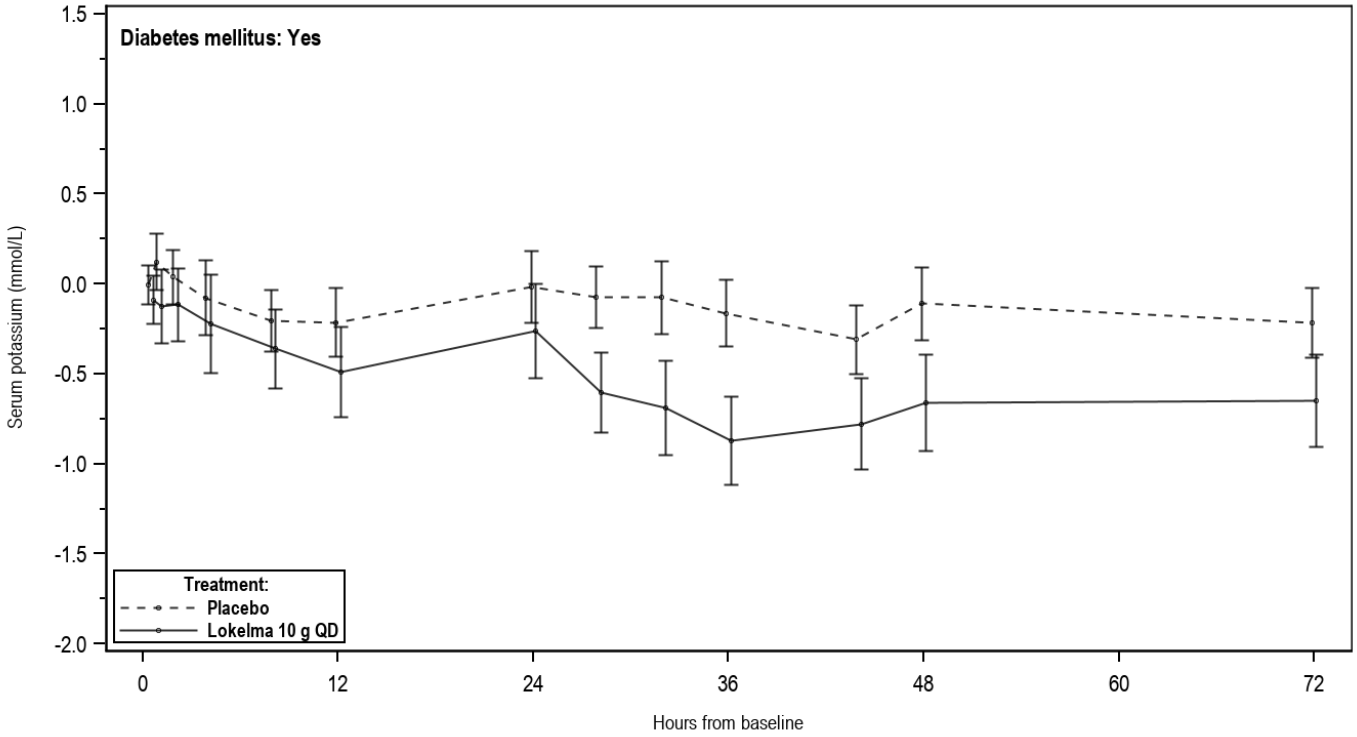
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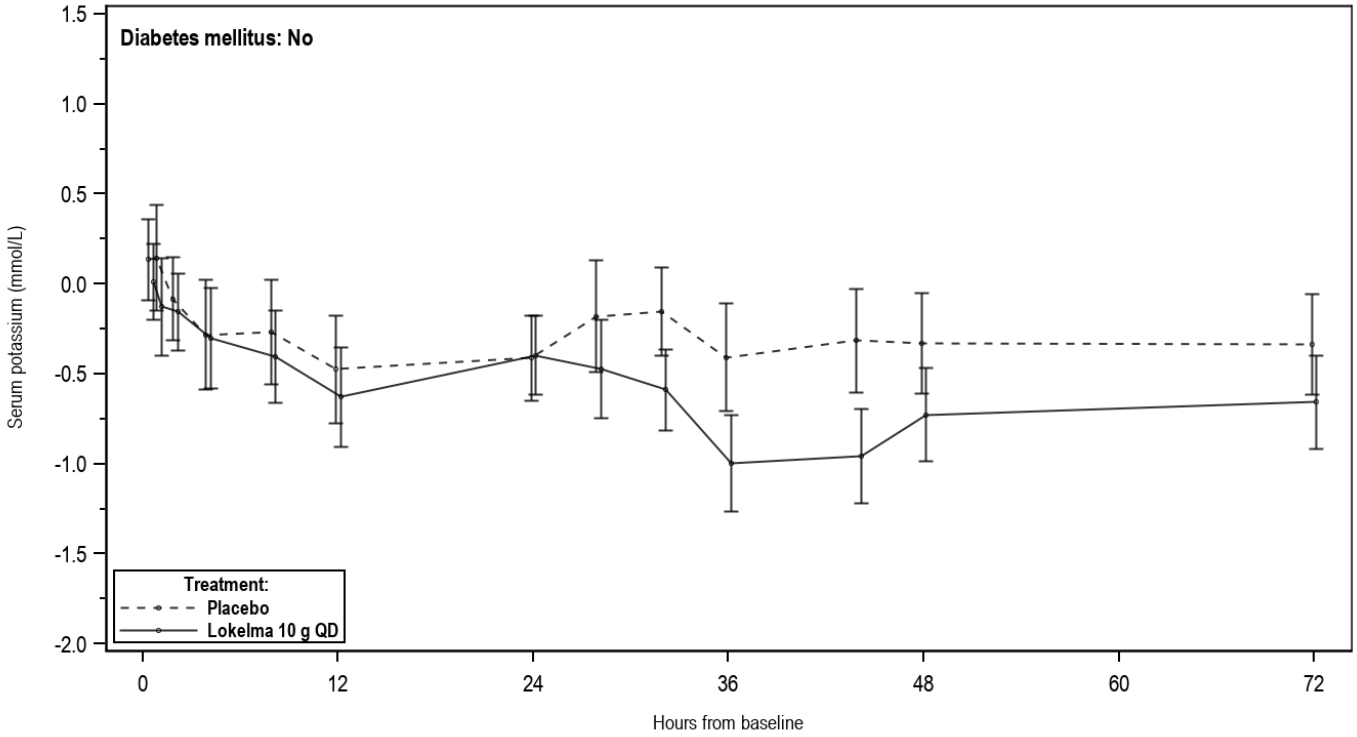
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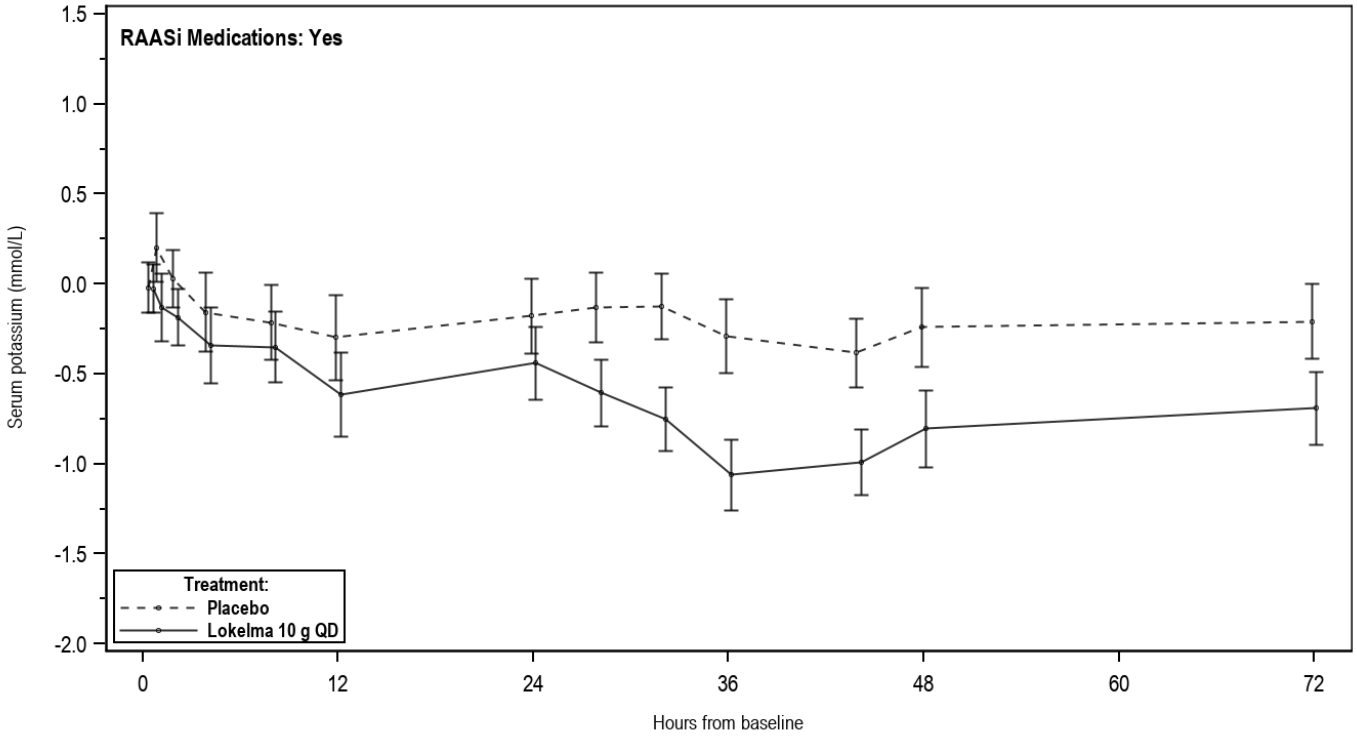
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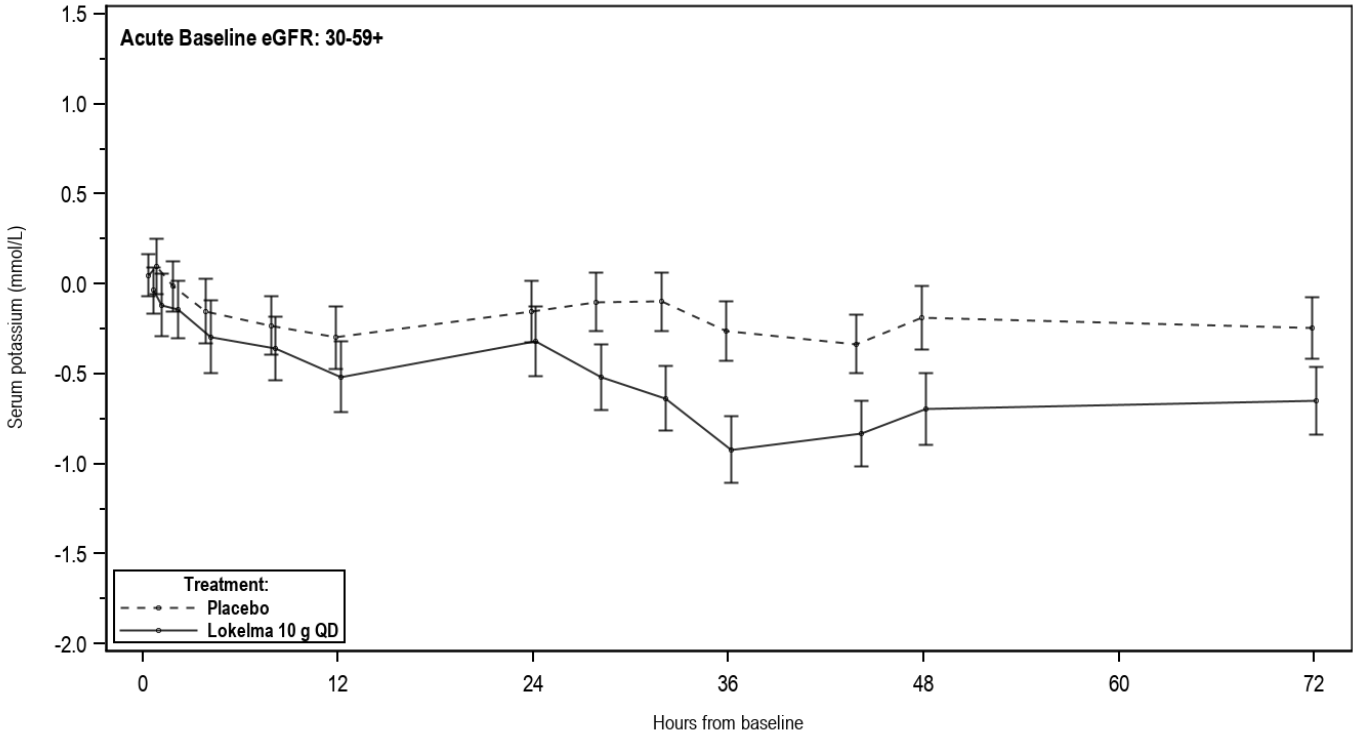
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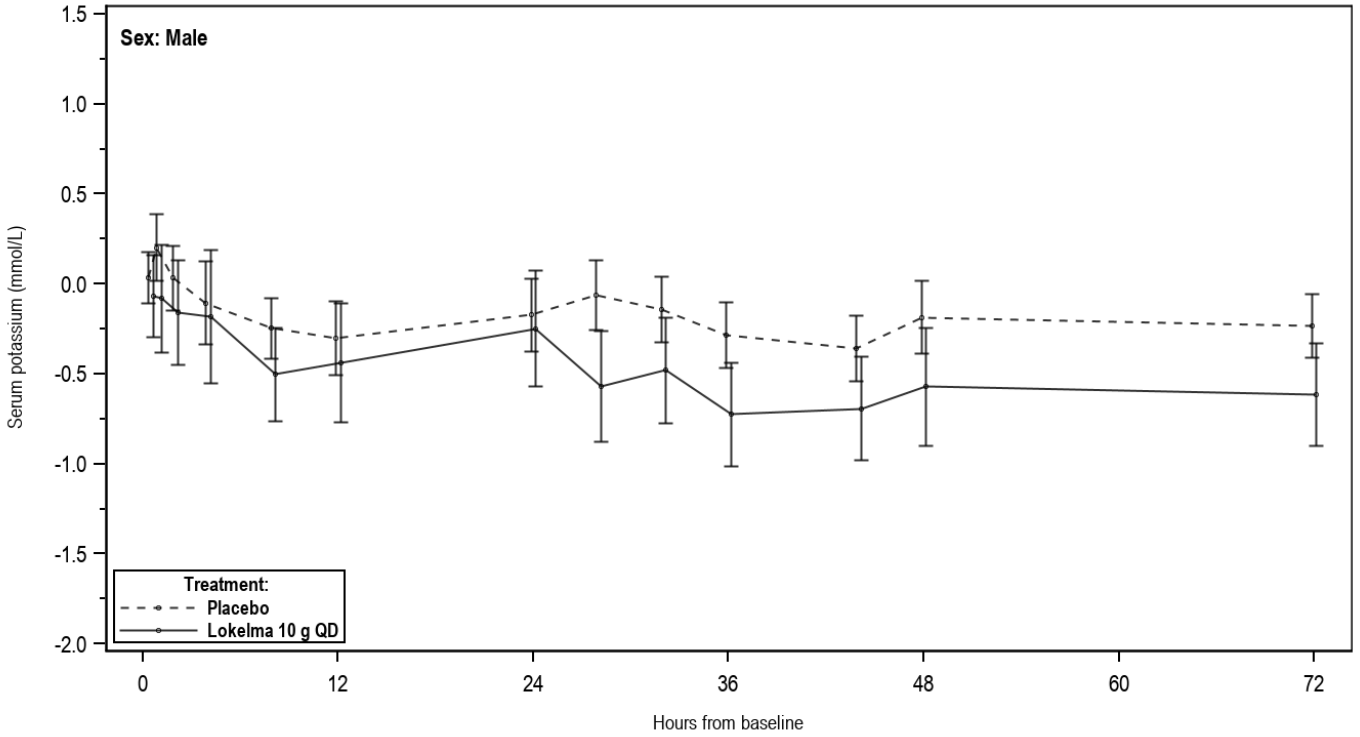
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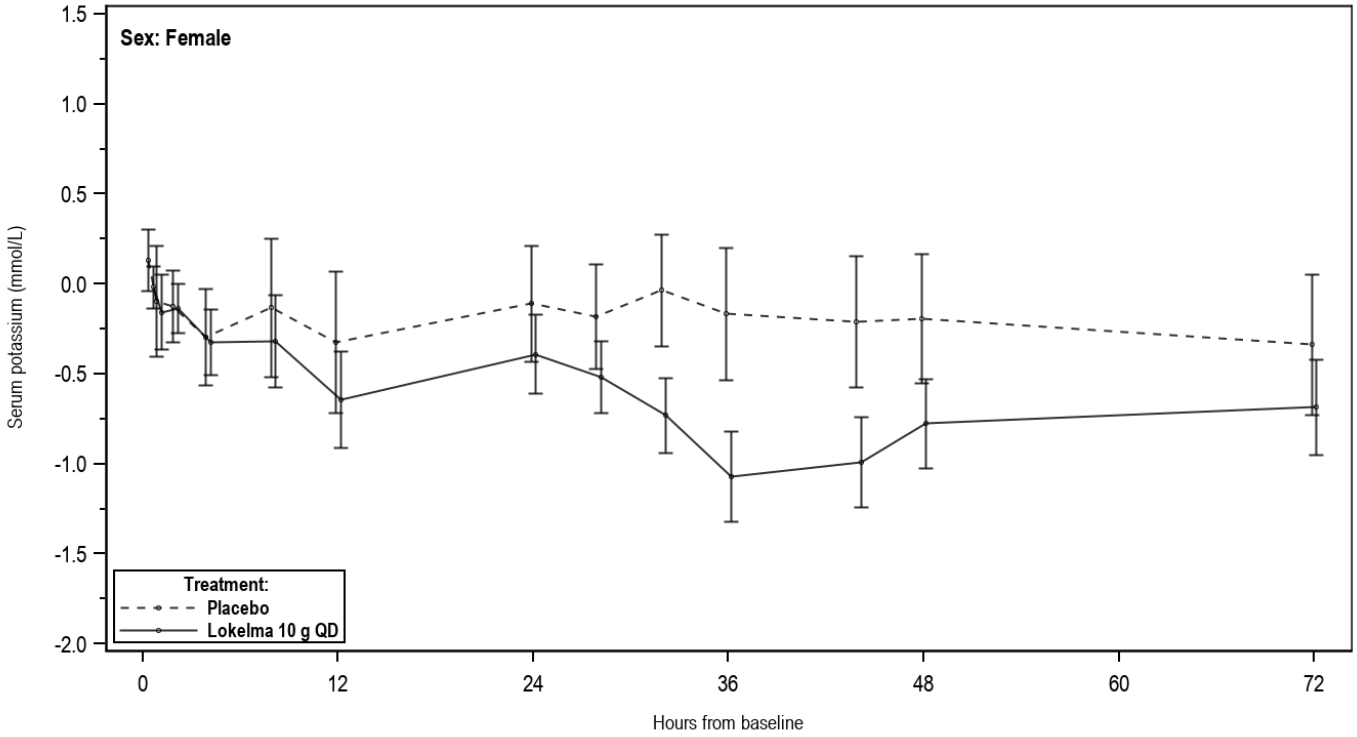
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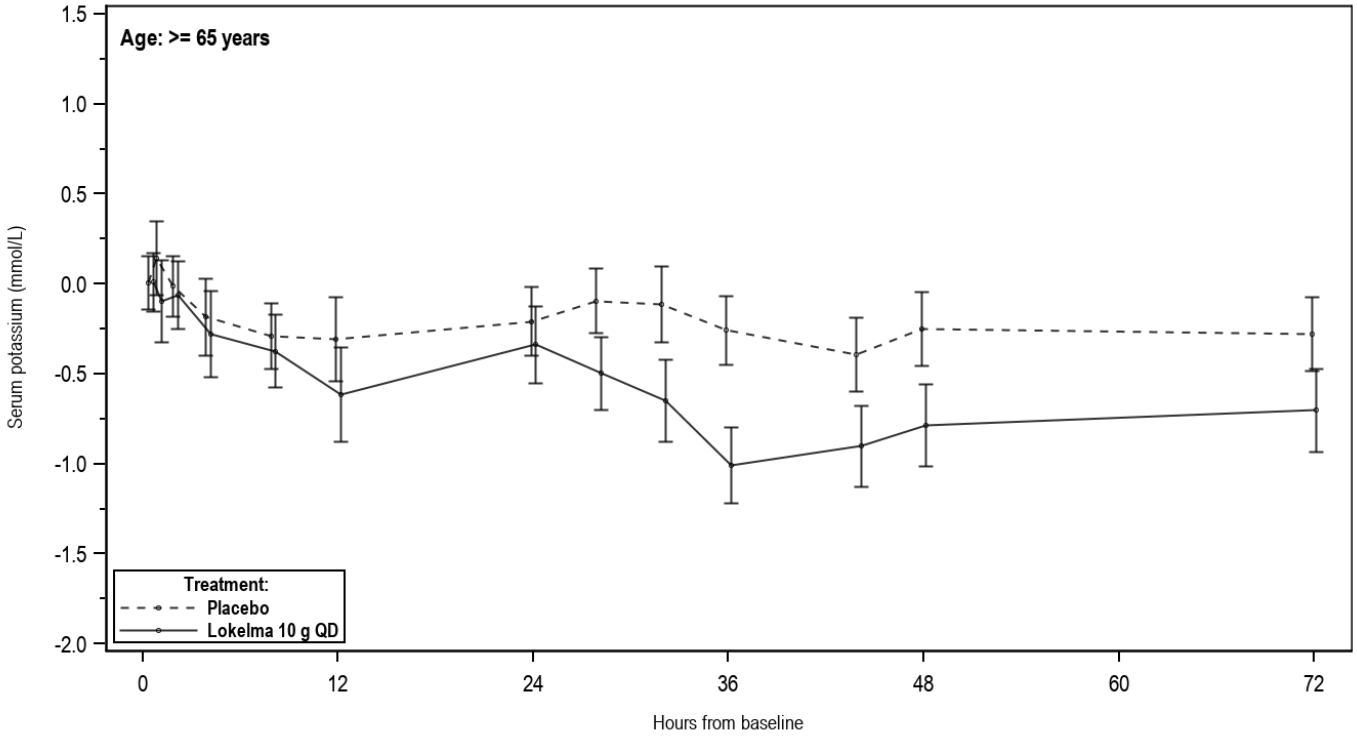
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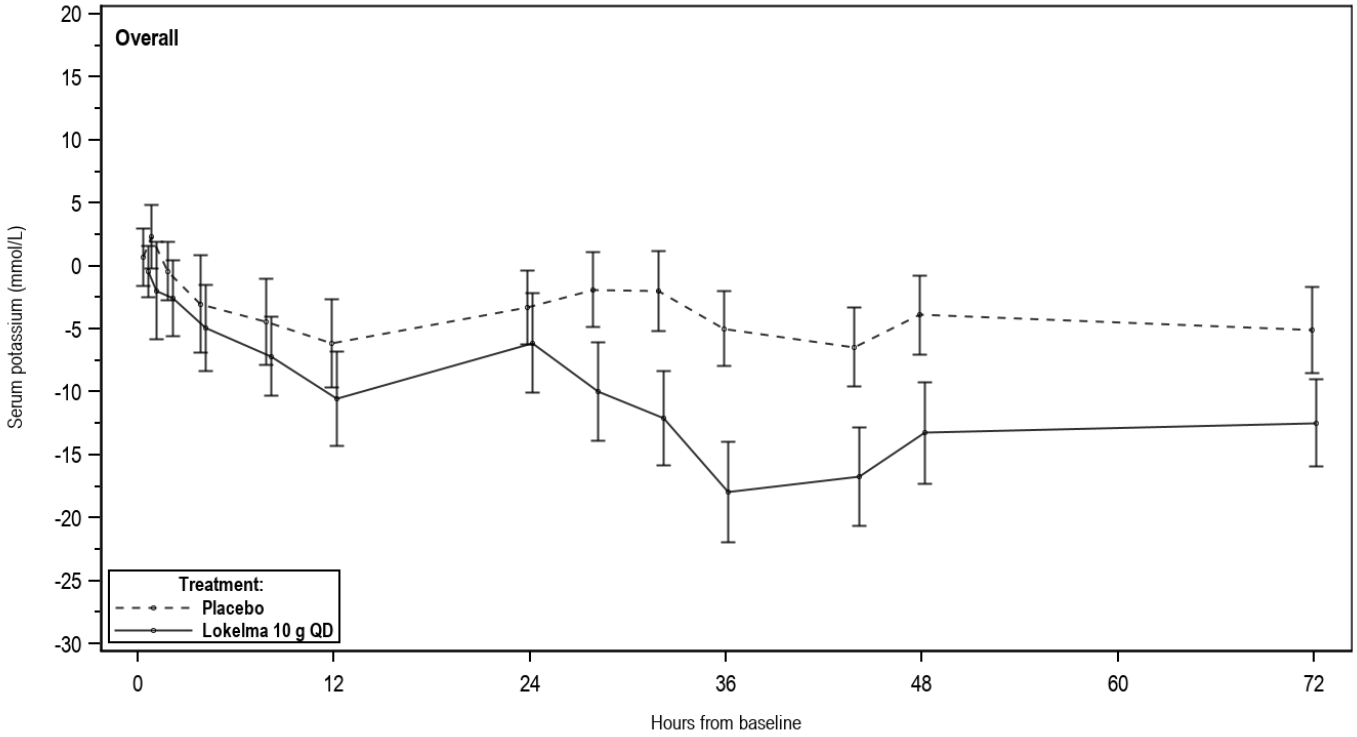
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Figure 1.1.2.4 - Study ZS-002: Serum potassium (mmol/L) over time up to 72 hours (Day 4 0hr pre-dose timepoint): % change from baseline, ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)



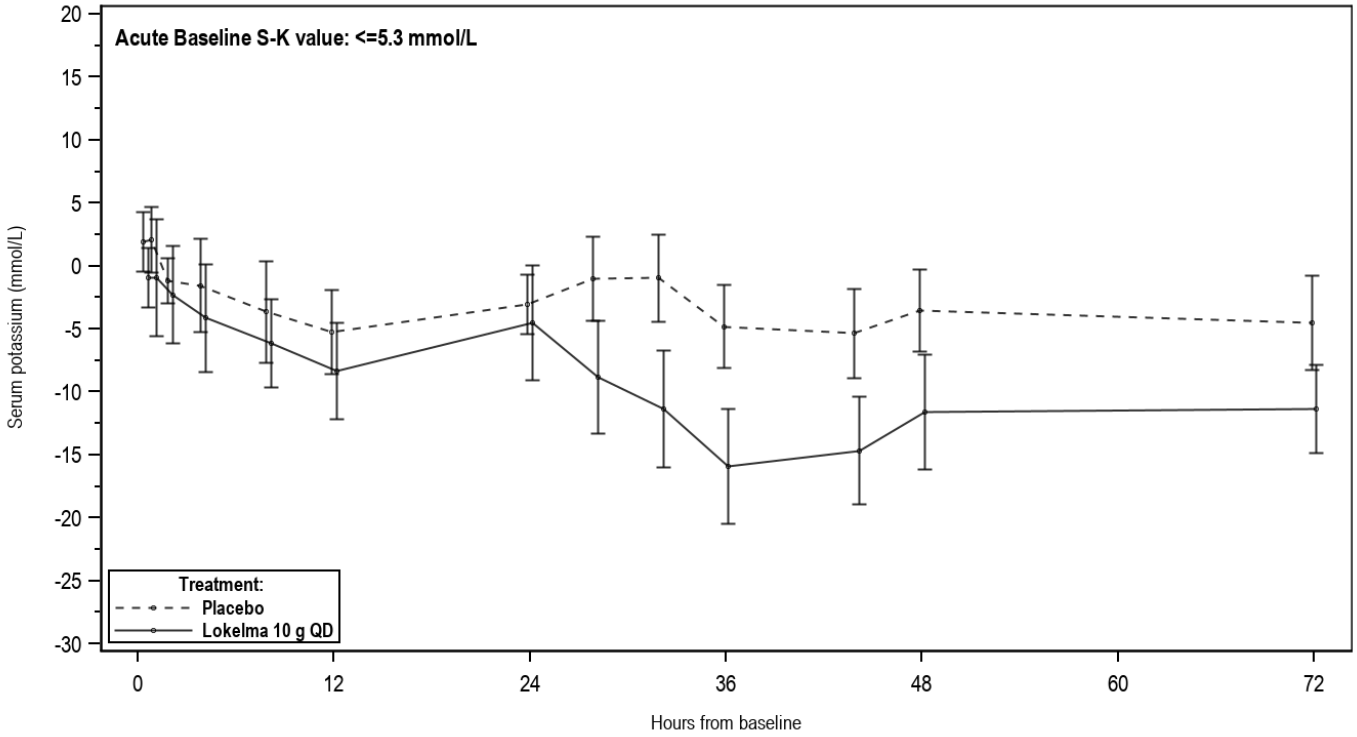
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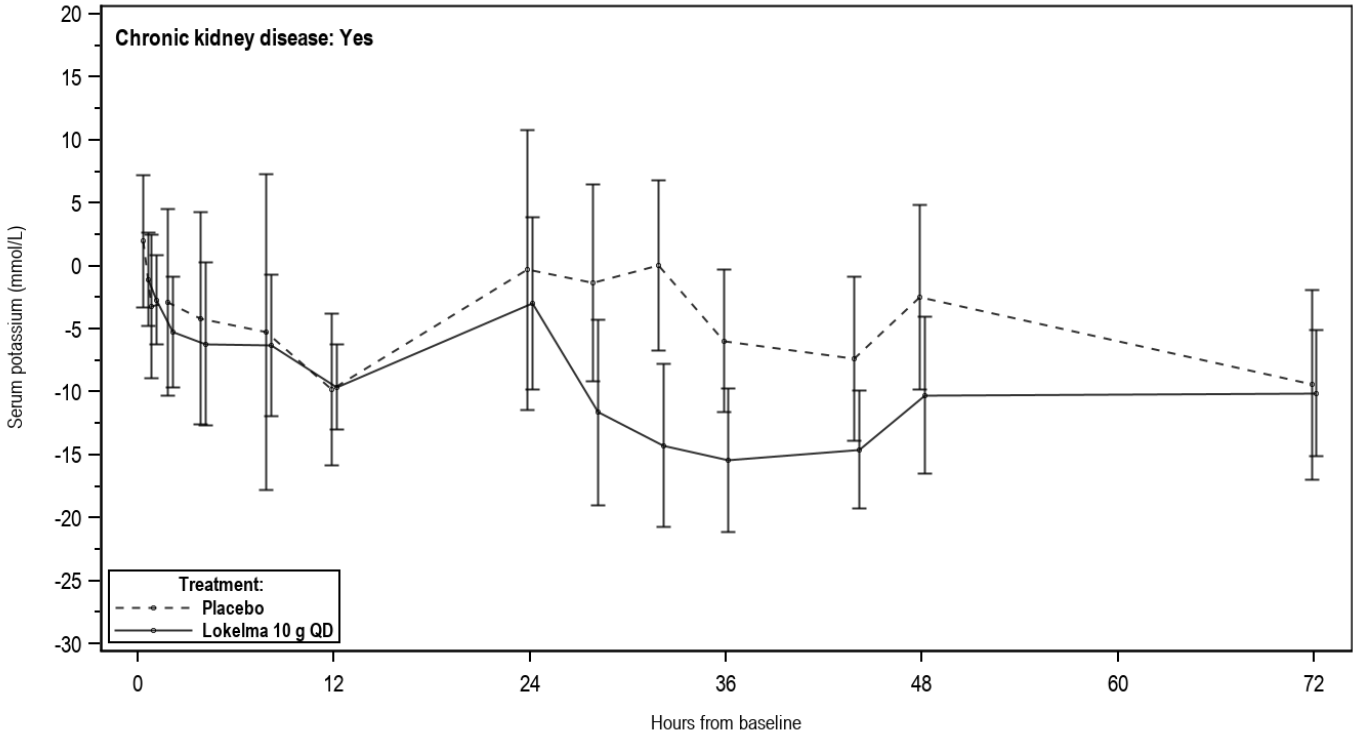
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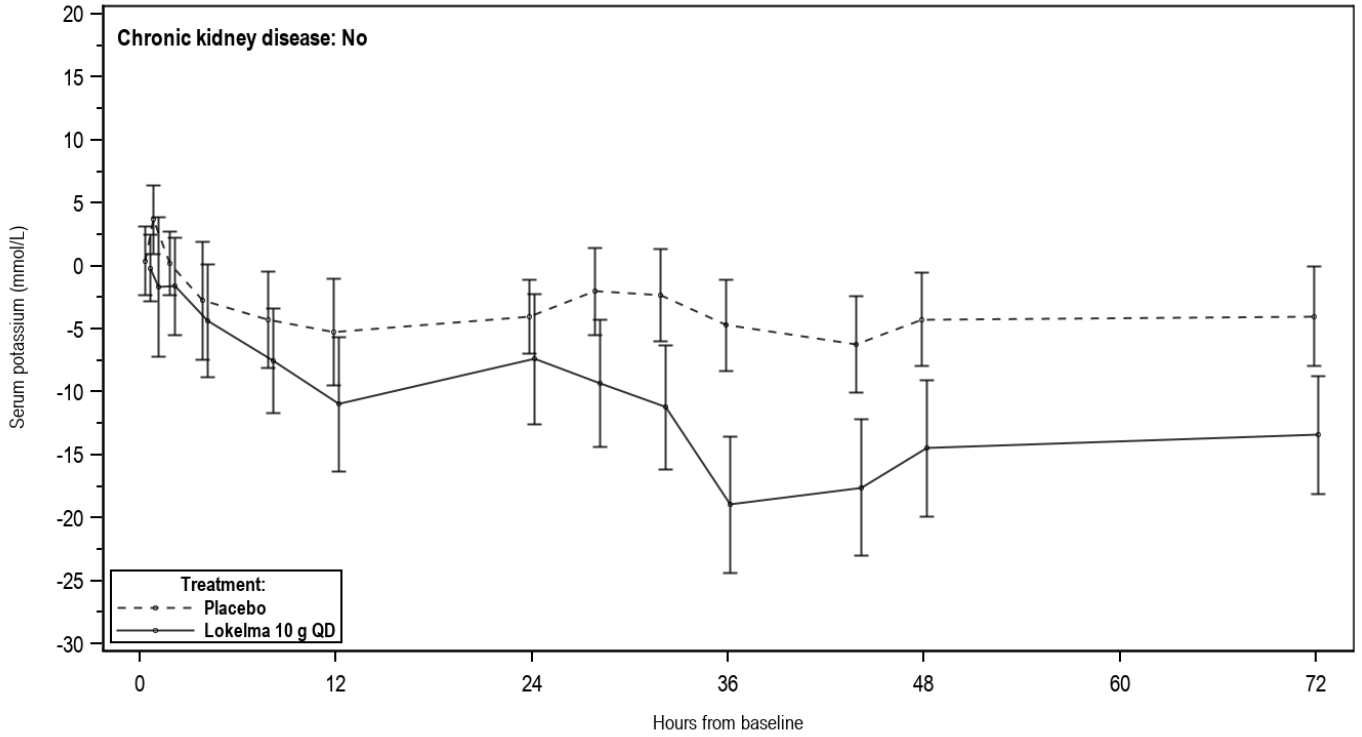
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.

f_zs002_sk_overtimem_c.pdf generated by zs002_overtime.sas at 23:32:13 on 19 January 2021

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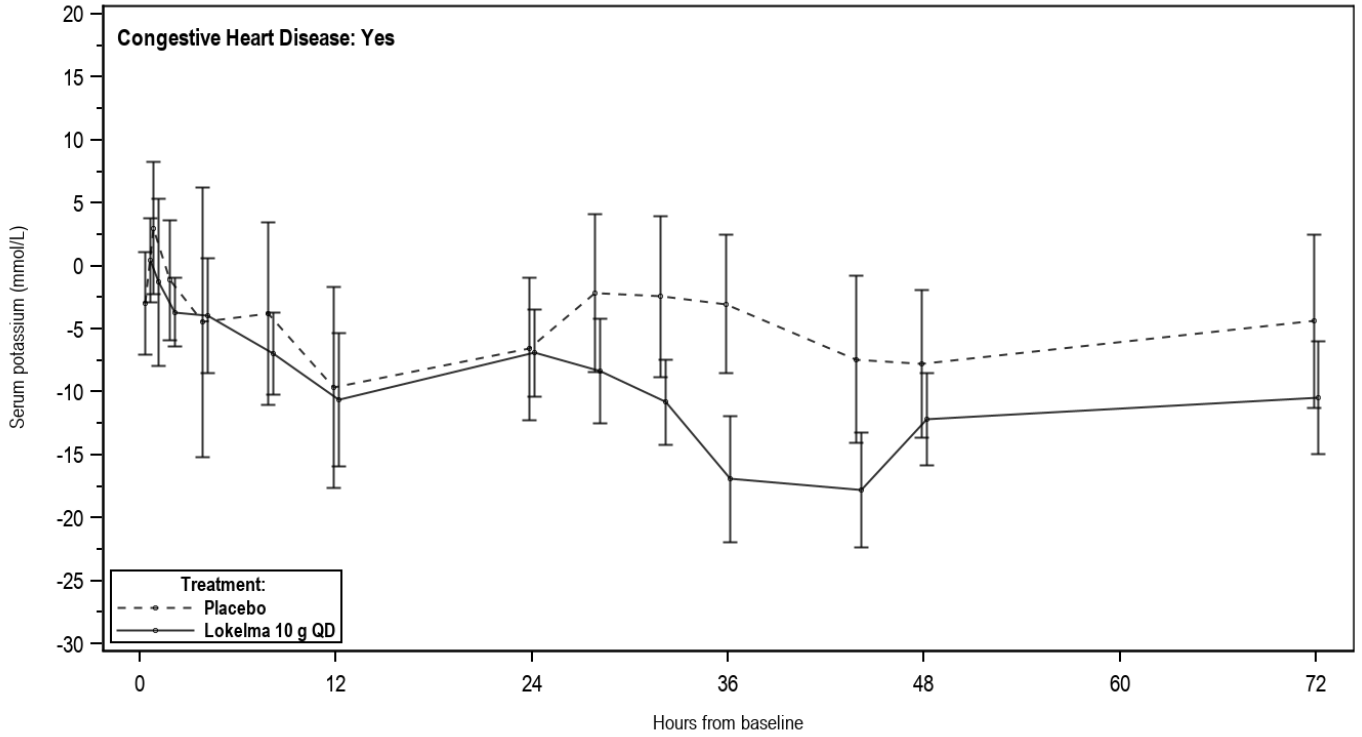
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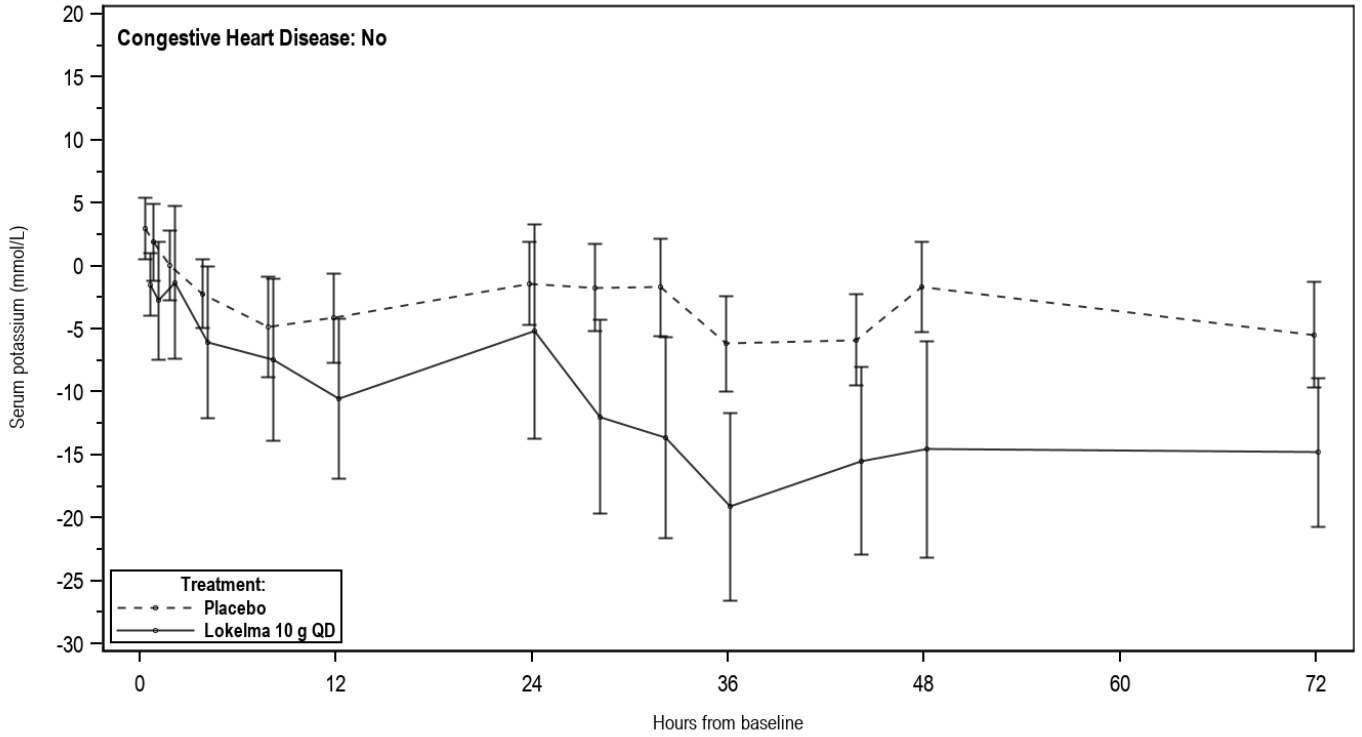
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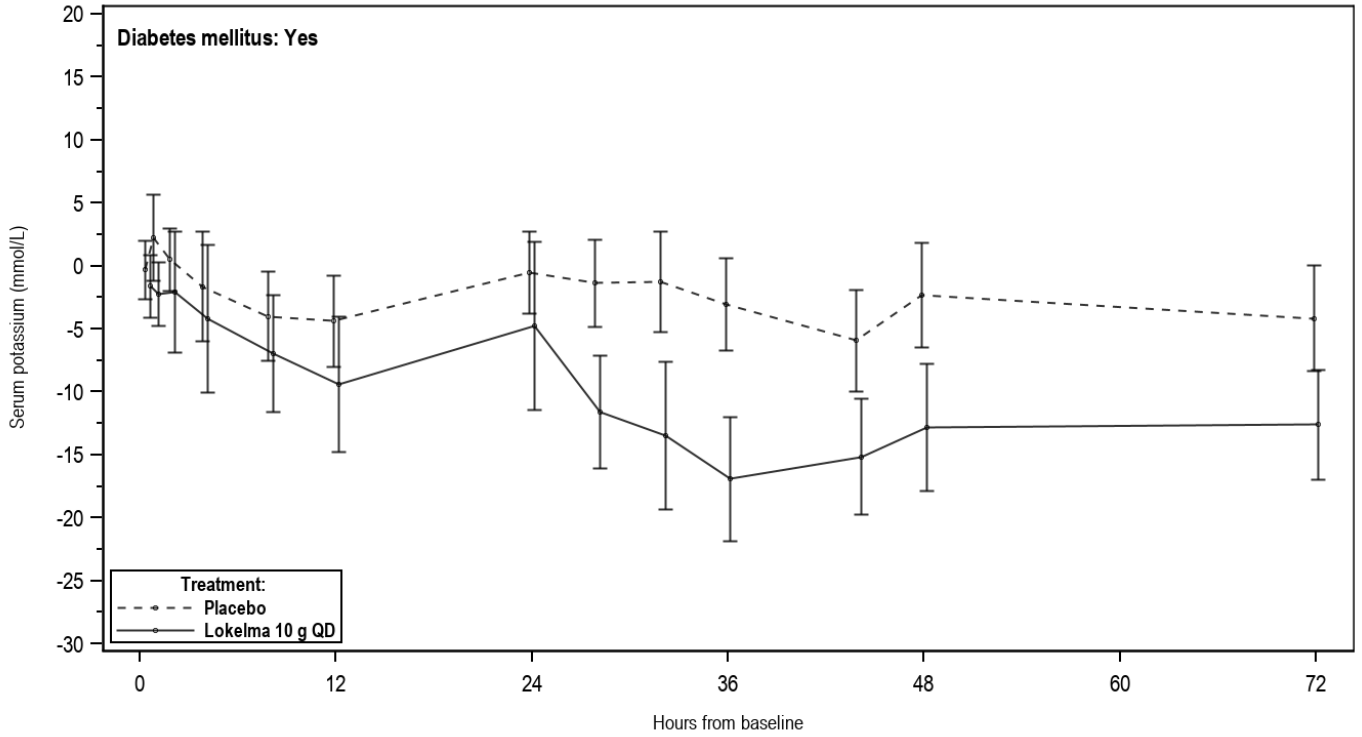
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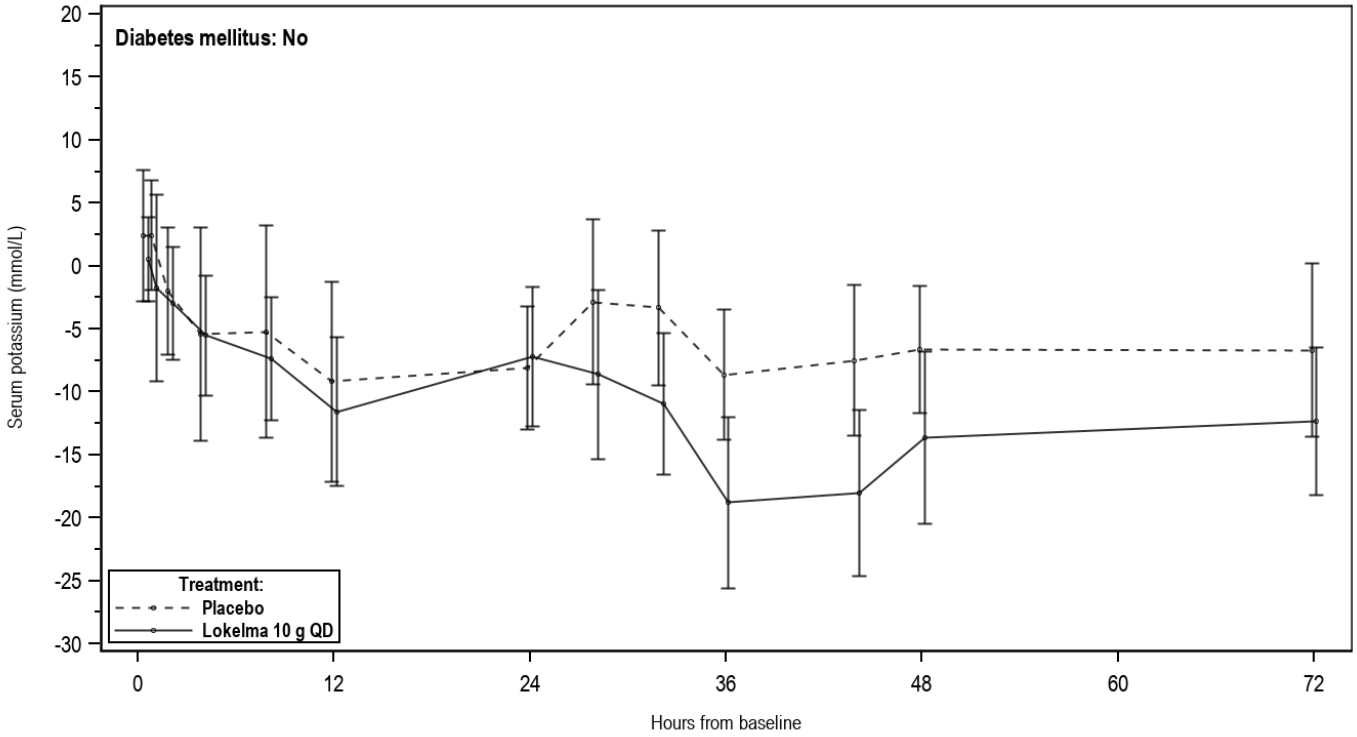
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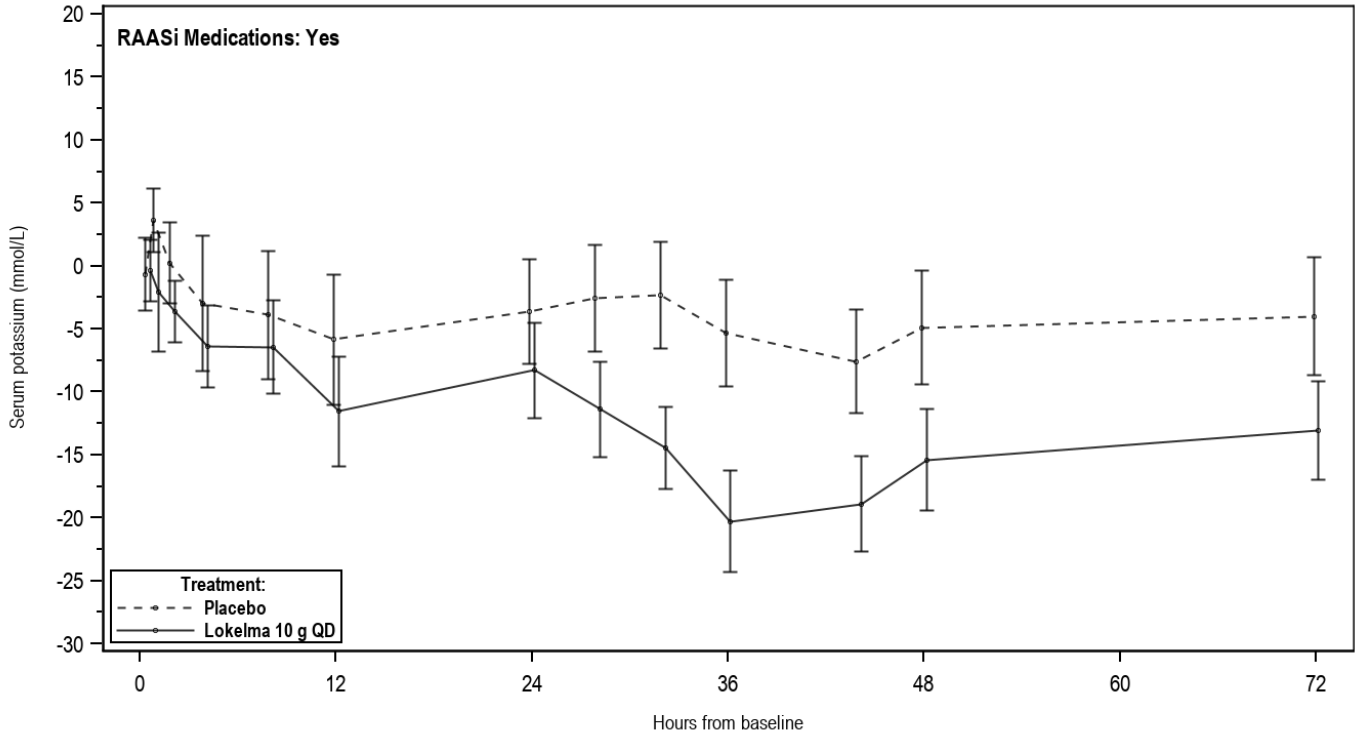
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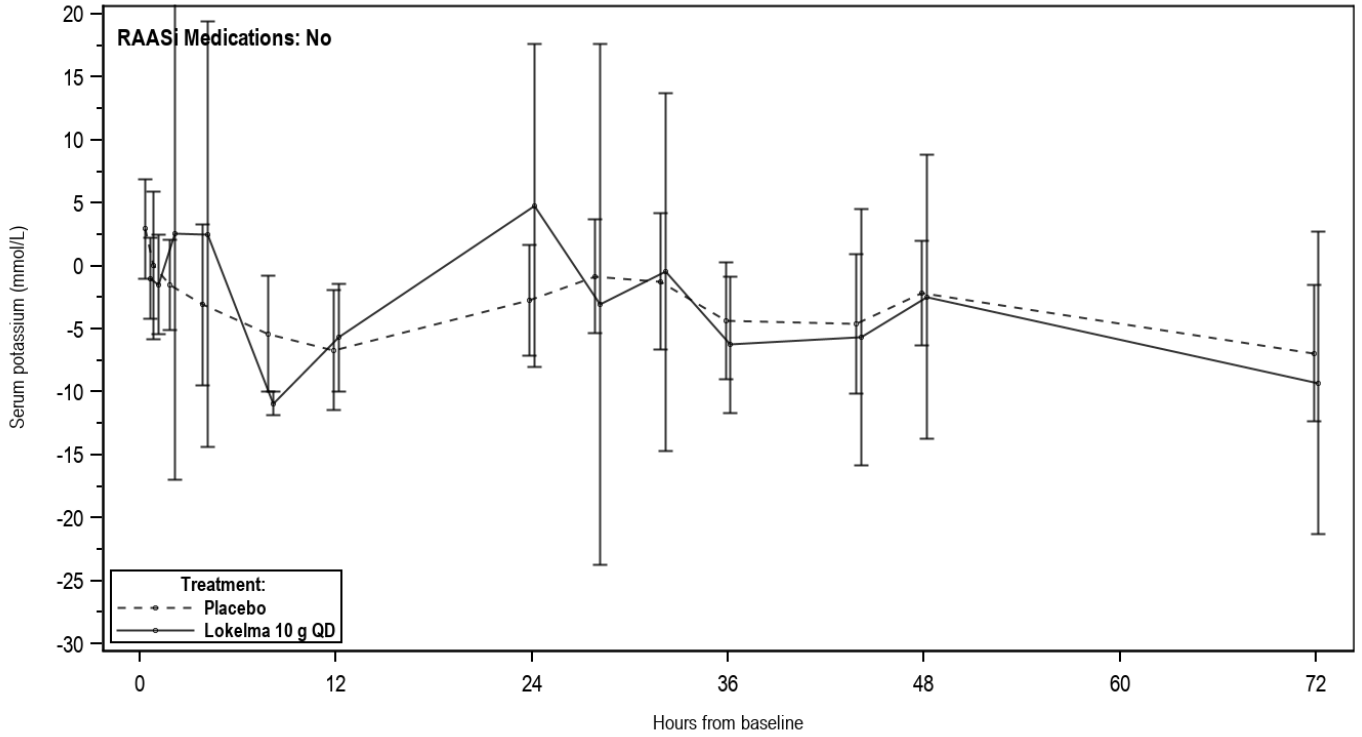
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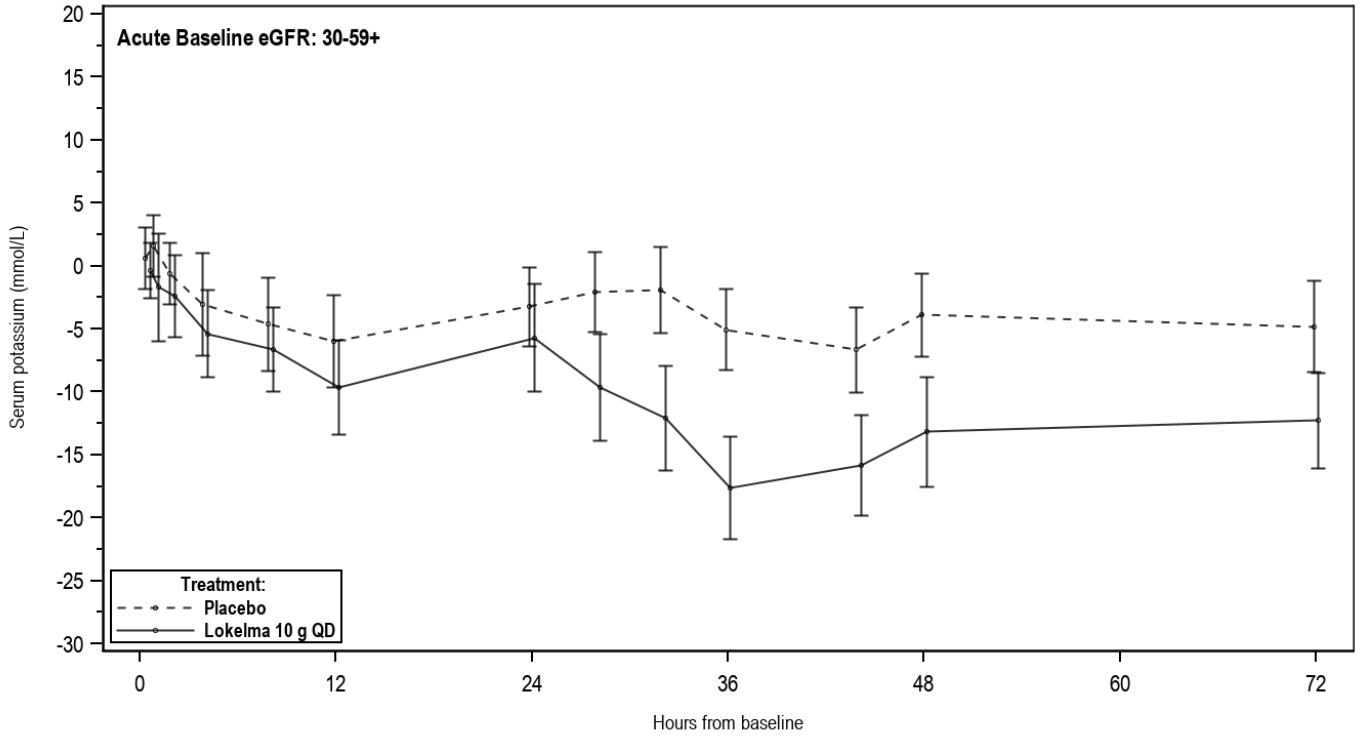
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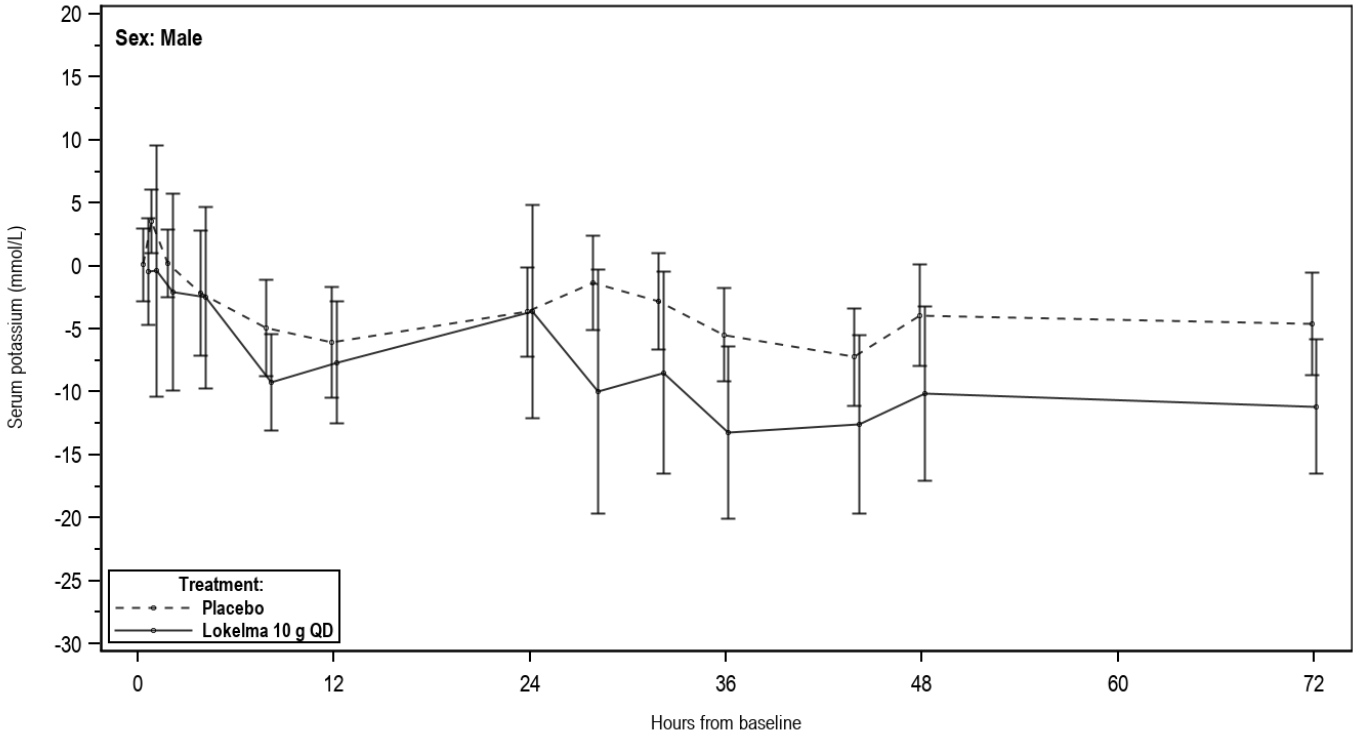
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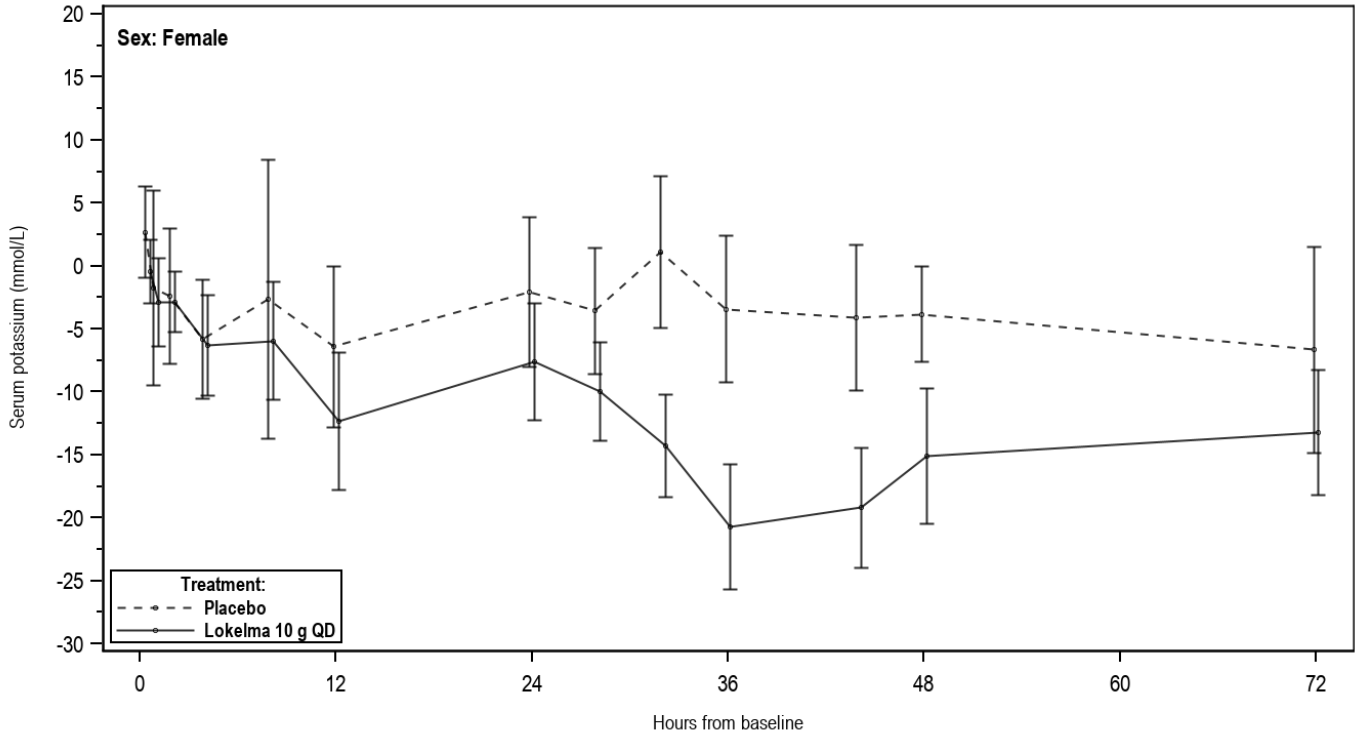
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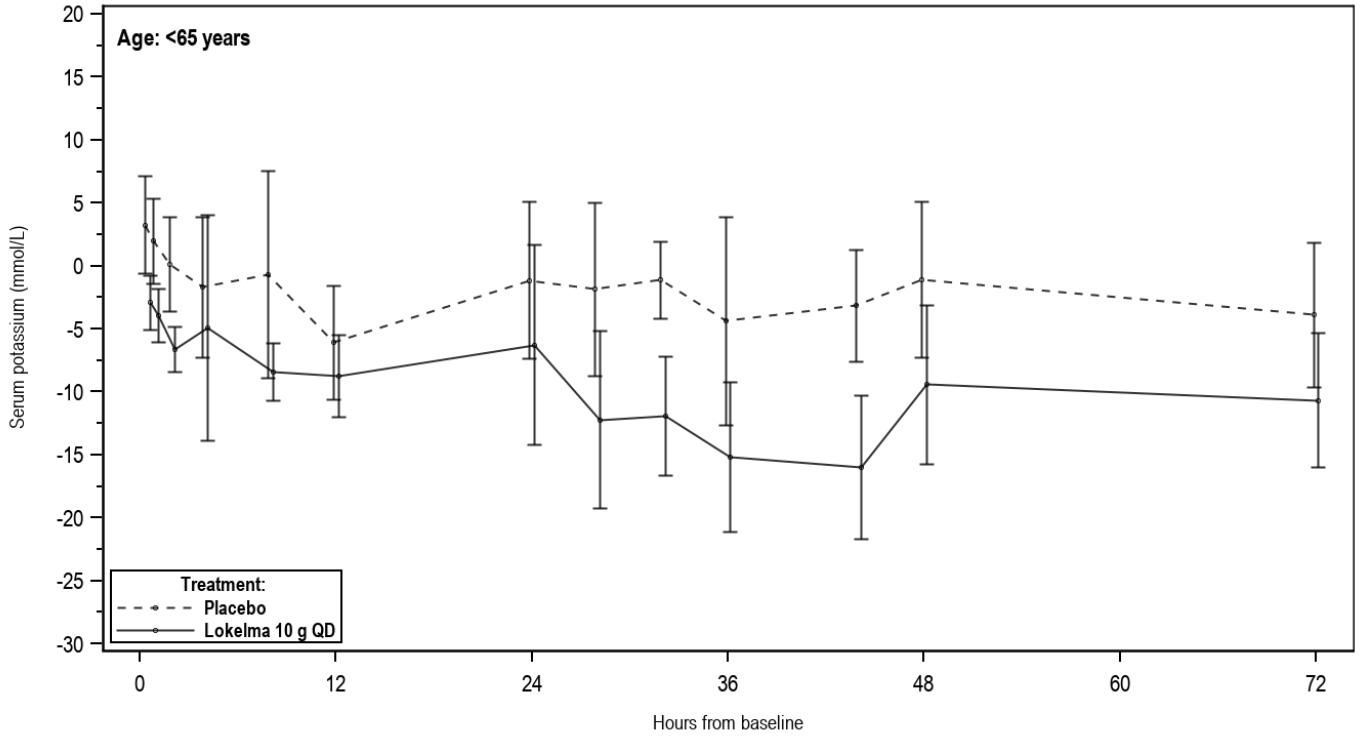
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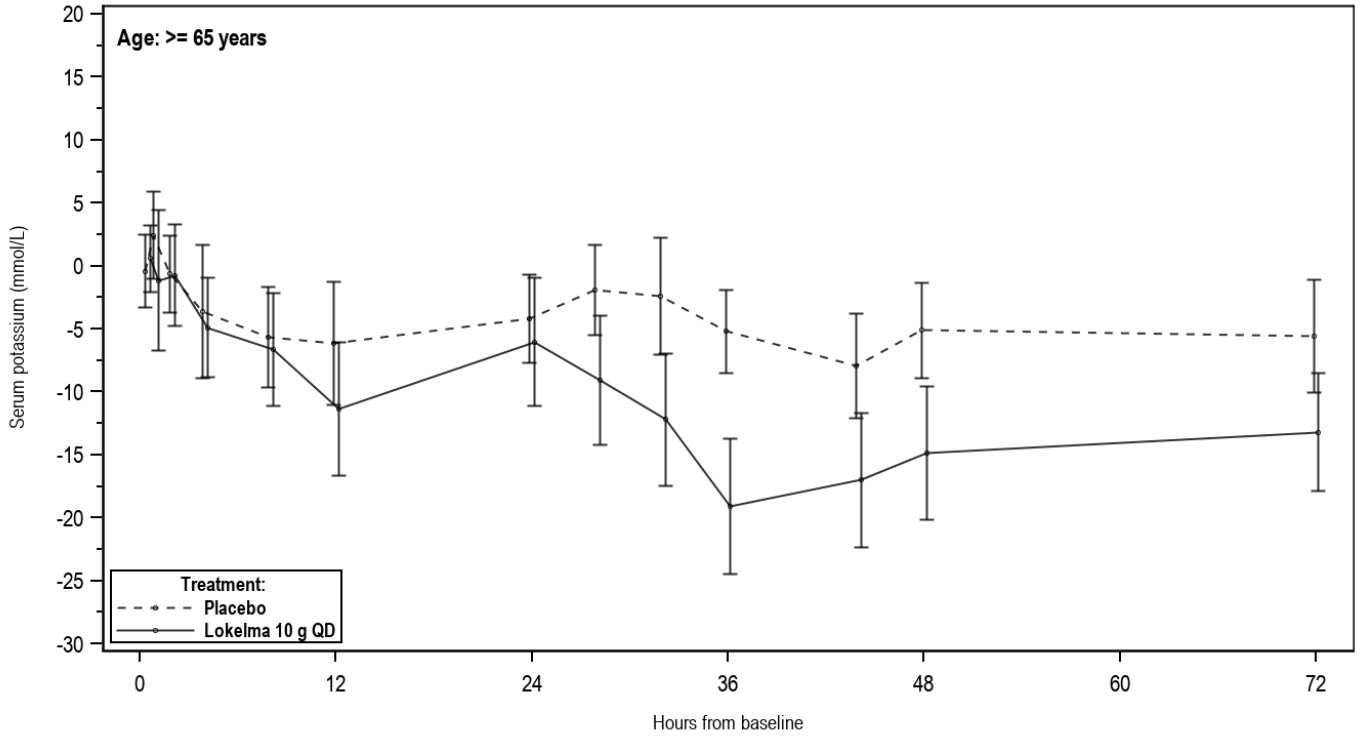
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Table 1.1.3.1 - Study ZS-002: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)					Lokelma 10g QD (N=24)							
Subgroup / Category	N	Patients with events [n(%)]	KM % at 12 hours	KM % at 24 hours	Median time (hours)	N	Patients with events [n(%)]	KM % at 12 hours	KM % at 24 hours	Median time (hours)	Hazard ratio (95% CI)	Hazard ratio p-value	p-value for interaction
Overall	30	22 (73.3%)	60.00	56.67	37.8	24	23 (95.8%)	37.50	25.00	7.6	2.19 (1.19, 4.02)	0.0118	
Chronic kidney disease													0.9900
No	24	17 (70.8%)	58.33	58.33	38.0	17	16 (94.1%)	41.18	23.53	8.0	2.08 (1.03, 4.21)	0.0407	
Yes	6	5 (83.3%)	66.67	50.00	25.8	7	7 (100.0%)	28.57	28.57	4.0	2.06 (0.58, 7.31)	0.2630	
Congestive heart disease													0.0649
No	19	13 (68.4%)	73.68	68.42	38.0	11	11 (100.0%)	27.27	18.18	4.0	5.10 (1.92, 13.52)	0.0010	
Yes	11	9 (81.8%)	36.36	36.36	4.0	13	12 (92.3%)	46.15	30.77	8.0	1.14 (0.47, 2.75)	0.7724	
Diabetes mellitus													0.6052
No	11	9 (81.8%)	54.55	54.55	38.0	13	12 (92.3%)	30.77	15.38	4.0	1.64 (0.67, 4.00)	0.2751	
Yes	19	13 (68.4%)	63.16	57.89	37.5	11	11 (100.0%)	45.45	36.36	8.0	2.58 (1.08, 6.18)	0.0338	
RAASi medications													0.9994
No	11	9 (81.8%)	45.45	45.45	8.0	4	4 (100.0%)	0.00	0.00	7.6	2.23 (0.61, 8.17)	0.2263	
Yes	19	13 (68.4%)	68.42	63.16	38.0	20	19 (95.0%)	45.00	30.00	6.0	2.41 (1.16, 5.00)	0.0187	
Sex													0.7612
Male	23	18 (78.3%)	60.87	56.52	37.5	9	9 (100.0%)	22.22	22.22	7.5	2.36 (1.03, 5.38)	0.0420	
Female	7	4 (57.1%)	57.14	57.14	38.0	15	14 (93.3%)	46.67	26.67	8.0	2.33 (0.72, 7.51)	0.1559	
Age (years)													0.1287
<65 years	9	6 (66.7%)	88.89	77.78	44.0	7	7 (100.0%)	14.29	14.29	4.0	10.38 (2.02, 53.29)	0.0050	
>=65 years	21	16 (76.2%)	47.62	47.62	8.0	17	16 (94.1%)	47.06	29.41	8.0	1.56 (0.77, 3.16)	0.2201	
Baseline S-K													-
<=5.3 mmol/L	25	18 (72.0%)	60.00	60.00	38.0	19	18 (94.7%)	42.11	31.58	8.0	-	-	
5.4-5.5 mmol/L	2	1 (50.0%)	50.00	50.00	NR	3	3 (100.0%)	33.33	0.00	4.0	-	-	
>5.5 mmol/L	3	3 (100.0%)	66.67	33.33	14.0	2	2 (100.0%)	0.00	0.00	2.5	-	-	
Baseline eGFR													-
15-29 ml/min/1.73m**2	1	1 (100.0%)	0.00	0.00	4.0	1	1 (100.0%)	0.00	0.00	4.0	-	-	
30-59 ml/min/1.73m**2	28	20 (71.4%)	60.71	57.14	37.8	22	21 (95.5%)	40.91	27.27	7.6	-	-	
>=60 ml/min/1.73m**2	1	1 (100.0%)	100.0	100.0	68.0	1	1 (100.0%)	0.00	0.00	8.0	-	-	

Hazard ratio derived from Cox proportional hazard model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present) and an interaction term for subgroup*treatment group were added.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
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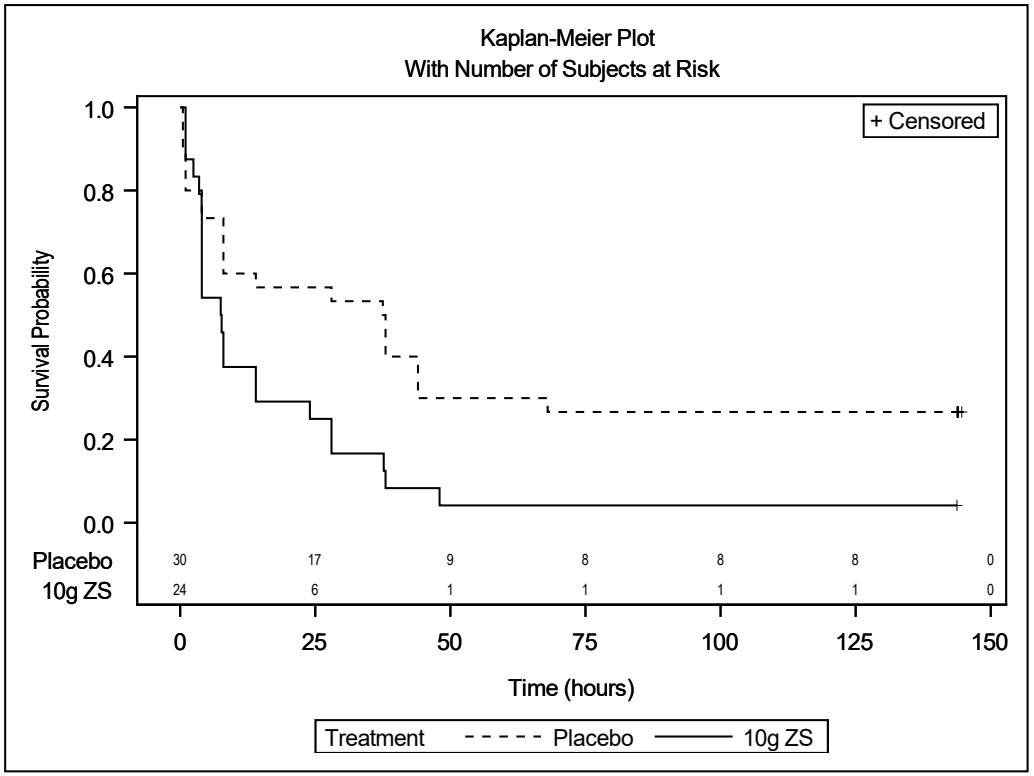
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Figure 1.1.3.2 - Study ZS-002: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

Overall



Plots shown for subgroups where interaction p-value is <=0.05

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Table 1.1.4.1 - Study ZS-002: Time to normalisation of serum potassium, ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)					Lokelma 10g QD (N=24)							
Subgroup / Category	N	Patients with events [n(%)]	KM % at 12 hours	KM % at 24 hours	Median time (hours)	N	Patients with events [n(%)]	KM % at 12 hours	KM % at 24 hours	Median time (hours)	Hazard ratio (95% CI)	Hazard ratio p-value	p-value for interaction
Overall	30	27 (90.0%)	20.00	20.00	2.0	24	24 (100.0%)	12.50	8.33	0.5	1.70 (0.96, 2.99)	0.0673	
Chronic kidney disease													0.7576
No	24	22 (91.7%)	20.83	20.83	3.0	17	17 (100.0%)	11.76	5.88	1.0	1.62 (0.84, 3.12)	0.1459	
Yes	6	5 (83.3%)	16.67	16.67	1.0	7	7 (100.0%)	14.29	14.29	0.5	1.91 (0.60, 6.13)	0.2741	
Congestive heart disease													0.0030
No	19	16 (84.2%)	31.58	31.58	4.0	11	11 (100.0%)	0.00	0.00	0.5	3.69 (1.55, 8.80)	0.0032	
Yes	11	11 (100.0%)	0.00	0.00	0.5	13	13 (100.0%)	23.08	15.38	1.0	0.55 (0.22, 1.34)	0.1888	
Diabetes mellitus													0.2373
No	11	11 (100.0%)	9.09	9.09	2.0	13	13 (100.0%)	15.38	7.69	1.0	1.22 (0.53, 2.80)	0.6369	
Yes	19	16 (84.2%)	26.32	26.32	3.5	11	11 (100.0%)	9.09	9.09	0.5	2.11 (0.95, 4.69)	0.0659	
RAASi medications													0.8685
No	11	11 (100.0%)	0.00	0.00	1.0	4	4 (100.0%)	0.00	0.00	0.5	5.19 (1.10, 24.49)	0.0375	
Yes	19	16 (84.2%)	31.58	31.58	4.0	20	20 (100.0%)	15.00	10.00	1.0	2.01 (1.00, 4.03)	0.0509	
Sex													0.1949
Male	23	20 (87.0%)	26.09	26.09	3.5	9	9 (100.0%)	11.11	11.11	0.5	2.11 (0.93, 4.80)	0.0743	
Female	7	7 (100.0%)	0.00	0.00	1.0	15	15 (100.0%)	13.33	6.67	1.0	0.97 (0.38, 2.49)	0.9515	
Age (years)													0.1371
<65 years	9	7 (77.8%)	33.33	33.33	2.0	7	7 (100.0%)	14.29	14.29	0.5	3.18 (1.04, 9.76)	0.0429	
>=65 years	21	20 (95.2%)	14.29	14.29	2.0	17	17 (100.0%)	11.76	5.88	1.0	1.31 (0.68, 2.54)	0.4167	
Baseline S-K													-
<=5.3 mmol/L	25	24 (96.0%)	12.00	12.00	2.0	19	19 (100.0%)	0.00	0.00	0.5	-	-	
5.4-5.5 mmol/L	2	1 (50.0%)	50.00	50.00	NR	3	3 (100.0%)	33.33	0.00	8.0	-	-	
>5.5 mmol/L	3	2 (66.7%)	66.67	66.67	44.0	2	2 (100.0%)	100.0	100.0	33.0	-	-	
Baseline eGFR													-
15-29 ml/min/1.73m**2	1	1 (100.0%)	0.00	0.00	4.0	1	1 (100.0%)	0.00	0.00	8.0	-	-	
30-59 ml/min/1.73m**2	28	25 (89.3%)	21.43	21.43	2.0	22	22 (100.0%)	13.64	9.09	0.5	-	-	
>=60 ml/min/1.73m**2	1	1 (100.0%)	0.00	0.00	0.5	1	1 (100.0%)	0.00	0.00	1.0	-	-	

Hazard ratio derived from Cox proportional hazard model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present) and an interaction term for subgroup*treatment group were added.
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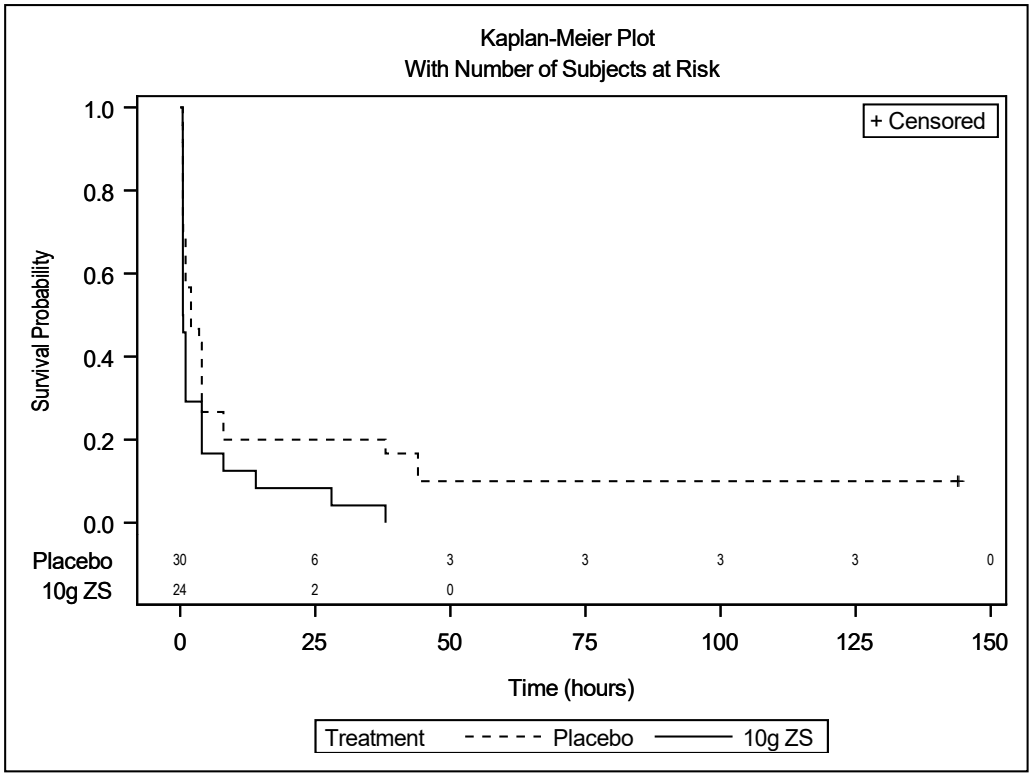
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Figure 1.1.4.2 - Study ZS-002: Time to normalisation of serum potassium, ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

Overall



Plots shown for subgroups where interaction p-value is <=0.05

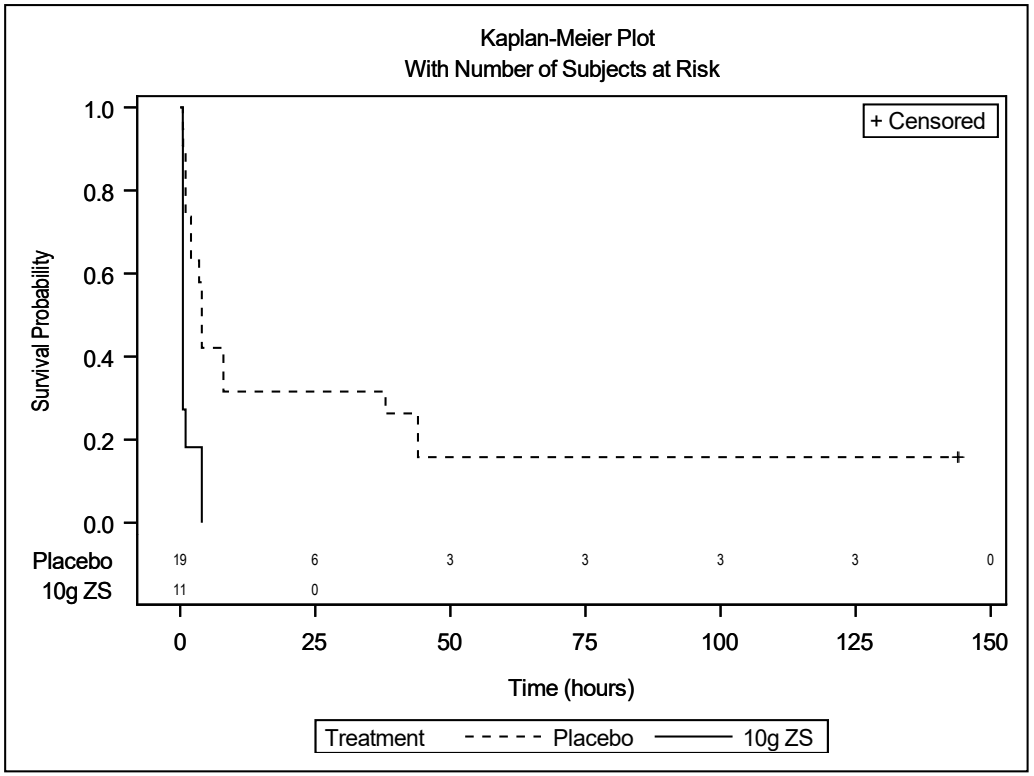
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Figure 1.1.4.2 - Study ZS-002: Time to normalisation of serum potassium, ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

Congestive heart disease: No



Plots shown for subgroups where interaction p-value is <=0.05

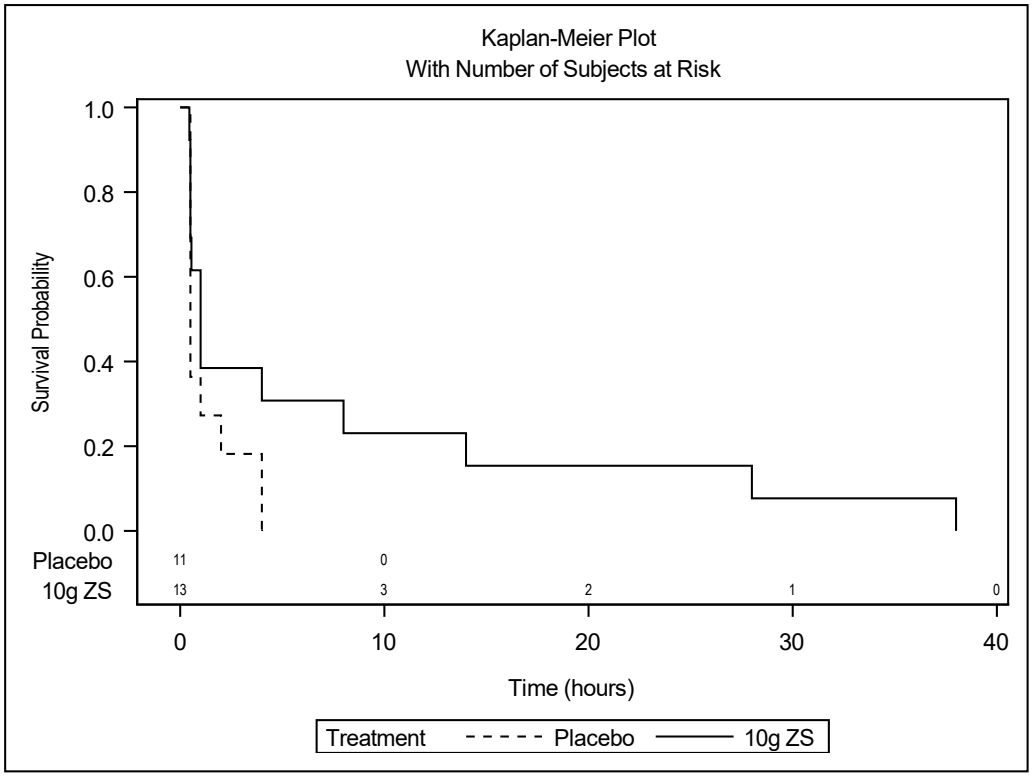
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Figure 1.1.4.2 - Study ZS-002: Time to normalisation of serum potassium, ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

Congestive heart disease: Yes



Plots shown for subgroups where interaction p-value is <=0.05

f_zs002_tte_norm generated by zs002ac_tte.sas at 15:38:10 on 19 January 2021

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Table 1.1.5.1 - Study ZS-002: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)		Lokelma 10g QD (N=24)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Overall											
Day 1 / 30-min Post 1st	29	9 (31.0%)	24	13 (54.2%)	2.63 (0.85, 8.08)	0.0923	1.75 (0.75, 4.08)	0.1990	23.1 (-12.6, 58.9)	0.2047	
Day 1 / 1-hr Post 1st	30	9 (30.0%)	24	15 (62.5%)	3.89 (1.25, 12.12)	0.0192	2.08 (0.91, 4.76)	0.0817	32.5 (-4.7, 69.7)	0.0869	
Day 1 / 2-hr Post 1st	30	14 (46.7%)	23	14 (60.9%)	1.78 (0.59, 5.35)	0.3064	1.30 (0.62, 2.74)	0.4821	14.2 (-26.0, 54.4)	0.4884	
Day 1 / 4-hr Post 1st	30	16 (53.3%)	24	16 (66.7%)	1.75 (0.58, 5.32)	0.3236	1.25 (0.63, 2.50)	0.5279	13.3 (-28.5, 55.2)	0.5322	
Day 1 / 4-hr Post 2nd	28	15 (53.6%)	24	17 (70.8%)	2.10 (0.67, 6.66)	0.2054	1.32 (0.66, 2.65)	0.4304	17.3 (-26.0, 60.5)	0.4338	
Day 1 / 4-hr Post 3rd	30	19 (63.3%)	24	20 (83.3%)	2.89 (0.78, 10.68)	0.1105	1.32 (0.70, 2.47)	0.3916	20.0 (-26.3, 66.3)	0.3973	
Day 2 / 0-hr	30	18 (60.0%)	24	17 (70.8%)	1.62 (0.52, 5.08)	0.4090	1.18 (0.61, 2.29)	0.6236	10.8 (-32.8, 54.4)	0.6264	
Day 2 / 4-hr Post 1st	29	13 (44.8%)	24	21 (87.5%)	8.62 (2.10, 35.42)	0.0028	1.95 (0.98, 3.90)	0.0581	42.7 (-2.0, 87.3)	0.0611	
Day 2 / 4-hr Post 2nd	28	10 (35.7%)	24	20 (83.3%)	9.00 (2.40, 33.78)	0.0011	2.33 (1.09, 4.98)	0.0287	47.6 (4.9, 90.3)	0.0289	
Day 2 / 4-hr Post 3rd	29	19 (65.5%)	24	23 (95.8%)	12.10 (1.42, 103.22)	0.0226	1.46 (0.80, 2.69)	0.2199	30.3 (-18.7, 79.3)	0.2254	
Day 2 / 20-hr Post 1st	29	18 (62.1%)	24	24 (100.0%)	n/a	n/a	1.61 (0.87, 2.97)	0.1261	37.9 (-11.3, 87.2)	0.1309	
Day 3 / 0-hr	30	14 (46.7%)	24	20 (83.3%)	5.71 (1.57, 20.78)	0.0081	1.79 (0.90, 3.54)	0.0961	36.7 (-7.3, 80.6)	0.1020	
Chronic kidney disease											
Day 1 / 30-min Post 1st											0.7401
No	23	7 (30.4%)	17	8 (47.1%)	2.03 (0.55, 7.47)	0.2860	1.55 (0.56, 4.26)	0.3997	16.6 (-23.0, 56.3)	0.4112	
Yes	6	2 (33.3%)	7	5 (71.4%)	5.00 (0.47, 52.96)	0.1814	2.14 (0.42, 11.04)	0.3623	38.1 (-39.7, 115.9)	0.3372	
Day 1 / 1-hr Post 1st											0.2632
No	24	5 (20.8%)	17	10 (58.8%)	5.43 (1.37, 21.57)	0.0162	2.82 (0.97, 8.26)	0.0581	38.0 (-2.8, 78.8)	0.0678	
Yes	6	4 (66.7%)	7	5 (71.4%)	1.25 (0.12, 13.24)	0.8530	1.07 (0.29, 3.99)	0.9181	4.8 (-85.7, 95.3)	0.9179	
Day 1 / 2-hr Post 1st											0.9840
No	24	10 (41.7%)	17	9 (52.9%)	1.57 (0.45, 5.50)	0.4767	1.27 (0.52, 3.13)	0.6022	11.3 (-31.9, 54.4)	0.6087	
Yes	6	4 (66.7%)	6	5 (83.3%)	2.50 (0.16, 38.60)	0.5117	1.25 (0.34, 4.65)	0.7394	16.7 (-81.3, 114.7)	0.7389	
Day 1 / 4-hr Post 1st											0.5411
No	24	12 (50.0%)	17	12 (70.6%)	2.40 (0.64, 8.94)	0.1920	1.41 (0.63, 3.14)	0.3983	20.6 (-28.4, 69.5)	0.4097	
Yes	6	4 (66.7%)	7	4 (57.1%)	0.67 (0.07, 6.41)	0.7255	0.86 (0.21, 3.43)	0.8274	-9.5 (-95.6, 76.5)	0.8283	
Day 1 / 4-hr Post 2nd											0.8785
No	23	12 (52.2%)	17	12 (70.6%)	2.20 (0.58, 8.28)	0.2439	1.35 (0.61, 3.01)	0.4590	18.4 (-31.2, 68.1)	0.4674	
Yes	5	3 (60.0%)	7	5 (71.4%)	1.67 (0.15, 18.87)	0.6800	1.19 (0.28, 4.98)	0.8113	11.4 (-80.9, 103.8)	0.8084	
Day 1 / 4-hr Post 3rd											0.6573
No	24	14 (58.3%)	17	14 (82.4%)	3.33 (0.75, 14.76)	0.1127	1.41 (0.67, 2.96)	0.3616	24.0 (-28.8, 76.9)	0.3732	
Yes	6	5 (83.3%)	7	6 (85.7%)	1.20 (0.06, 24.47)	0.9057	1.03 (0.31, 3.37)	0.9629	2.4 (-97.8, 102.6)	0.9629	
Day 2 / 0-hr											0.7762
No	24	15 (62.5%)	17	12 (70.6%)	1.44 (0.38, 5.45)	0.5913	1.13 (0.53, 2.41)	0.7534	8.1 (-42.9, 59.0)	0.7557	
Yes	6	3 (50.0%)	7	5 (71.4%)	2.50 (0.25, 24.71)	0.4332	1.43 (0.34, 5.98)	0.6253	21.4 (-63.0, 105.8)	0.6187	
Day 2 / 4-hr Post 1st											0.9461
No	23	10 (43.5%)	17	14 (82.4%)	6.07 (1.36, 27.05)	0.0181	1.89 (0.84, 4.26)	0.1229	38.9 (-12.0, 89.7)	0.1341	
Yes	6	3 (50.0%)	7	7 (100.0%)	n/a	n/a	2.00 (0.52, 7.73)	0.3152	50.0 (-43.2, 143.2)	0.2931	

OR, RR and ARR derived from model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
Patients are included in the count of patients meeting criteria if the patients' serum potassium is in normal range at the timepoint. This is the definition used in the majority of the study CSR's. ZS-002 CSR table 14.2.3 is an exception as it counts patients in normal range before the timepoint even if the patient is not still in normal range at the timepoint. The normal range used in ZS-002 CSR (3.5 to 4.9) has been retained. All other studies define normal range as 3.5 to 5.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 1.1.5.1 - Study ZS-002: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)		Lokelma 10g QD (N=24)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Chronic kidney disease *(contd.)*											
Day 2 / 4-hr Post 2nd											0.7013
No	24	9 (37.5%)	17	14 (82.4%)	7.78 (1.74, 34.71)	0.0072	2.20 (0.95, 5.07)	0.0656	44.9 (-4.8, 94.5)	0.0764	
Yes	4	1 (25.0%)	7	6 (85.7%)	18.00 (0.81, 399.03)	0.0676	3.43 (0.41, 28.48)	0.2540	60.7 (-23.6, 145.0)	0.1580	
Day 2 / 4-hr Post 3rd											0.9573
No	23	15 (65.2%)	17	16 (94.1%)	8.53 (0.95, 76.62)	0.0556	1.44 (0.71, 2.92)	0.3074	28.9 (-27.8, 85.6)	0.3179	
Yes	6	4 (66.7%)	7	7 (100.0%)	n/a	n/a	1.50 (0.44, 5.12)	0.5177	33.3 (-65.4, 132.1)	0.5083	
Day 2 / 20-hr Post 1st											0.7319
No	23	15 (65.2%)	17	17 (100.0%)	n/a	n/a	1.53 (0.77, 3.07)	0.2276	34.8 (-23.1, 92.7)	0.2388	
Yes	6	3 (50.0%)	7	7 (100.0%)	n/a	n/a	2.00 (0.52, 7.73)	0.3152	50.0 (-43.2, 143.2)	0.2931	
Day 3 / 0-hr											0.8213
No	24	11 (45.8%)	17	13 (76.5%)	3.84 (0.97, 15.25)	0.0557	1.67 (0.75, 3.72)	0.2115	30.6 (-19.0, 80.3)	0.2262	
Yes	6	3 (50.0%)	7	7 (100.0%)	n/a	n/a	2.00 (0.52, 7.73)	0.3152	50.0 (-43.2, 143.2)	0.2931	
Congestive heart disease											
Day 1 / 30-min Post 1st											0.0155
No	18	2 (11.1%)	11	8 (72.7%)	21.33 (2.94, 154.55)	0.0025	6.55 (1.39, 30.82)	0.0175	61.6 (8.9, 114.3)	0.0219	
Yes	11	7 (63.6%)	13	5 (38.5%)	0.36 (0.07, 1.88)	0.2243	0.60 (0.19, 1.90)	0.3898	-25.2 (-83.1, 32.8)	0.3946	
Day 1 / 1-hr Post 1st											0.3431
No	19	4 (21.1%)	11	7 (63.6%)	6.56 (1.26, 34.20)	0.0255	3.02 (0.88, 10.33)	0.0776	42.6 (-8.9, 94.0)	0.1048	
Yes	11	5 (45.5%)	13	8 (61.5%)	1.92 (0.38, 9.80)	0.4328	1.35 (0.44, 4.14)	0.5951	16.1 (-42.3, 74.4)	0.5891	
Day 1 / 2-hr Post 1st											0.4020
No	19	7 (36.8%)	11	7 (63.6%)	3.00 (0.64, 14.02)	0.1626	1.73 (0.61, 4.92)	0.3065	26.8 (-27.7, 81.3)	0.3350	
Yes	11	7 (63.6%)	12	7 (58.3%)	0.80 (0.15, 4.30)	0.7947	0.92 (0.32, 2.61)	0.8707	-5.3 (-69.3, 58.6)	0.8709	
Day 1 / 4-hr Post 1st											0.1775
No	19	9 (47.4%)	11	10 (90.9%)	11.11 (1.18, 104.81)	0.0355	1.92 (0.78, 4.72)	0.1560	43.5 (-20.7, 107.8)	0.1843	
Yes	11	7 (63.6%)	13	6 (46.2%)	0.49 (0.09, 2.53)	0.3944	0.73 (0.24, 2.16)	0.5637	-17.5 (-77.4, 42.4)	0.5672	
Day 1 / 4-hr Post 2nd											0.8248
No	17	9 (52.9%)	11	7 (63.6%)	1.56 (0.33, 7.36)	0.5775	1.20 (0.45, 3.23)	0.7150	10.7 (-47.8, 69.2)	0.7200	
Yes	11	6 (54.5%)	13	10 (76.9%)	2.78 (0.48, 16.03)	0.2534	1.41 (0.51, 3.88)	0.5056	22.4 (-42.3, 87.0)	0.4974	
Day 1 / 4-hr Post 3rd											0.5401
No	19	11 (57.9%)	11	10 (90.9%)	7.27 (0.77, 68.89)	0.0837	1.57 (0.67, 3.70)	0.3017	33.0 (-32.9, 98.9)	0.3263	
Yes	11	8 (72.7%)	13	10 (76.9%)	1.25 (0.20, 7.96)	0.8132	1.06 (0.42, 2.68)	0.9059	4.2 (-65.2, 73.6)	0.9056	
Day 2 / 0-hr											0.6007
No	19	9 (47.4%)	11	7 (63.6%)	1.94 (0.42, 8.92)	0.3922	1.34 (0.50, 3.61)	0.5580	16.3 (-40.1, 72.7)	0.5718	
Yes	11	9 (81.8%)	13	10 (76.9%)	0.74 (0.10, 5.49)	0.7690	0.94 (0.38, 2.31)	0.8932	-4.9 (-76.5, 66.7)	0.8934	
Day 2 / 4-hr Post 1st											0.5621
No	18	7 (38.9%)	11	10 (90.9%)	15.71 (1.63, 151.12)	0.0171	2.34 (0.89, 6.14)	0.0849	52.0 (-11.3, 115.3)	0.1071	
Yes	11	6 (54.5%)	13	11 (84.6%)	4.58 (0.67, 31.20)	0.1198	1.55 (0.57, 4.19)	0.3870	30.1 (-36.3, 96.4)	0.3746	

OR, RR and ARR derived from model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
Patients are included in the count of patients meeting criteria if the patients' serum potassium is in normal range at the timepoint. This is the definition used in the majority of the study CSR's. ZS-002 CSR table 14.2.3 is an exception as it counts patients in normal range before the timepoint even if the patient is not still in normal range at the timepoint. The normal range used in ZS-002 CSR (3.5 to 4.9) has been retained. All other studies define normal range as 3.5 to 5.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 1.1.5.1 - Study ZS-002: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)		Lokelma 10g QD (N=24)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Congestive heart disease *(contd.)*											
Day 2 / 4-hr Post 2nd											0.9962
No	17	6 (35.3%)	11	9 (81.8%)	8.25 (1.33, 51.26)	0.0236	2.32 (0.83, 6.51)	0.1107	46.5 (-13.9, 107.0)	0.1315	
Yes	11	4 (36.4%)	13	11 (84.6%)	9.62 (1.38, 67.23)	0.0224	2.33 (0.74, 7.31)	0.1481	48.3 (-13.2, 109.7)	0.1235	
Day 2 / 4-hr Post 3rd											0.8232
No	18	12 (66.7%)	11	10 (90.9%)	5.00 (0.51, 48.75)	0.1660	1.36 (0.59, 3.16)	0.4688	24.2 (-43.6, 92.0)	0.4835	
Yes	11	7 (63.6%)	13	13 (100.0%)	n/a	n/a	1.57 (0.63, 3.94)	0.3350	36.4 (-35.6, 108.3)	0.3219	
Day 2 / 20-hr Post 1st											0.6674
No	18	10 (55.6%)	11	11 (100.0%)	n/a	n/a	1.80 (0.76, 4.24)	0.1785	44.4 (-24.0, 112.8)	0.2028	
Yes	11	8 (72.7%)	13	13 (100.0%)	n/a	n/a	1.37 (0.57, 3.32)	0.4785	27.3 (-46.9, 101.4)	0.4708	
Day 3 / 0-hr											0.3994
No	19	6 (31.6%)	11	8 (72.7%)	5.78 (1.12, 29.85)	0.0363	2.30 (0.80, 6.64)	0.1224	41.1 (-15.2, 97.5)	0.1526	
Yes	11	8 (72.7%)	13	12 (92.3%)	4.50 (0.39, 51.28)	0.2258	1.27 (0.52, 3.10)	0.6014	19.6 (-53.0, 92.2)	0.5970	
Diabetes mellitus											
Day 1 / 30-min Post 1st											0.8934
No	11	3 (27.3%)	13	6 (46.2%)	2.29 (0.41, 12.73)	0.3456	1.69 (0.42, 6.77)	0.4569	18.9 (-29.2, 67.0)	0.4419	
Yes	18	6 (33.3%)	11	7 (63.6%)	3.50 (0.73, 16.85)	0.1182	1.91 (0.64, 5.68)	0.2451	30.3 (-23.9, 84.5)	0.2728	
Day 1 / 1-hr Post 1st											0.8973
No	11	3 (27.3%)	13	8 (61.5%)	4.27 (0.75, 24.18)	0.1012	2.26 (0.60, 8.51)	0.2294	34.3 (-18.4, 86.9)	0.2020	
Yes	19	6 (31.6%)	11	7 (63.6%)	3.79 (0.79, 18.11)	0.0948	2.02 (0.68, 6.00)	0.2079	32.1 (-21.4, 85.5)	0.2401	
Day 1 / 2-hr Post 1st											0.6490
No	11	6 (54.5%)	12	7 (58.3%)	1.17 (0.22, 6.08)	0.8548	1.07 (0.36, 3.18)	0.9039	3.8 (-57.6, 65.2)	0.9038	
Yes	19	8 (42.1%)	11	7 (63.6%)	2.41 (0.52, 11.10)	0.2604	1.51 (0.55, 4.17)	0.4249	21.5 (-33.9, 77.0)	0.4465	
Day 1 / 4-hr Post 1st											0.7672
No	11	7 (63.6%)	13	9 (69.2%)	1.29 (0.23, 7.05)	0.7723	1.09 (0.41, 2.92)	0.8672	5.6 (-59.7, 70.9)	0.8667	
Yes	19	9 (47.4%)	11	7 (63.6%)	1.94 (0.42, 8.92)	0.3922	1.34 (0.50, 3.61)	0.5580	16.3 (-40.1, 72.7)	0.5718	
Day 1 / 4-hr Post 2nd											0.7466
No	10	6 (60.0%)	13	9 (69.2%)	1.50 (0.27, 8.45)	0.6457	1.15 (0.41, 3.24)	0.7860	9.2 (-56.7, 75.2)	0.7839	
Yes	18	9 (50.0%)	11	8 (72.7%)	2.67 (0.53, 13.43)	0.2345	1.45 (0.56, 3.77)	0.4406	22.7 (-37.3, 82.8)	0.4583	
Day 1 / 4-hr Post 3rd											0.9682
No	11	7 (63.6%)	13	11 (84.6%)	3.14 (0.45, 21.96)	0.2483	1.33 (0.52, 3.43)	0.5556	21.0 (-47.7, 89.7)	0.5496	
Yes	19	12 (63.2%)	11	9 (81.8%)	2.62 (0.44, 15.78)	0.2916	1.30 (0.55, 3.07)	0.5572	18.7 (-45.6, 83.0)	0.5695	
Day 2 / 0-hr											0.3788
No	11	9 (81.8%)	13	9 (69.2%)	0.50 (0.07, 3.45)	0.4821	0.85 (0.34, 2.13)	0.7231	-12.6 (-82.6, 57.4)	0.7246	
Yes	19	9 (47.4%)	11	8 (72.7%)	2.96 (0.60, 14.73)	0.1843	1.54 (0.59, 3.98)	0.3776	25.4 (-33.8, 84.5)	0.4007	
Day 2 / 4-hr Post 1st											0.5455
No	10	5 (50.0%)	13	10 (76.9%)	3.33 (0.56, 19.95)	0.1872	1.54 (0.53, 4.50)	0.4316	26.9 (-37.8, 91.7)	0.4152	
Yes	19	8 (42.1%)	11	11 (100.0%)	n/a	n/a	2.37 (0.96, 5.90)	0.0627	57.9 (-8.0, 123.8)	0.0851	

OR, RR and ARR derived from model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
Patients are included in the count of patients meeting criteria if the patients' serum potassium is in normal range at the timepoint. This is the definition used in the majority of the study CSR's. ZS-002 CSR table 14.2.3 is an exception as it counts patients in normal range before the timepoint even if the patient is not still in normal range at the timepoint. The normal range used in ZS-002 CSR (3.5 to 4.9) has been retained. All other studies define normal range as 3.5 to 5.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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26/02/2021

Lokelma

Table 1.1.5.1 - Study ZS-002: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

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	Placebo (N=30)		Lokelma 10g QD (N=24)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Diabetes mellitus *(contd.)*											
Day 2 / 4-hr Post 2nd											0.7219
No	10	3 (30.0%)	13	11 (84.6%)	12.83 (1.69, 97.17)	0.0135	2.82 (0.79, 10.11)	0.1114	54.6 (-5.8, 115.1)	0.0765	
Yes	18	7 (38.9%)	11	9 (81.8%)	7.07 (1.17, 42.84)	0.0333	2.10 (0.78, 5.65)	0.1400	42.9 (-17.8, 103.7)	0.1659	
Day 2 / 4-hr Post 3rd											0.5183
No	10	8 (80.0%)	13	12 (92.3%)	3.00 (0.23, 38.87)	0.4006	1.15 (0.47, 2.82)	0.7539	12.3 (-63.9, 88.5)	0.7515	
Yes	19	11 (57.9%)	11	11 (100.0%)	n/a	n/a	1.73 (0.75, 3.98)	0.1999	42.1 (-26.2, 110.4)	0.2268	
Day 2 / 20-hr Post 1st											0.7645
No	10	7 (70.0%)	13	13 (100.0%)	n/a	n/a	1.43 (0.57, 3.58)	0.4468	30.0 (-45.1, 105.1)	0.4338	
Yes	19	11 (57.9%)	11	11 (100.0%)	n/a	n/a	1.73 (0.75, 3.98)	0.1999	42.1 (-26.2, 110.4)	0.2268	
Day 3 / 0-hr											0.5436
No	11	6 (54.5%)	13	10 (76.9%)	2.78 (0.48, 16.03)	0.2534	1.41 (0.51, 3.88)	0.5056	22.4 (-42.3, 87.0)	0.4974	
Yes	19	8 (42.1%)	11	10 (90.9%)	13.75 (1.45, 130.24)	0.0223	2.16 (0.85, 5.47)	0.1047	48.8 (-14.6, 112.3)	0.1317	
RAASi medications											
Day 1 / 30-min Post 1st											0.2816
No	11	3 (27.3%)	4	4 (100.0%)	n/a	n/a	3.67 (0.82, 16.38)	0.0889	72.7 (-30.0, 175.5)	0.1653	
Yes	18	6 (33.3%)	20	9 (45.0%)	1.64 (0.44, 6.11)	0.4639	1.35 (0.48, 3.79)	0.5691	11.7 (-28.0, 51.4)	0.5646	
Day 1 / 1-hr Post 1st											0.8468
No	11	5 (45.5%)	4	4 (100.0%)	n/a	n/a	2.20 (0.59, 8.19)	0.2398	54.5 (-51.2, 160.3)	0.3122	
Yes	19	4 (21.1%)	20	11 (55.0%)	4.58 (1.12, 18.80)	0.0345	2.61 (0.83, 8.20)	0.1000	33.9 (-4.6, 72.4)	0.0839	
Day 1 / 2-hr Post 1st											0.5986
No	11	6 (54.5%)	4	2 (50.0%)	0.83 (0.08, 8.24)	0.8761	0.92 (0.19, 4.54)	0.9151	-4.5 (-86.4, 77.3)	0.9134	
Yes	19	8 (42.1%)	19	12 (63.2%)	2.36 (0.64, 8.68)	0.1972	1.50 (0.61, 3.67)	0.3744	21.1 (-25.1, 67.2)	0.3711	
Day 1 / 4-hr Post 1st											0.4869
No	11	7 (63.6%)	4	2 (50.0%)	0.57 (0.06, 5.77)	0.6354	0.79 (0.16, 3.78)	0.7636	-13.6 (-97.4, 70.2)	0.7498	
Yes	19	9 (47.4%)	20	14 (70.0%)	2.59 (0.70, 9.64)	0.1553	1.48 (0.64, 3.41)	0.3607	22.6 (-25.3, 70.6)	0.3552	
Day 1 / 4-hr Post 2nd											0.7064
No	10	8 (80.0%)	4	4 (100.0%)	n/a	n/a	1.25 (0.38, 4.15)	0.7156	20.0 (-92.6, 132.6)	0.7277	
Yes	18	7 (38.9%)	20	13 (65.0%)	2.92 (0.78, 10.92)	0.1118	1.67 (0.67, 4.19)	0.2732	26.1 (-19.5, 71.7)	0.2616	
Day 1 / 4-hr Post 3rd											0.9946
No	11	8 (72.7%)	4	4 (100.0%)	n/a	n/a	1.37 (0.41, 4.57)	0.6030	27.3 (-82.9, 137.5)	0.6276	
Yes	19	11 (57.9%)	20	16 (80.0%)	2.91 (0.70, 12.09)	0.1418	1.38 (0.64, 2.98)	0.4090	22.1 (-29.9, 74.1)	0.4050	
Day 2 / 0-hr											0.2693
No	11	7 (63.6%)	4	1 (25.0%)	0.19 (0.01, 2.50)	0.2069	0.39 (0.05, 3.19)	0.3821	-38.6 (-106.6, 29.4)	0.2654	
Yes	19	11 (57.9%)	20	16 (80.0%)	2.91 (0.70, 12.09)	0.1418	1.38 (0.64, 2.98)	0.4090	22.1 (-29.9, 74.1)	0.4050	
Day 2 / 4-hr Post 1st											0.3212
No	11	7 (63.6%)	4	3 (75.0%)	1.71 (0.13, 22.51)	0.6817	1.18 (0.30, 4.56)	0.8118	11.4 (-85.7, 108.4)	0.8185	
Yes	18	6 (33.3%)	20	18 (90.0%)	18.00 (3.10, 104.53)	0.0013	2.70 (1.07, 6.80)	0.0351	56.7 (7.3, 106.1)	0.0245	

OR, RR and ARR derived from model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
Patients are included in the count of patients meeting criteria if the patients' serum potassium is in normal range at the timepoint. This is the definition used in the majority of the study CSR's. ZS-002 CSR table 14.2.3 is an exception as it counts patients in normal range before the timepoint even if the patient is not still in normal range at the timepoint. The normal range used in ZS-002 CSR (3.5 to 4.9) has been retained. All other studies define normal range as 3.5 to 5.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 1.1.5.1 - Study ZS-002: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)		Lokelma 10g QD (N=24)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
RAASi medications *(contd.)*											
Day 2 / 4-hr Post 2nd											0.3458
No	9	4 (44.4%)	4	2 (50.0%)	1.25 (0.12, 13.24)	0.8530	1.12 (0.21, 6.14)	0.8918	5.6 (-76.3, 87.4)	0.8942	
Yes	19	6 (31.6%)	20	18 (90.0%)	19.50 (3.38, 112.45)	0.0009	2.85 (1.13, 7.18)	0.0263	58.4 (9.8, 107.1)	0.0186	
Day 2 / 4-hr Post 3rd											0.8647
No	11	8 (72.7%)	4	4 (100.0%)	n/a	n/a	1.37 (0.41, 4.57)	0.6030	27.3 (-82.9, 137.5)	0.6276	
Yes	18	11 (61.1%)	20	19 (95.0%)	12.09 (1.31, 111.65)	0.0280	1.55 (0.74, 3.27)	0.2442	33.9 (-22.0, 89.8)	0.2351	
Day 2 / 20-hr Post 1st											0.9558
No	11	7 (63.6%)	4	4 (100.0%)	n/a	n/a	1.57 (0.46, 5.37)	0.4708	36.4 (-72.4, 145.1)	0.5122	
Yes	18	11 (61.1%)	20	20 (100.0%)	n/a	n/a	1.64 (0.78, 3.42)	0.1895	38.9 (-17.9, 95.7)	0.1795	
Day 3 / 0-hr											0.9203
No	11	5 (45.5%)	4	3 (75.0%)	3.60 (0.28, 46.36)	0.3259	1.65 (0.39, 6.90)	0.4929	29.5 (-64.2, 123.3)	0.5368	
Yes	19	9 (47.4%)	20	17 (85.0%)	6.30 (1.37, 28.85)	0.0178	1.79 (0.80, 4.03)	0.1561	37.6 (-13.3, 88.5)	0.1473	
Sex											
Day 1 / 30-min Post 1st											0.6296
Male	22	8 (36.4%)	9	6 (66.7%)	3.50 (0.68, 17.96)	0.1333	1.83 (0.64, 5.28)	0.2617	30.3 (-28.7, 89.3)	0.3141	
Female	7	1 (14.3%)	15	7 (46.7%)	5.25 (0.50, 54.89)	0.1662	3.27 (0.40, 26.55)	0.2682	32.4 (-12.1, 76.9)	0.1537	
Day 1 / 1-hr Post 1st											0.1127
Male	23	5 (21.7%)	9	7 (77.8%)	12.60 (1.97, 80.76)	0.0075	3.58 (1.14, 11.27)	0.0295	56.0 (-4.6, 116.7)	0.0703	
Female	7	4 (57.1%)	15	8 (53.3%)	0.86 (0.14, 5.23)	0.8673	0.93 (0.28, 3.10)	0.9103	-3.8 (-70.9, 63.3)	0.9114	
Day 1 / 2-hr Post 1st											0.5633
Male	23	9 (39.1%)	9	5 (55.6%)	1.94 (0.41, 9.24)	0.4031	1.42 (0.48, 4.24)	0.5298	16.4 (-38.6, 71.4)	0.5583	
Female	7	5 (71.4%)	14	9 (64.3%)	0.72 (0.10, 5.17)	0.7439	0.90 (0.30, 2.69)	0.8502	-7.1 (-82.5, 68.2)	0.8527	
Day 1 / 4-hr Post 1st											0.1935
Male	23	9 (39.1%)	9	6 (66.7%)	3.11 (0.62, 15.71)	0.1695	1.70 (0.61, 4.79)	0.3121	27.5 (-31.6, 86.7)	0.3616	
Female	7	7 (100.0%)	15	10 (66.7%)	n/a	n/a	0.67 (0.25, 1.75)	0.4106	-33.3 (-118.2, 51.5)	0.4412	
Day 1 / 4-hr Post 2nd											0.7049
Male	22	12 (54.5%)	9	8 (88.9%)	6.67 (0.71, 62.74)	0.0972	1.63 (0.67, 3.99)	0.2847	34.3 (-34.6, 103.2)	0.3286	
Female	6	3 (50.0%)	15	9 (60.0%)	1.50 (0.22, 10.08)	0.6765	1.20 (0.32, 4.43)	0.7845	10.0 (-58.8, 78.8)	0.7758	
Day 1 / 4-hr Post 3rd											0.9411
Male	23	14 (60.9%)	9	7 (77.8%)	2.25 (0.38, 13.35)	0.3721	1.28 (0.52, 3.17)	0.5964	16.9 (-48.9, 82.8)	0.6148	
Female	7	5 (71.4%)	15	13 (86.7%)	2.60 (0.28, 23.81)	0.3978	1.21 (0.43, 3.40)	0.7133	15.2 (-63.1, 93.6)	0.7031	
Day 2 / 0-hr											0.3426
Male	23	15 (65.2%)	9	5 (55.6%)	0.67 (0.14, 3.20)	0.6127	0.85 (0.31, 2.34)	0.7562	-9.7 (-68.5, 49.2)	0.7475	
Female	7	3 (42.9%)	15	12 (80.0%)	5.33 (0.75, 37.86)	0.0941	1.87 (0.53, 6.61)	0.3336	37.1 (-29.2, 103.5)	0.2725	
Day 2 / 4-hr Post 1st											0.6318
Male	22	9 (40.9%)	9	8 (88.9%)	11.56 (1.22, 109.18)	0.0327	2.17 (0.84, 5.63)	0.1103	48.0 (-19.2, 115.1)	0.1613	
Female	7	4 (57.1%)	15	13 (86.7%)	4.87 (0.59, 40.26)	0.1414	1.52 (0.49, 4.65)	0.4663	29.5 (-43.7, 102.7)	0.4291	

OR, RR and ARR derived from model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
Patients are included in the count of patients meeting criteria if the patients' serum potassium is in normal range at the timepoint. This is the definition used in the majority of the study CSR's. ZS-002 CSR table 14.2.3 is an exception as it counts patients in normal range before the timepoint even if the patient is not still in normal range at the timepoint. The normal range used in ZS-002 CSR (3.5 to 4.9) has been retained. All other studies define normal range as 3.5 to 5.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 1.1.5.1 - Study ZS-002: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)		Lokelma 10g QD (N=24)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Sex *(contd.)*											
Day 2 / 4-hr Post 2nd											0.6485
Male	22	8 (36.4%)	9	6 (66.7%)	3.50 (0.68, 17.96)	0.1333	1.83 (0.64, 5.28)	0.2617	30.3 (-28.7, 89.3)	0.3141	
Female	6	2 (33.3%)	15	14 (93.3%)	28.00 (1.99, 394.40)	0.0135	2.80 (0.64, 12.32)	0.1732	60.0 (-7.3, 127.3)	0.0804	
Day 2 / 4-hr Post 3rd											0.8789
Male	22	15 (68.2%)	9	9 (100.0%)	n/a	n/a	1.47 (0.64, 3.35)	0.3637	31.8 (-42.1, 105.7)	0.3986	
Female	7	4 (57.1%)	15	14 (93.3%)	10.50 (0.84, 130.66)	0.0676	1.63 (0.54, 4.96)	0.3868	36.2 (-38.1, 110.5)	0.3400	
Day 2 / 20-hr Post 1st											0.5413
Male	22	15 (68.2%)	9	9 (100.0%)	n/a	n/a	1.47 (0.64, 3.35)	0.3637	31.8 (-42.1, 105.7)	0.3986	
Female	7	3 (42.9%)	15	15 (100.0%)	n/a	n/a	2.33 (0.68, 8.06)	0.1803	57.1 (-12.9, 127.2)	0.1101	
Day 3 / 0-hr											0.6123
Male	23	10 (43.5%)	9	8 (88.9%)	10.40 (1.11, 97.33)	0.0401	2.04 (0.81, 5.18)	0.1317	45.4 (-21.8, 112.6)	0.1856	
Female	7	4 (57.1%)	15	12 (80.0%)	3.00 (0.42, 21.30)	0.2719	1.40 (0.45, 4.34)	0.5600	22.9 (-49.1, 94.9)	0.5338	
Age (years)											
Day 1 / 30-min Post 1st											0.3757
<65 years	9	2 (22.2%)	7	5 (71.4%)	8.75 (0.90, 84.80)	0.0612	3.21 (0.62, 16.57)	0.1628	49.2 (-20.6, 119.0)	0.1669	
>=65 years	20	7 (35.0%)	17	8 (47.1%)	1.65 (0.44, 6.20)	0.4579	1.34 (0.49, 3.71)	0.5673	12.1 (-29.6, 53.7)	0.5705	
Day 1 / 1-hr Post 1st											0.7102
<65 years	9	3 (33.3%)	7	6 (85.7%)	12.00 (0.96, 150.69)	0.0543	2.57 (0.64, 10.28)	0.1817	52.4 (-25.9, 130.7)	0.1896	
>=65 years	21	6 (28.6%)	17	9 (52.9%)	2.81 (0.73, 10.77)	0.1313	1.85 (0.66, 5.21)	0.2419	24.4 (-17.1, 65.8)	0.2493	
Day 1 / 2-hr Post 1st											0.7189
<65 years	9	5 (55.6%)	7	6 (85.7%)	4.80 (0.40, 58.01)	0.2173	1.54 (0.47, 5.06)	0.4739	30.2 (-54.0, 114.3)	0.4822	
>=65 years	21	9 (42.9%)	16	8 (50.0%)	1.33 (0.36, 4.93)	0.6661	1.17 (0.45, 3.02)	0.7511	7.1 (-37.4, 51.7)	0.7533	
Day 1 / 4-hr Post 1st											0.4462
<65 years	9	5 (55.6%)	7	3 (42.9%)	0.60 (0.08, 4.40)	0.6153	0.77 (0.18, 3.23)	0.7223	-12.7 (-81.4, 56.0)	0.7172	
>=65 years	21	11 (52.4%)	17	13 (76.5%)	2.95 (0.72, 12.11)	0.1322	1.46 (0.65, 3.26)	0.3557	24.1 (-27.7, 75.9)	0.3623	
Day 1 / 4-hr Post 2nd											0.8018
<65 years	7	4 (57.1%)	7	6 (85.7%)	4.50 (0.34, 60.15)	0.2556	1.50 (0.42, 5.32)	0.5299	28.6 (-60.0, 117.1)	0.5271	
>=65 years	21	11 (52.4%)	17	11 (64.7%)	1.67 (0.45, 6.19)	0.4456	1.24 (0.54, 2.85)	0.6202	12.3 (-36.9, 61.5)	0.6234	
Day 1 / 4-hr Post 3rd											0.7554
<65 years	9	5 (55.6%)	7	6 (85.7%)	4.80 (0.40, 58.01)	0.2173	1.54 (0.47, 5.06)	0.4739	30.2 (-54.0, 114.3)	0.4822	
>=65 years	21	14 (66.7%)	17	14 (82.4%)	2.33 (0.50, 10.91)	0.2815	1.24 (0.59, 2.59)	0.5761	15.7 (-39.8, 71.2)	0.5796	
Day 2 / 0-hr											0.8726
<65 years	9	5 (55.6%)	7	5 (71.4%)	2.00 (0.24, 16.36)	0.5181	1.29 (0.37, 4.44)	0.6911	15.9 (-63.4, 95.2)	0.6949	
>=65 years	21	13 (61.9%)	17	12 (70.6%)	1.48 (0.38, 5.78)	0.5756	1.14 (0.52, 2.50)	0.7430	8.7 (-43.5, 60.9)	0.7445	
Day 2 / 4-hr Post 1st											0.9579
<65 years	8	4 (50.0%)	7	7 (100.0%)	n/a	n/a	2.00 (0.59, 6.83)	0.2688	50.0 (-38.8, 138.8)	0.2699	
>=65 years	21	9 (42.9%)	17	14 (82.4%)	6.22 (1.36, 28.37)	0.0182	1.92 (0.83, 4.44)	0.1263	39.5 (-11.9, 90.9)	0.1323	

OR, RR and ARR derived from model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
Patients are included in the count of patients meeting criteria if the patients' serum potassium is in normal range at the timepoint. This is the definition used in the majority of the study CSR's. ZS-002 CSR table 14.2.3 is an exception as it counts patients in normal range before the timepoint even if the patient is not still in normal range at the timepoint. The normal range used in ZS-002 CSR (3.5 to 4.9) has been retained. All other studies define normal range as 3.5 to 5.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 1.1.5.1 - Study ZS-002: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)		Lokelma 10g QD (N=24)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Age (years) *(contd.)*											
Day 2 / 4-hr Post 2nd											0.7092
<65 years	9	4 (44.4%)	7	6 (85.7%)	7.50 (0.62, 90.61)	0.1131	1.93 (0.54, 6.83)	0.3089	41.3 (-40.0, 122.5)	0.3194	
>=65 years	19	6 (31.6%)	17	14 (82.4%)	10.11 (2.09, 48.99)	0.0041	2.61 (1.00, 6.79)	0.0495	50.8 (0.8, 100.8)	0.0465	
Day 2 / 4-hr Post 3rd											0.8447
<65 years	8	6 (75.0%)	7	7 (100.0%)	n/a	n/a	1.33 (0.45, 3.97)	0.6051	25.0 (-70.3, 120.3)	0.6073	
>=65 years	21	13 (61.9%)	17	16 (94.1%)	9.85 (1.09, 89.21)	0.0420	1.52 (0.73, 3.16)	0.2619	32.2 (-24.9, 89.3)	0.2688	
Day 2 / 20-hr Post 1st											0.8754
<65 years	9	6 (66.7%)	7	7 (100.0%)	n/a	n/a	1.50 (0.50, 4.46)	0.4661	33.3 (-58.0, 124.6)	0.4742	
>=65 years	20	12 (60.0%)	17	17 (100.0%)	n/a	n/a	1.67 (0.80, 3.49)	0.1755	40.0 (-18.4, 98.4)	0.1796	
Day 3 / 0-hr											0.6550
<65 years	9	4 (44.4%)	7	7 (100.0%)	n/a	n/a	2.25 (0.66, 7.69)	0.1957	55.6 (-30.4, 141.5)	0.2051	
>=65 years	21	10 (47.6%)	17	13 (76.5%)	3.57 (0.87, 14.65)	0.0767	1.61 (0.70, 3.66)	0.2601	28.9 (-22.1, 79.8)	0.2673	
Baseline S-K											
Day 1 / 30-min Post 1st											-
<=5.3 mmol/L	24	8 (33.3%)	19	13 (68.4%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	2	1 (50.0%)	3	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	3	0 (0.0%)	2	0 (0.0%)	-	-	-	-	-	-	
Day 1 / 1-hr Post 1st											-
<=5.3 mmol/L	25	9 (36.0%)	19	15 (78.9%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	2	0 (0.0%)	3	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	3	0 (0.0%)	2	0 (0.0%)	-	-	-	-	-	-	
Day 1 / 2-hr Post 1st											-
<=5.3 mmol/L	25	13 (52.0%)	18	14 (77.8%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	2	0 (0.0%)	3	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	3	1 (33.3%)	2	0 (0.0%)	-	-	-	-	-	-	
Day 1 / 4-hr Post 1st											-
<=5.3 mmol/L	25	14 (56.0%)	19	15 (78.9%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	2	1 (50.0%)	3	1 (33.3%)	-	-	-	-	-	-	
>5.5 mmol/L	3	1 (33.3%)	2	0 (0.0%)	-	-	-	-	-	-	
Day 1 / 4-hr Post 2nd											-
<=5.3 mmol/L	23	14 (60.9%)	19	15 (78.9%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	2	0 (0.0%)	3	2 (66.7%)	-	-	-	-	-	-	
>5.5 mmol/L	3	1 (33.3%)	2	0 (0.0%)	-	-	-	-	-	-	
Day 1 / 4-hr Post 3rd											-
<=5.3 mmol/L	25	17 (68.0%)	19	17 (89.5%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	2	1 (50.0%)	3	3 (100.0%)	-	-	-	-	-	-	
>5.5 mmol/L	3	1 (33.3%)	2	0 (0.0%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
Patients are included in the count of patients meeting criteria if the patients' serum potassium is in normal range at the timepoint. This is the definition used in the majority of the study CSR's. ZS-002 CSR table 14.2.3 is an exception as it counts patients in normal range before the timepoint even if the patient is not still in normal range at the timepoint. The normal range used in ZS-002 CSR (3.5 to 4.9) has been retained. All other studies define normal range as 3.5 to 5.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 1.1.5.1 - Study ZS-002: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)		Lokelma 10g QD (N=24)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Baseline S-K *(contd.)*											
Day 2 / 0-hr											-
<=5.3 mmol/L	25	16 (64.0%)	19	15 (78.9%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	2	1 (50.0%)	3	2 (66.7%)	-	-	-	-	-	-	
>5.5 mmol/L	3	1 (33.3%)	2	0 (0.0%)	-	-	-	-	-	-	
Day 2 / 4-hr Post 1st											-
<=5.3 mmol/L	24	13 (54.2%)	19	18 (94.7%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	2	0 (0.0%)	3	2 (66.7%)	-	-	-	-	-	-	
>5.5 mmol/L	3	0 (0.0%)	2	1 (50.0%)	-	-	-	-	-	-	
Day 2 / 4-hr Post 2nd											-
<=5.3 mmol/L	23	10 (43.5%)	19	17 (89.5%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	2	0 (0.0%)	3	3 (100.0%)	-	-	-	-	-	-	
>5.5 mmol/L	3	0 (0.0%)	2	0 (0.0%)	-	-	-	-	-	-	
Day 2 / 4-hr Post 3rd											-
<=5.3 mmol/L	24	19 (79.2%)	19	18 (94.7%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	2	0 (0.0%)	3	3 (100.0%)	-	-	-	-	-	-	
>5.5 mmol/L	3	0 (0.0%)	2	2 (100.0%)	-	-	-	-	-	-	
Day 2 / 20-hr Post 1st											-
<=5.3 mmol/L	24	16 (66.7%)	19	19 (100.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	2	1 (50.0%)	3	3 (100.0%)	-	-	-	-	-	-	
>5.5 mmol/L	3	1 (33.3%)	2	2 (100.0%)	-	-	-	-	-	-	
Day 3 / 0-hr											-
<=5.3 mmol/L	25	13 (52.0%)	19	16 (84.2%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	2	1 (50.0%)	3	2 (66.7%)	-	-	-	-	-	-	
>5.5 mmol/L	3	0 (0.0%)	2	2 (100.0%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
Patients are included in the count of patients meeting criteria if the patients' serum potassium is in normal range at the timepoint. This is the definition used in the majority of the study CSR's. ZS-002 CSR table 14.2.3 is an exception as it counts patients in normal range before the timepoint even if the patient is not still in normal range at the timepoint. The normal range used in ZS-002 CSR (3.5 to 4.9) has been retained. All other studies define normal range as 3.5 to 5.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 1.1.5.1 - Study ZS-002: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)		Lokelma 10g QD (N=24)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Baseline eGFR											
Day 1 / 30-min Post 1st											-
15-29 ml/min/1.73m**2	1	0 (0.0%)	1	0 (0.0%)	-	-	-	-	-	-	
30-59 ml/min/1.73m**2	27	8 (29.6%)	22	13 (59.1%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	1	1 (100.0%)	1	0 (0.0%)	-	-	-	-	-	-	
Day 1 / 1-hr Post 1st											-
15-29 ml/min/1.73m**2	1	0 (0.0%)	1	0 (0.0%)	-	-	-	-	-	-	
30-59 ml/min/1.73m**2	28	9 (32.1%)	22	14 (63.6%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	1	0 (0.0%)	1	1 (100.0%)	-	-	-	-	-	-	
Day 1 / 2-hr Post 1st											-
15-29 ml/min/1.73m**2	1	0 (0.0%)	1	0 (0.0%)	-	-	-	-	-	-	
30-59 ml/min/1.73m**2	28	13 (46.4%)	21	13 (61.9%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	
Day 1 / 4-hr Post 1st											-
15-29 ml/min/1.73m**2	1	1 (100.0%)	1	0 (0.0%)	-	-	-	-	-	-	
30-59 ml/min/1.73m**2	28	15 (53.6%)	22	16 (72.7%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	1	0 (0.0%)	1	0 (0.0%)	-	-	-	-	-	-	
Day 1 / 4-hr Post 2nd											-
15-29 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	
30-59 ml/min/1.73m**2	26	13 (50.0%)	22	15 (68.2%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	
Day 1 / 4-hr Post 3rd											-
15-29 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	
30-59 ml/min/1.73m**2	28	17 (60.7%)	22	18 (81.8%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	
Day 2 / 0-hr											-
15-29 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	
30-59 ml/min/1.73m**2	28	16 (57.1%)	22	15 (68.2%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	
Day 2 / 4-hr Post 1st											-
15-29 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	
30-59 ml/min/1.73m**2	27	11 (40.7%)	22	19 (86.4%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	
Day 2 / 4-hr Post 2nd											-
15-29 ml/min/1.73m**2	1	0 (0.0%)	1	1 (100.0%)	-	-	-	-	-	-	
30-59 ml/min/1.73m**2	26	9 (34.6%)	22	18 (81.8%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
Patients are included in the count of patients meeting criteria if the patients' serum potassium is in normal range at the timepoint. This is the definition used in the majority of the study CSR's. ZS-002 CSR table 14.2.3 is an exception as it counts patients in normal range before the timepoint even if the patient is not still in normal range at the timepoint. The normal range used in ZS-002 CSR (3.5 to 4.9) has been retained. All other studies define normal range as 3.5 to 5.
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'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 1.1.5.1 - Study ZS-002: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=30)		Lokelma 10g QD (N=24)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Baseline eGFR *(contd.)*											
Day 2 / 4-hr Post 3rd											-
15-29 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	
30-59 ml/min/1.73m**2	27	17 (63.0%)	22	21 (95.5%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	
Day 2 / 20-hr Post 1st											-
15-29 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	
30-59 ml/min/1.73m**2	27	16 (59.3%)	22	22 (100.0%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	
Day 3 / 0-hr											-
15-29 ml/min/1.73m**2	1	0 (0.0%)	1	1 (100.0%)	-	-	-	-	-	-	
30-59 ml/min/1.73m**2	28	13 (46.4%)	22	18 (81.8%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	1	1 (100.0%)	1	1 (100.0%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with treatment group.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
Patients are included in the count of patients meeting criteria if the patients' serum potassium is in normal range at the timepoint. This is the definition used in the majority of the study CSR's. ZS-002 CSR table 14.2.3 is an exception as it counts patients in normal range before the timepoint even if the patient is not still in normal range at the timepoint. The normal range used in ZS-002 CSR (3.5 to 4.9) has been retained. All other studies define normal range as 3.5 to 5.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 1.2.1.1 - Study ZS-002: Subjects experiencing any adverse event (AE), ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	30	3 (10.0%)	24	7 (29.2%)	3.71 (0.84 , 16.32)	0.0833	2.92 (0.84 , 10.09)	0.0910	19.17 (-1.95 , 40.28)	0.0752	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 1.2.1.2 - Study ZS-002: Subjects experiencing any serious adverse event (SAE), ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	30	0 (0.0%)	24	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 1.2.1.3 - Study ZS-002: Subjects experiencing any AE leading to discontinuation of study medication (DAE), ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	30	0 (0.0%)	24	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 1.2.1.4 - Study ZS-002: Subjects experiencing any AE graded as severe, ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	30	0 (0.0%)	24	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 1.2.1.5 - Study ZS-002: Subjects experiencing any AE graded as non-severe, ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	30	3 (10.0%)	24	7 (29.2%)	3.71 (0.84 , 16.32)	0.0833	2.92 (0.84 , 10.09)	0.0910	19.17 (-1.95 , 40.28)	0.0752	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 1.2.1.6 - Study ZS-002: Subjects experiencing any AE resulting in death, ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	30	0 (0.0%)	24	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_zs002_ae_death.pdf generated by zs002ac_ae_soc_pt.sas at 16:15:24 on 25 February 2021

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Table 1.2.1.7 - Study ZS-002: Adverse events leading to discontinuation (DAE) by SOC and PT, ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10 g ZS (N=24)	
Subgroup / Category / SOC / PT	N	n (%)	N	n (%)
No data for listing				

t_zs002_ae_dae_socpt.pdf generated by zs002ac_ae_soc_pt.sas at 16:15:56 on 25 February 2021

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Table 1.2.1.8 - Study ZS-002: Adverse events (AE) by SOC and PT occurring in at least 10% of subjects in any treatment group, ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	30	3 (10.0%)	24	7 (29.2%)	3.71 (0.84 , 16.32)	0.0833	2.92 (0.84 , 10.09)	0.0910	19.17 (-1.95 , 40.28)	0.0752	
Gastrointestinal disorders: All	30	2 (6.7%)	24	4 (16.7%)	2.80 (0.47 , 16.80)	0.2600	2.50 (0.50 , 12.51)	0.2647	10.00 (-7.38 , 27.38)	0.2594	
Gastrointestinal disorders: Vomiting	30	1 (3.3%)	24	3 (12.5%)	4.14 (0.40 , 42.66)	0.2322	3.75 (0.42 , 33.80)	0.2387	9.17 (-5.54 , 23.87)	0.2219	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

t_zs002_ae_any_socpt.pdf generated by zs002ac_ae_soc_pt.sas at 16:15:42 on 25 February 2021

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Table 1.2.1.9 - Study ZS-002: Serious adverse events (SAE) by SOC and PT occurring in at least 5% of subjects in any treatment group, ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	30	0 (0.0%)	24	0 (0.0%)							

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 1.2.1.10 - Study ZS-002: AEs graded as severe by SOC and PT occurring in at least 5% of subjects in any treatment group, ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	30	0 (0.0%)	24	0 (0.0%)							

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 1.2.1.11 - Study ZS-002: AEs graded as non-severe by SOC and PT occurring in at least 10% of subjects in any treatment group, ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	30	3 (10.0%)	24	7 (29.2%)	3.71 (0.84 , 16.32)	0.0833	2.92 (0.84 , 10.09)	0.0910	19.17 (-1.95 , 40.28)	0.0752	
Gastrointestinal disorders: All	30	2 (6.7%)	24	4 (16.7%)	2.80 (0.47 , 16.80)	0.2600	2.50 (0.50 , 12.51)	0.2647	10.00 (-7.38 , 27.38)	0.2594	
Gastrointestinal disorders: Vomiting	30	1 (3.3%)	24	3 (12.5%)	4.14 (0.40 , 42.66)	0.2322	3.75 (0.42 , 33.80)	0.2387	9.17 (-5.54 , 23.87)	0.2219	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 1.2.2.1 - Study ZS-002: AEs of special interest: urinary tract infection—subjects experiencing any adverse event (AE), ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	30	0 (0.0%)	24	1 (4.2%)	3.89 (0.15 , 99.97)	0.4117	3.72 (0.16 , 87.42)	0.4147	4.17 (-3.83 , 12.16)	0.3070	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 1.2.2.2 - Study ZS-002: AEs of special interest: urinary tract infection—subjects experiencing any serious adverse event (SAE), ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	30	0 (0.0%)	24	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 1.2.2.3 - Study ZS-002: AEs of special interest: urinary tract infection—subjects experiencing any AE graded as severe, ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	30	0 (0.0%)	24	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 1.2.2.4 - Study ZS-002: AEs of special interest: urinary tract infection—subjects experiencing any AE graded as non-severe, ZS 10g TID vs. combined placebo, overall and by subgroups (safety population)

	Placebo (N=30)		10g ZS (N=24)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	30	0 (0.0%)	24	1 (4.2%)	3.89 (0.15 , 99.97)	0.4117	3.72 (0.16 , 87.42)	0.4147	4.17 (-3.83 , 12.16)	0.3070	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Anhang 4-G3: Studie ZS002J

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Table 8.1.1.1 - Study ZS-002 Japan: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value
Overall	33	36					
Through 24 hours							
Time			0.00003	0.000517	0.07	0.9470	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00397	0.000663	-5.99	<.0001	
Through 48 hours							
Time			-0.00008	0.000309	-0.27	0.7915	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00498	0.000399	-12.48	<.0001	
Acute Baseline S-K value							0.3727
<=5.3 mmol/L	7	12					
Through 24 hours							
Time			0.00136	0.001256	1.08	0.2951	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00423	0.001515	-2.79	0.0071	
Through 48 hours							
Time			0.00096	0.000883	1.08	0.2934	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00586	0.001066	-5.50	<.0001	
5.4-5.5 mmol/L	13	13					
Through 24 hours							
Time			-0.00040	0.000739	-0.54	0.5953	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00371	0.001004	-3.70	0.0004	
Through 48 hours							
Time			-0.00024	0.000361	-0.65	0.5203	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00454	0.000488	-9.30	<.0001	
>5.5 mmol/L	13	11					
Through 24 hours							
Time			-0.00001	0.000845	-0.01	0.9882	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00518	0.001010	-5.13	<.0001	
Through 48 hours							
Time			-0.00040	0.000472	-0.85	0.4071	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00531	0.000573	-9.27	<.0001	
Chronic kidney disease							0.0404
Yes	26	26					
Through 24 hours							
Time			-0.00011	0.000571	-0.20	0.8436	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00395	0.000760	-5.19	<.0001	
Through 48 hours							
Time			-0.00035	0.000299	-1.18	0.2450	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00501	0.000407	-12.30	<.0001	

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.

Interaction p-values are based on analysis through 48 hours.

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Table 8.1.1.1 - Study ZS-002 Japan: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value
Chronic kidney disease *(contd.)*							
No	7	10					
Through 24 hours							
Time			0.00025	0.001425	0.17	0.8646	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00384	0.001616	-2.37	0.0214	
Through 48 hours							
Time			0.00052	0.000848	0.61	0.5486	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00464	0.000935	-4.96	<.0001	
Congestive Heart Disease							0.9744
Yes	4	3					
Through 24 hours							
Time			-0.00068	0.001675	-0.41	0.7003	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00475	0.002475	-1.92	0.0685	
Through 48 hours							
Time			-0.00009	0.001094	-0.08	0.9409	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00524	0.001662	-3.15	0.0030	
No	29	33					
Through 24 hours							
Time			0.00014	0.000560	0.24	0.8094	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00394	0.000708	-5.56	<.0001	
Through 48 hours							
Time			-0.00007	0.000328	-0.22	0.8236	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00498	0.000414	-12.04	<.0001	
Diabetes mellitus							0.8198
Yes	16	24					
Through 24 hours							
Time			-0.00001	0.000780	-0.01	0.9947	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00388	0.000938	-4.14	<.0001	
Through 48 hours							
Time			0.00015	0.000487	0.31	0.7587	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00520	0.000585	-8.89	<.0001	
No	17	12					
Through 24 hours							
Time			0.00003	0.000683	0.05	0.9605	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00402	0.000981	-4.10	<.0001	
Through 48 hours							
Time			-0.00032	0.000371	-0.86	0.3998	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00474	0.000540	-8.78	<.0001	

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.

Interaction p-values are based on analysis through 48 hours.

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Table 8.1.1.1 - Study ZS-002 Japan: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value
RAASi Medications							0.9746
Yes	27	26					
Through 24 hours							
Time			-0.00001	0.000582	-0.01	0.9920	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00379	0.000764	-4.97	<.0001	
Through 48 hours							
Time			-0.00013	0.000338	-0.37	0.7114	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00494	0.000441	-11.20	<.0001	
No	6	10					
Through 24 hours							
Time			0.00018	0.001180	0.15	0.8797	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00445	0.001393	-3.19	0.0025	
Through 48 hours							
Time			0.00003	0.000788	0.04	0.9662	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00505	0.000968	-5.22	<.0001	
Acute Baseline eGFR							0.0279
<15	11	9					
Through 24 hours							
Time			0.00058	0.000901	0.65	0.5248	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00406	0.001306	-3.11	0.0029	
Through 48 hours							
Time			-0.00021	0.000465	-0.46	0.6500	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00461	0.000682	-6.76	<.0001	
15-29+	11	13					
Through 24 hours							
Time			-0.00103	0.000901	-1.15	0.2637	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00420	0.001110	-3.79	0.0003	
Through 48 hours							
Time			-0.00071	0.000513	-1.39	0.1792	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00531	0.000635	-8.36	<.0001	
30-59+	11	11					
Through 24 hours							
Time			0.00003	0.000870	0.03	0.9755	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00357	0.001198	-2.98	0.0040	
Through 48 hours							
Time			0.00032	0.000523	0.61	0.5505	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00474	0.000730	-6.49	<.0001	

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.

Interaction p-values are based on analysis through 48 hours.

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Table 8.1.1.1 - Study ZS-002 Japan: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value
Acute Baseline eGFR *(contd.)*							
>=60	0	3					
Through 24 hours							
Time			NC	NC	NC	NC	
10g ZS time-treatment interaction (Ref: Placebo*Time)			NC	NC	NC	NC	
Through 48 hours							
Time			NC	NC	NC	NC	
10g ZS time-treatment interaction (Ref: Placebo*Time)			NC	NC	NC	NC	
Sex							0.0828
Male	23	28					
Through 24 hours							
Time			-0.00080	0.000652	-1.23	0.2249	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00315	0.000805	-3.92	0.0001	
Through 48 hours							
Time			-0.00031	0.000374	-0.84	0.4045	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00454	0.000458	-9.91	<.0001	
Female	10	8					
Through 24 hours							
Time			0.00196	0.000888	2.20	0.0426	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00614	0.001174	-5.23	<.0001	
Through 48 hours							
Time			0.00037	0.000505	0.72	0.4792	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00622	0.000739	-8.42	<.0001	
Age							0.2848
<65 years	1	5					
Through 24 hours							
Time			-0.00558	0.002264	-2.47	0.0693	
10g ZS time-treatment interaction (Ref: Placebo*Time)			0.00226	0.001890	1.19	0.2481	
Through 48 hours							
Time			-0.00265	0.001878	-1.41	0.2313	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00209	0.001999	-1.05	0.3022	
>=65 years	32	31					
Through 24 hours							
Time			0.00019	0.000525	0.37	0.7137	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00420	0.000692	-6.06	<.0001	
Through 48 hours							
Time			0.00001	0.000314	0.02	0.9807	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00513	0.000411	-12.48	<.0001	

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.

Interaction p-values are based on analysis through 48 hours.

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Overall																
Baseline																
Absolute value	33	5.65 (0.423)	5.5 (5.4, 5.8)	5.2, 6.6			36	5.46 (0.369)	5.4 (5.2, 5.7)	5.0, 6.8						
1 hour																
Absolute value	33	5.52 (0.570)	5.3 (5.1, 5.9)	4.7, 6.8			36	5.09 (0.402)	5.2 (4.8, 5.4)	4.2, 5.8						
Change from baseline	33	-0.13 (0.320)	-0.2 (-0.3, 0.1)	-0.8, 0.5	-0.10 (0.060)	(-0.22, 0.02)	36	-0.37 (0.345)	-0.4 (-0.6, -0.1)	-1.0, 0.6	-0.39 (0.057)	(-0.50, -0.28)	-0.29 (-0.46, -0.12)	0.0008	-0.74 (-1.22, -0.25)	
Percent change from baseline	33	-2.32 (5.602)	-3.2 (-6.2, 1.9)	-13.8, 8.4			36	-6.72 (6.290)	-8.3 (-10.5, -2.2)	-18.4, 12.3						
2 hours																
Absolute value	32	5.28 (0.560)	5.1 (4.9, 5.6)	4.4, 6.5			36	4.95 (0.384)	5.0 (4.8, 5.2)	4.2, 5.9						
Change from baseline	32	-0.33 (0.301)	-0.3 (-0.6, -0.2)	-0.9, 0.5	-0.31 (0.062)	(-0.43, -0.19)	36	-0.50 (0.398)	-0.5 (-0.8, -0.2)	-1.4, 0.4	-0.52 (0.059)	(-0.64, -0.40)	-0.21 (-0.38, -0.04)	0.0169	-0.48 (-0.97, 0.00)	
Percent change from baseline	32	-6.06 (5.397)	-6.5 (-9.9, -3.9)	-16.6, 7.4			36	-9.07 (6.877)	-8.8 (-14.5, -4.3)	-23.4, 6.8						
4 hours																
Absolute value	32	5.18 (0.516)	5.2 (4.9, 5.5)	4.4, 6.1			36	4.92 (0.446)	5.0 (4.7, 5.3)	4.0, 5.9						
Change from baseline	32	-0.43 (0.308)	-0.4 (-0.7, -0.2)	-1.1, 0.0	-0.41 (0.061)	(-0.53, -0.29)	36	-0.53 (0.361)	-0.6 (-0.8, -0.2)	-1.2, 0.2	-0.55 (0.057)	(-0.66, -0.44)	-0.14 (-0.31, 0.03)	0.1024	-0.29 (-0.77, 0.18)	
Percent change from baseline	32	-7.77 (5.621)	-6.8 (-12.1, -2.8)	-19.6, 0.0			36	-9.70 (6.528)	-10.5 (-14.3, -3.3)	-22.3, 3.2						
24 hours																
Absolute value	31	5.38 (0.471)	5.3 (5.0, 5.7)	4.6, 6.6			36	4.76 (0.329)	4.8 (4.6, 5.0)	4.1, 5.4						
Change from baseline	31	-0.22 (0.352)	-0.3 (-0.5, 0.0)	-0.9, 0.5	-0.19 (0.062)	(-0.32, -0.07)	36	-0.69 (0.380)	-0.7 (-0.9, -0.4)	-1.9, 0.0	-0.71 (0.057)	(-0.83, -0.60)	-0.52 (-0.69, -0.35)	<.0001	-1.30 (-1.83, -0.77)	
Percent change from baseline	31	-3.81 (6.236)	-5.0 (-9.1, 0.9)	-15.6, 9.1			36	-12.51 (6.295)	-13.0 (-17.3, -7.9)	-28.2, 1.0						
25 hours																
Absolute value	31	5.33 (0.468)	5.3 (5.1, 5.6)	4.1, 6.3			36	4.46 (0.333)	4.5 (4.3, 4.7)	3.7, 5.2						
Change from baseline	31	-0.27 (0.312)	-0.2 (-0.4, -0.2)	-1.2, 0.4	-0.24 (0.066)	(-0.37, -0.10)	36	-1.00 (0.448)	-1.0 (-1.1, -0.7)	-2.6, -0.3	-1.02 (0.061)	(-1.14, -0.89)	-0.78 (-0.96, -0.60)	<.0001	-1.87 (-2.45, -1.30)	
Percent change from baseline	31	-4.77 (5.665)	-4.1 (-7.7, -2.7)	-22.3, 7.5			36	-18.06 (7.045)	-18.4 (-21.0, -13.1)	-38.5, -5.8						
28 hours																
Absolute value	31	5.19 (0.519)	5.2 (4.8, 5.5)	4.2, 6.3			36	4.33 (0.374)	4.4 (4.0, 4.6)	3.7, 5.2						
Change from baseline	31	-0.41 (0.427)	-0.5 (-0.8, -0.1)	-1.1, 0.5	-0.38 (0.070)	(-0.52, -0.24)	36	-1.12 (0.387)	-1.1 (-1.3, -0.9)	-2.0, -0.3	-1.14 (0.065)	(-1.27, -1.01)	-0.76 (-0.96, -0.57)	<.0001	-1.77 (-2.33, -1.20)	
Percent change from baseline	31	-7.21 (7.609)	-7.6 (-14.2, -1.8)	-20.4, 9.8			36	-20.47 (6.380)	-20.5 (-24.4, -16.2)	-33.9, -5.9						
48 hours																
Absolute value	31	5.36 (0.382)	5.4 (5.1, 5.6)	4.6, 6.1			36	4.16 (0.466)	4.2 (4.0, 4.5)	2.9, 5.2						
Change from baseline	31	-0.24 (0.339)	-0.2 (-0.5, -0.0)	-1.0, 0.5	-0.21 (0.071)	(-0.35, -0.07)	36	-1.30 (0.476)	-1.3 (-1.6, -1.1)	-2.5, -0.2	-1.31 (0.066)	(-1.44, -1.18)	-1.10 (-1.30, -0.91)	<.0001	-2.53 (-3.18, -1.89)	
Percent change from baseline	31	-4.06 (5.934)	-2.9 (-8.0, -0.5)	-15.6, 9.4			36	-23.64 (8.274)	-24.1 (-27.3, -19.4)	-44.0, -3.4						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

Lokelma

Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value																0.1220
<=5.3 mmol/L																
Baseline																
Absolute value	7	5.24 (0.045)	5.2 (5.2, 5.3)	5.2, 5.3			12	5.11 (0.088)	5.1 (5.1, 5.2)	5.0, 5.3						
1 hour																
Absolute value	7	5.16 (0.172)	5.1 (5.0, 5.4)	5.0, 5.4			12	4.77 (0.436)	4.7 (4.5, 5.0)	4.2, 5.7						
Change from baseline	7	-0.08 (0.139)	-0.1 (-0.2, 0.1)	-0.2, 0.1	0.04 (0.152)	(-0.28, 0.35)	12	-0.33 (0.464)	-0.4 (-0.7, -0.0)	-1.0, 0.6	-0.40 (0.112)	(-0.64, -0.17)	-0.44 (-0.86, -0.02)	0.0404	-0.66 (-1.62, 0.30)	
Percent change from baseline	7	-1.58 (2.649)	-2.4 (-3.4, 1.9)	-4.3, 2.4			12	-6.49 (9.001)	-8.7 (-12.8, -0.6)	-18.4, 12.3						
2 hours																
Absolute value	7	4.80 (0.208)	4.8 (4.7, 5.0)	4.4, 5.0			12	4.69 (0.309)	4.8 (4.4, 4.9)	4.2, 5.2						
Change from baseline	7	-0.44 (0.234)	-0.4 (-0.6, -0.2)	-0.9, -0.2	-0.32 (0.121)	(-0.57, -0.07)	12	-0.41 (0.349)	-0.4 (-0.7, -0.2)	-1.0, 0.1	-0.48 (0.087)	(-0.67, -0.30)	-0.16 (-0.51, 0.18)	0.3340	0.08 (-0.85, 1.01)	
Percent change from baseline	7	-8.36 (4.399)	-7.2 (-10.9, -4.3)	-16.6, -4.3			12	-8.06 (6.770)	-7.5 (-13.9, -3.4)	-18.4, 2.5						
4 hours																
Absolute value	7	4.80 (0.311)	4.8 (4.4, 5.1)	4.4, 5.2			12	4.57 (0.360)	4.7 (4.3, 4.9)	4.0, 5.0						
Change from baseline	7	-0.44 (0.305)	-0.4 (-0.8, -0.1)	-0.9, -0.1	-0.32 (0.147)	(-0.63, -0.01)	12	-0.54 (0.365)	-0.6 (-0.8, -0.2)	-1.2, -0.1	-0.61 (0.108)	(-0.84, -0.38)	-0.29 (-0.69, 0.12)	0.1557	-0.29 (-1.23, 0.65)	
Percent change from baseline	7	-8.39 (5.813)	-7.5 (-15.4, -2.4)	-16.6, -1.4			12	-10.55 (7.124)	-10.6 (-16.2, -3.2)	-22.3, -1.5						
24 hours																
Absolute value	7	5.11 (0.389)	5.3 (4.6, 5.5)	4.6, 5.5			12	4.59 (0.350)	4.7 (4.3, 4.9)	4.1, 5.0						
Change from baseline	7	-0.13 (0.360)	-0.0 (-0.6, 0.2)	-0.6, 0.3	-0.01 (0.155)	(-0.33, 0.32)	12	-0.51 (0.360)	-0.5 (-0.8, -0.2)	-1.2, 0.0	-0.58 (0.114)	(-0.82, -0.34)	-0.58 (-1.00, -0.15)	0.0105	-1.08 (-2.08, -0.09)	
Percent change from baseline	7	-2.42 (6.911)	-0.0 (-11.1, 4.3)	-12.0, 5.3			12	-10.05 (7.006)	-9.3 (-16.1, -4.6)	-21.9, 1.0						
25 hours																
Absolute value	7	4.96 (0.541)	4.9 (4.6, 5.5)	4.1, 5.7			12	4.26 (0.360)	4.3 (4.0, 4.5)	3.7, 4.9						
Change from baseline	7	-0.28 (0.535)	-0.3 (-0.6, 0.3)	-1.2, 0.4	-0.16 (0.177)	(-0.53, 0.21)	12	-0.85 (0.383)	-0.9 (-1.0, -0.5)	-1.6, -0.3	-0.92 (0.131)	(-1.19, -0.64)	-0.75 (-1.23, -0.27)	0.0038	-1.28 (-2.30, -0.26)	
Percent change from baseline	7	-5.39 (10.155)	-5.3 (-12.0, 5.3)	-22.3, 7.5			12	-16.57 (7.353)	-17.1 (-20.2, -10.6)	-29.5, -5.8						
28 hours																
Absolute value	7	4.91 (0.491)	5.0 (4.4, 5.4)	4.2, 5.4			12	4.04 (0.287)	4.0 (3.8, 4.2)	3.7, 4.7						
Change from baseline	7	-0.33 (0.486)	-0.2 (-0.8, 0.1)	-1.1, 0.2	-0.21 (0.156)	(-0.53, 0.12)	12	-1.06 (0.304)	-1.1 (-1.2, -0.9)	-1.6, -0.4	-1.13 (0.115)	(-1.38, -0.89)	-0.93 (-1.36, -0.50)	0.0002	-1.95 (-3.07, -0.83)	
Percent change from baseline	7	-6.21 (9.253)	-3.4 (-15.8, 1.9)	-20.4, 3.3			12	-20.82 (5.818)	-21.2 (-24.6, -18.4)	-29.5, -7.4						
48 hours																
Absolute value	7	5.23 (0.431)	5.4 (4.9, 5.5)	4.6, 5.8			12	3.93 (0.572)	4.0 (3.7, 4.4)	2.9, 4.9						
Change from baseline	7	-0.01 (0.389)	0.2 (-0.3, 0.2)	-0.6, 0.5	0.11 (0.210)	(-0.33, 0.55)	12	-1.18 (0.597)	-1.2 (-1.5, -0.8)	-2.3, -0.2	-1.25 (0.157)	(-1.58, -0.92)	-1.36 (-1.93, -0.79)	<.0001	-2.20 (-3.36, -1.03)	
Percent change from baseline	7	-0.26 (7.434)	3.3 (-6.2, 4.3)	-11.1, 9.4			12	-23.07 (11.515)	-22.6 (-29.4, -15.9)	-44.0, -3.4						
5.4-5.5 mmol/L																
Baseline																
Absolute value	13	5.45 (0.058)	5.5 (5.4, 5.5)	5.4, 5.5			13	5.42 (0.049)	5.4 (5.4, 5.5)	5.4, 5.5						
1 hour																
Absolute value	13	5.24 (0.325)	5.3 (4.9, 5.4)	4.7, 5.8			13	5.12 (0.277)	5.2 (4.8, 5.4)	4.8, 5.5						
Change from baseline	13	-0.21 (0.308)	-0.2 (-0.4, -0.1)	-0.8, 0.3	-0.20 (0.081)	(-0.37, -0.04)	13	-0.30 (0.255)	-0.2 (-0.5, -0.1)	-0.6, 0.0	-0.30 (0.081)	(-0.47, -0.13)	-0.10 (-0.34, 0.14)	0.4045	-0.32 (-1.09, 0.45)	
Percent change from baseline	13	-3.82 (5.664)	-3.2 (-8.4, -1.8)	-13.8, 5.0			13	-5.51 (4.730)	-3.7 (-10.3, -2.3)	-11.1, 0.9						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

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	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value *(contd.)*																
5.4-5.5 mmol/L *(contd.)*																
2 hours																
Absolute value	13	5.10 (0.252)	5.1 (4.9, 5.2)	4.7, 5.7			13	5.05 (0.399)	5.1 (4.9, 5.2)	4.3, 5.9						
Change from baseline	13	-0.35 (0.266)	-0.4 (-0.5, -0.2)	-0.7, 0.3	-0.34 (0.090)	(-0.53, -0.16)	13	-0.37 (0.363)	-0.4 (-0.5, -0.2)	-1.1, 0.4	-0.37 (0.090)	(-0.56, -0.18)	-0.03 (-0.29, 0.24)	0.8249	-0.07 (-0.84, 0.70)	
Percent change from baseline	13	-6.33 (4.892)	-7.3 (-9.8, -4.1)	-13.4, 6.0			13	-6.82 (6.727)	-6.8 (-8.8, -3.3)	-19.6, 6.8						
4 hours																
Absolute value	13	5.02 (0.329)	5.2 (4.9, 5.2)	4.4, 5.4			13	5.02 (0.398)	5.1 (4.8, 5.3)	4.2, 5.7						
Change from baseline	13	-0.43 (0.336)	-0.3 (-0.6, -0.2)	-1.1, 0.0	-0.43 (0.100)	(-0.63, -0.22)	13	-0.41 (0.372)	-0.4 (-0.7, -0.1)	-1.1, 0.2	-0.41 (0.100)	(-0.62, -0.20)	0.02 (-0.28, 0.31)	0.9033	0.07 (-0.70, 0.84)	
Percent change from baseline	13	-7.89 (6.166)	-6.2 (-10.9, -3.3)	-19.6, 0.0			13	-7.51 (6.892)	-6.4 (-11.9, -2.3)	-21.5, 3.2						
24 hours																
Absolute value	13	5.20 (0.356)	5.2 (5.0, 5.4)	4.6, 5.9			13	4.74 (0.266)	4.7 (4.6, 4.9)	4.4, 5.3						
Change from baseline	13	-0.25 (0.360)	-0.3 (-0.5, 0.1)	-0.9, 0.4	-0.24 (0.089)	(-0.43, -0.06)	13	-0.68 (0.278)	-0.8 (-0.9, -0.5)	-1.1, -0.1	-0.69 (0.089)	(-0.87, -0.50)	-0.44 (-0.71, -0.18)	0.0019	-1.36 (-2.21, -0.51)	
Percent change from baseline	13	-4.50 (6.594)	-6.2 (-9.1, 0.9)	-15.6, 6.8			13	-12.58 (5.089)	-14.2 (-16.7, -9.7)	-19.3, -1.9						
25 hours																
Absolute value	13	5.18 (0.174)	5.2 (5.1, 5.3)	4.9, 5.5			13	4.54 (0.263)	4.5 (4.4, 4.7)	4.0, 4.9						
Change from baseline	13	-0.27 (0.198)	-0.2 (-0.4, -0.2)	-0.6, 0.1	-0.27 (0.067)	(-0.41, -0.13)	13	-0.88 (0.280)	-0.9 (-1.1, -0.7)	-1.5, -0.5	-0.89 (0.067)	(-1.03, -0.75)	-0.62 (-0.82, -0.42)	<.0001	-2.53 (-3.56, -1.50)	
Percent change from baseline	13	-4.92 (3.606)	-4.1 (-6.8, -2.8)	-11.6, 2.3			13	-16.27 (5.105)	-17.1 (-19.6, -12.6)	-26.6, -9.3						
28 hours																
Absolute value	13	5.05 (0.410)	5.0 (4.8, 5.2)	4.4, 5.9			13	4.50 (0.329)	4.5 (4.3, 4.7)	3.9, 5.2						
Change from baseline	13	-0.39 (0.418)	-0.4 (-0.7, -0.3)	-1.0, 0.5	-0.39 (0.103)	(-0.60, -0.18)	13	-0.92 (0.306)	-0.9 (-1.1, -0.8)	-1.5, -0.3	-0.92 (0.103)	(-1.14, -0.71)	-0.54 (-0.84, -0.24)	0.0012	-1.45 (-2.31, -0.58)	
Percent change from baseline	13	-7.18 (7.677)	-6.5 (-12.7, -5.6)	-18.9, 9.8			13	-17.01 (5.685)	-16.3 (-20.0, -13.8)	-28.1, -5.9						
48 hours																
Absolute value	13	5.22 (0.276)	5.3 (5.1, 5.4)	4.6, 5.5			13	4.17 (0.377)	4.1 (4.0, 4.4)	3.5, 4.8						
Change from baseline	13	-0.23 (0.276)	-0.1 (-0.3, -0.1)	-0.9, 0.1	-0.23 (0.090)	(-0.41, -0.04)	13	-1.25 (0.352)	-1.3 (-1.5, -1.1)	-1.9, -0.7	-1.26 (0.090)	(-1.44, -1.07)	-1.03 (-1.29, -0.77)	<.0001	-3.23 (-4.40, -2.06)	
Percent change from baseline	13	-4.22 (5.073)	-1.9 (-6.0, -1.4)	-15.6, 0.9			13	-23.12 (6.594)	-24.1 (-26.6, -20.0)	-34.6, -11.9						
>5.5 mmol/L																
Baseline																
Absolute value	13	6.07 (0.371)	6.1 (5.7, 6.3)	5.6, 6.6			11	5.88 (0.338)	5.8 (5.7, 5.9)	5.6, 6.8						
1 hour																
Absolute value	13	6.00 (0.577)	6.0 (5.5, 6.5)	5.0, 6.8			11	5.38 (0.218)	5.4 (5.3, 5.5)	5.0, 5.8						
Change from baseline	13	-0.07 (0.396)	-0.2 (-0.4, 0.3)	-0.7, 0.5	-0.03 (0.099)	(-0.24, 0.17)	11	-0.50 (0.274)	-0.5 (-0.6, -0.3)	-1.0, -0.1	-0.53 (0.106)	(-0.75, -0.31)	-0.50 (-0.80, -0.19)	0.0028	-1.25 (-2.12, -0.37)	
Percent change from baseline	13	-1.23 (6.639)	-3.4 (-6.3, 5.4)	-12.3, 8.4			11	-8.39 (4.182)	-8.9 (-10.4, -5.4)	-15.0, -2.2						
2 hours																
Absolute value	12	5.77 (0.590)	5.9 (5.1, 6.3)	5.0, 6.5			11	5.12 (0.309)	5.2 (4.9, 5.4)	4.5, 5.6						
Change from baseline	12	-0.26 (0.367)	-0.3 (-0.6, -0.0)	-0.7, 0.5	-0.23 (0.109)	(-0.46, -0.01)	11	-0.77 (0.392)	-0.7 (-0.9, -0.5)	-1.4, -0.1	-0.79 (0.115)	(-1.03, -0.55)	-0.56 (-0.89, -0.23)	0.0021	-1.34 (-2.24, -0.43)	
Percent change from baseline	12	-4.42 (6.248)	-4.3 (-9.8, -0.7)	-12.3, 7.4			11	-12.85 (6.106)	-12.2 (-15.4, -8.8)	-23.4, -2.2						
4 hours																
Absolute value	12	5.59 (0.521)	5.8 (5.1, 6.1)	4.7, 6.1			11	5.21 (0.330)	5.1 (5.0, 5.3)	4.8, 5.9						
Change from baseline	12	-0.43 (0.305)	-0.4 (-0.7, -0.2)	-1.0, -0.1	-0.41 (0.092)	(-0.60, -0.21)	11	-0.68 (0.316)	-0.7 (-0.9, -0.5)	-1.2, -0.0	-0.70 (0.097)	(-0.90, -0.50)	-0.29 (-0.58, -0.01)	0.0437	-0.78 (-1.63, 0.07)	

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value *(contd.)*																
>5.5 mmol/L *(contd.)*																
4 hours *(contd.)*																
Percent change from baseline	12	-7.29 (5.352)	-6.2 (-12.1, -2.6)	-17.5, -1.2			11	-11.37 (5.113)	-11.3 (-14.9, -8.2)	-20.3, -0.4						
24 hours																
Absolute value	11	5.76 (0.411)	5.7 (5.4, 6.1)	5.2, 6.6			11	4.98 (0.264)	4.9 (4.8, 5.3)	4.6, 5.4						
Change from baseline	11	-0.24 (0.361)	-0.3 (-0.4, 0.0)	-0.8, 0.5	-0.21 (0.106)	(-0.43, 0.02)	11	-0.90 (0.429)	-0.9 (-1.1, -0.6)	-1.9, -0.3	-0.93 (0.105)	(-1.15, -0.70)	-0.72 (-1.04, -0.41)	0.0001	-1.67 (-2.64, -0.70)	
Percent change from baseline	11	-3.89 (5.818)	-5.4 (-7.1, 0.0)	-12.6, 9.1			11	-15.11 (6.243)	-16.1 (-18.7, -10.5)	-28.2, -5.8						
25 hours																
Absolute value	11	5.75 (0.359)	5.7 (5.4, 6.1)	5.3, 6.3			11	4.58 (0.299)	4.6 (4.3, 4.7)	4.2, 5.2						
Change from baseline	11	-0.26 (0.269)	-0.2 (-0.6, -0.2)	-0.6, 0.3	-0.20 (0.113)	(-0.44, 0.04)	11	-1.30 (0.549)	-1.1 (-1.6, -1.0)	-2.6, -0.4	-1.33 (0.114)	(-1.57, -1.08)	-1.13 (-1.47, -0.78)	<.0001	-2.42 (-3.52, -1.32)	
Percent change from baseline	11	-4.21 (4.260)	-3.6 (-9.2, -2.6)	-9.6, 4.1			11	-21.80 (7.790)	-19.6 (-26.8, -17.9)	-38.5, -7.6						
28 hours																
Absolute value	11	5.53 (0.508)	5.5 (5.2, 6.1)	4.6, 6.3			11	4.45 (0.339)	4.5 (4.2, 4.7)	3.9, 5.0						
Change from baseline	11	-0.48 (0.432)	-0.5 (-1.0, -0.1)	-1.1, 0.3	-0.42 (0.117)	(-0.67, -0.18)	11	-1.43 (0.387)	-1.2 (-1.8, -1.2)	-2.0, -0.9	-1.45 (0.118)	(-1.70, -1.21)	-1.03 (-1.38, -0.68)	<.0001	-2.33 (-3.41, -1.25)	
Percent change from baseline	11	-7.88 (7.100)	-7.8 (-15.7, -1.8)	-18.9, 4.1			11	-24.17 (5.970)	-21.4 (-30.3, -20.0)	-33.9, -16.1						
48 hours																
Absolute value	11	5.62 (0.349)	5.8 (5.2, 5.9)	5.1, 6.1			11	4.41 (0.305)	4.3 (4.2, 4.5)	4.1, 5.2						
Change from baseline	11	-0.38 (0.321)	-0.4 (-0.6, -0.1)	-1.0, 0.0	-0.36 (0.102)	(-0.58, -0.15)	11	-1.48 (0.447)	-1.5 (-1.6, -1.2)	-2.5, -0.7	-1.50 (0.101)	(-1.71, -1.29)	-1.14 (-1.44, -0.83)	<.0001	-2.80 (-3.98, -1.63)	
Percent change from baseline	11	-6.29 (5.094)	-7.1 (-10.1, -1.8)	-15.1, 0.9			11	-24.88 (6.259)	-25.3 (-27.1, -21.4)	-37.0, -12.2						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Chronic kidney disease																0.8922
Yes																
Baseline																
Absolute value	26	5.68 (0.434)	5.5 (5.4, 6.1)	5.2, 6.6			26	5.45 (0.268)	5.4 (5.3, 5.6)	5.0, 6.0						
1 hour																
Absolute value	26	5.56 (0.551)	5.4 (5.2, 5.9)	4.7, 6.6			26	5.11 (0.366)	5.3 (4.8, 5.4)	4.3, 5.7						
Change from baseline	26	-0.12 (0.303)	-0.2 (-0.3, 0.1)	-0.8, 0.5	-0.10 (0.065)	(-0.23, 0.03)	26	-0.35 (0.344)	-0.4 (-0.6, -0.1)	-1.0, 0.6	-0.36 (0.065)	(-0.49, -0.23)	-0.26 (-0.45, -0.07)	0.0077	-0.68 (-1.24, -0.12)	
Percent change from baseline	26	-2.23 (5.341)	-3.3 (-6.2, 1.9)	-13.8, 7.4			26	-6.26 (6.419)	-7.4 (-10.7, -2.3)	-18.1, 12.3						
2 hours																
Absolute value	25	5.32 (0.544)	5.1 (5.0, 5.7)	4.4, 6.5			26	4.93 (0.394)	5.0 (4.7, 5.2)	4.3, 5.9						
Change from baseline	25	-0.33 (0.294)	-0.3 (-0.5, -0.2)	-0.9, 0.5	-0.31 (0.069)	(-0.45, -0.17)	26	-0.52 (0.380)	-0.5 (-0.8, -0.3)	-1.4, 0.4	-0.53 (0.068)	(-0.67, -0.40)	-0.22 (-0.42, -0.02)	0.0281	-0.56 (-1.12, 0.00)	
Percent change from baseline	25	-5.90 (5.288)	-5.8 (-9.7, -4.1)	-16.6, 7.4			26	-9.42 (6.789)	-8.8 (-14.7, -6.0)	-23.4, 6.8						
4 hours																
Absolute value	25	5.21 (0.522)	5.2 (4.9, 5.5)	4.4, 6.1			26	4.96 (0.408)	5.0 (4.7, 5.3)	4.1, 5.7						
Change from baseline	25	-0.43 (0.295)	-0.4 (-0.7, -0.2)	-1.1, 0.0	-0.42 (0.070)	(-0.56, -0.28)	26	-0.49 (0.383)	-0.5 (-0.9, -0.1)	-1.2, 0.2	-0.51 (0.068)	(-0.65, -0.37)	-0.09 (-0.29, 0.10)	0.3429	-0.18 (-0.73, 0.37)	
Percent change from baseline	25	-7.73 (5.413)	-6.5 (-11.1, -3.3)	-19.6, 0.0			26	-9.01 (6.908)	-8.5 (-14.9, -2.4)	-21.5, 3.2						
24 hours																
Absolute value	25	5.42 (0.484)	5.3 (5.0, 5.7)	4.6, 6.6			26	4.76 (0.319)	4.8 (4.6, 4.9)	4.1, 5.4						
Change from baseline	25	-0.23 (0.352)	-0.3 (-0.4, 0.0)	-0.9, 0.5	-0.21 (0.065)	(-0.34, -0.08)	26	-0.69 (0.308)	-0.8 (-0.9, -0.5)	-1.2, -0.1	-0.71 (0.064)	(-0.84, -0.58)	-0.50 (-0.68, -0.31)	<.0001	-1.41 (-2.03, -0.80)	
Percent change from baseline	25	-3.99 (6.141)	-5.0 (-7.8, 0.5)	-15.6, 9.1			26	-12.66 (5.479)	-14.3 (-17.1, -8.5)	-21.9, -1.9						
25 hours																
Absolute value	25	5.36 (0.510)	5.3 (5.1, 5.7)	4.1, 6.3			26	4.45 (0.350)	4.5 (4.3, 4.7)	3.7, 5.2						
Change from baseline	25	-0.29 (0.329)	-0.2 (-0.5, -0.2)	-1.2, 0.4	-0.27 (0.070)	(-0.41, -0.13)	26	-1.00 (0.381)	-1.1 (-1.3, -0.7)	-1.6, -0.3	-1.02 (0.069)	(-1.16, -0.88)	-0.75 (-0.95, -0.55)	<.0001	-2.00 (-2.68, -1.33)	
Percent change from baseline	25	-5.12 (5.967)	-3.7 (-9.2, -2.7)	-22.3, 7.5			26	-18.27 (6.659)	-19.1 (-22.0, -12.6)	-29.5, -5.8						
28 hours																
Absolute value	25	5.18 (0.570)	5.1 (4.7, 5.5)	4.2, 6.3			26	4.29 (0.369)	4.3 (4.0, 4.5)	3.7, 5.2						
Change from baseline	25	-0.46 (0.443)	-0.5 (-0.8, -0.3)	-1.1, 0.5	-0.44 (0.082)	(-0.61, -0.28)	26	-1.16 (0.389)	-1.1 (-1.4, -0.9)	-2.0, -0.3	-1.18 (0.081)	(-1.34, -1.01)	-0.73 (-0.97, -0.50)	<.0001	-1.68 (-2.32, -1.04)	
Percent change from baseline	25	-8.15 (7.885)	-7.8 (-14.2, -5.6)	-20.4, 9.8			26	-21.19 (6.601)	-21.1 (-25.1, -18.0)	-33.9, -5.9						
48 hours																
Absolute value	25	5.38 (0.392)	5.4 (5.1, 5.8)	4.6, 6.1			26	4.09 (0.445)	4.2 (3.8, 4.4)	2.9, 4.8						
Change from baseline	25	-0.26 (0.344)	-0.2 (-0.5, -0.1)	-1.0, 0.5	-0.25 (0.071)	(-0.39, -0.10)	26	-1.36 (0.383)	-1.4 (-1.6, -1.1)	-2.3, -0.6	-1.38 (0.070)	(-1.52, -1.24)	-1.13 (-1.33, -0.93)	<.0001	-3.02 (-3.82, -2.22)	
Percent change from baseline	25	-4.52 (5.949)	-3.2 (-8.0, -1.4)	-15.6, 9.4			26	-25.04 (7.256)	-24.5 (-29.0, -20.4)	-44.0, -11.3						
No																
Baseline																
Absolute value	7	5.53 (0.384)	5.4 (5.2, 5.7)	5.2, 6.3			10	5.47 (0.574)	5.3 (5.1, 5.8)	5.0, 6.8						
1 hour																
Absolute value	7	5.39 (0.662)	5.1 (5.0, 5.5)	4.9, 6.8			10	5.03 (0.501)	5.0 (4.6, 5.4)	4.2, 5.8						
Change from baseline	7	-0.14 (0.404)	-0.1 (-0.5, 0.1)	-0.7, 0.5	-0.11 (0.154)	(-0.45, 0.22)	10	-0.44 (0.356)	-0.5 (-0.5, -0.1)	-1.0, 0.0	-0.44 (0.129)	(-0.72, -0.16)	-0.33 (-0.77, 0.11)	0.1300	-0.81 (-1.81, 0.20)	
Percent change from baseline	7	-2.68 (6.953)	-2.4 (-9.7, 2.4)	-12.3, 8.4			10	-7.90 (6.103)	-9.0 (-10.1, -2.0)	-18.4, 0.9						

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Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
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	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Chronic kidney disease *(contd.)*																
No *(contd.)*																
2 hours																
Absolute value	7	5.17 (0.647)	5.0 (4.7, 5.5)	4.7, 6.5			10	5.00 (0.374)	5.0 (4.8, 5.4)	4.2, 5.4						
Change from baseline	7	-0.35 (0.347)	-0.4 (-0.7, -0.1)	-0.7, 0.2	-0.33 (0.147)	(-0.64, -0.01)	10	-0.47 (0.461)	-0.3 (-0.7, -0.2)	-1.4, 0.0	-0.47 (0.123)	(-0.73, -0.21)	-0.14 (-0.55, 0.27)	0.4666	-0.28 (-1.25, 0.69)	
Percent change from baseline	7	-6.61 (6.180)	-7.2 (-12.3, -1.8)	-13.4, 3.6			10	-8.18 (7.391)	-5.8 (-12.2, -3.0)	-20.9, 1.0						
4 hours																
Absolute value	7	5.09 (0.521)	5.1 (4.7, 5.2)	4.5, 6.1			10	4.84 (0.546)	4.8 (4.4, 5.1)	4.0, 5.9						
Change from baseline	7	-0.44 (0.378)	-0.4 (-0.9, -0.1)	-1.0, -0.1	-0.41 (0.136)	(-0.72, -0.11)	10	-0.63 (0.289)	-0.7 (-0.8, -0.4)	-1.2, -0.2	-0.63 (0.114)	(-0.88, -0.38)	-0.22 (-0.61, 0.18)	0.2486	-0.59 (-1.58, 0.40)	
Percent change from baseline	7	-7.94 (6.784)	-7.1 (-17.1, -2.4)	-17.5, -1.4			10	-11.51 (5.304)	-11.6 (-13.7, -7.4)	-22.3, -3.0						
24 hours																
Absolute value	6	5.23 (0.418)	5.4 (4.9, 5.5)	4.6, 5.7			10	4.78 (0.371)	5.0 (4.4, 5.0)	4.2, 5.3						
Change from baseline	6	-0.17 (0.381)	-0.2 (-0.5, 0.2)	-0.6, 0.3	-0.19 (0.161)	(-0.54, 0.16)	10	-0.69 (0.545)	-0.6 (-0.9, -0.4)	-1.9, 0.0	-0.69 (0.121)	(-0.95, -0.43)	-0.50 (-0.93, -0.06)	0.0291	-1.07 (-2.14, 0.01)	
Percent change from baseline	6	-3.07 (7.177)	-3.6 (-9.7, 4.3)	-11.1, 5.3			10	-12.12 (8.396)	-12.1 (-17.6, -6.4)	-28.2, 1.0						
25 hours																
Absolute value	6	5.22 (0.223)	5.2 (5.1, 5.4)	4.9, 5.5			10	4.48 (0.301)	4.5 (4.2, 4.7)	4.1, 4.9						
Change from baseline	6	-0.18 (0.231)	-0.3 (-0.3, -0.2)	-0.3, 0.3	-0.14 (0.149)	(-0.49, 0.21)	10	-0.99 (0.615)	-0.9 (-1.0, -0.7)	-2.6, -0.4	-0.99 (0.116)	(-1.27, -0.71)	-0.85 (-1.29, -0.40)	0.0026	-1.58 (-2.73, -0.43)	
Percent change from baseline	6	-3.33 (4.306)	-5.3 (-5.4, -3.3)	-6.0, 5.3			10	-17.50 (8.328)	-17.3 (-18.4, -13.7)	-38.5, -7.1						
28 hours																
Absolute value	6	5.22 (0.232)	5.3 (5.0, 5.4)	4.9, 5.5			10	4.44 (0.386)	4.6 (4.1, 4.7)	3.8, 5.0						
Change from baseline	6	-0.18 (0.281)	-0.1 (-0.5, 0.0)	-0.5, 0.2	-0.20 (0.108)	(-0.44, 0.03)	10	-1.03 (0.385)	-1.0 (-1.2, -0.9)	-1.8, -0.4	-1.03 (0.081)	(-1.21, -0.85)	-0.83 (-1.12, -0.53)	<.0001	-2.41 (-3.73, -1.10)	
Percent change from baseline	6	-3.30 (5.126)	-2.6 (-8.8, 0.5)	-9.7, 3.3			10	-18.61 (5.646)	-19.4 (-21.2, -15.6)	-26.7, -7.4						
48 hours																
Absolute value	6	5.28 (0.360)	5.4 (5.2, 5.5)	4.6, 5.6			10	4.35 (0.488)	4.3 (4.0, 4.8)	3.7, 5.2						
Change from baseline	6	-0.12 (0.316)	-0.1 (-0.4, 0.2)	-0.6, 0.2	-0.17 (0.193)	(-0.59, 0.25)	10	-1.12 (0.655)	-1.1 (-1.5, -0.7)	-2.5, -0.2	-1.12 (0.144)	(-1.43, -0.81)	-0.95 (-1.47, -0.43)	0.0017	-1.80 (-2.99, -0.61)	
Percent change from baseline	6	-2.14 (5.994)	-1.1 (-7.1, 3.3)	-11.1, 4.3			10	-20.02 (9.992)	-21.0 (-27.0, -12.2)	-37.0, -3.4						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Congestive Heart Disease																
Yes																
Baseline																
Absolute value	4	5.47 (0.410)	5.3 (5.2, 5.7)	5.2, 6.1			3	5.68 (0.250)	5.7 (5.4, 5.9)	5.4, 5.9						
1 hour																
Absolute value	4	5.45 (0.733)	5.2 (5.0, 6.0)	4.9, 6.5			3	5.43 (0.058)	5.4 (5.4, 5.5)	5.4, 5.5						
Change from baseline	4	-0.02 (0.378)	-0.0 (-0.3, 0.3)	-0.4, 0.4			3	-0.25 (0.254)	-0.2 (-0.5, -0.0)	-0.5, -0.0						
Percent change from baseline	4	-0.61 (6.715)	-0.5 (-5.9, 4.7)	-8.4, 7.0			3	-4.28 (4.252)	-3.5 (-8.9, -0.5)	-8.9, -0.5						
2 hours																
Absolute value	4	5.18 (0.640)	5.0 (4.8, 5.6)	4.7, 6.1			3	5.23 (0.058)	5.2 (5.2, 5.3)	5.2, 5.3						
Change from baseline	4	-0.29 (0.251)	-0.3 (-0.5, -0.1)	-0.6, 0.0			3	-0.45 (0.303)	-0.5 (-0.7, -0.1)	-0.7, -0.1						
Percent change from baseline	4	-5.60 (4.754)	-6.0 (-9.1, -2.1)	-10.9, 0.4			3	-7.77 (5.041)	-8.8 (-12.2, -2.3)	-12.2, -2.3						
4 hours																
Absolute value	4	5.30 (0.503)	5.2 (5.0, 5.6)	4.8, 6.0			3	5.20 (0.173)	5.3 (5.0, 5.3)	5.0, 5.3						
Change from baseline	4	-0.17 (0.142)	-0.1 (-0.3, -0.1)	-0.4, -0.1			3	-0.48 (0.313)	-0.6 (-0.7, -0.1)	-0.7, -0.1						
Percent change from baseline	4	-3.18 (2.802)	-2.1 (-5.0, -1.3)	-7.2, -1.2			3	-8.38 (5.331)	-10.5 (-12.3, -2.3)	-12.3, -2.3						
24 hours																
Absolute value	4	5.30 (0.483)	5.5 (5.0, 5.6)	4.6, 5.7			3	4.80 (0.436)	4.6 (4.5, 5.3)	4.5, 5.3						
Change from baseline	4	-0.17 (0.370)	-0.2 (-0.5, 0.1)	-0.6, 0.2			3	-0.88 (0.240)	-0.9 (-1.1, -0.6)	-1.1, -0.6						
Percent change from baseline	4	-3.02 (6.931)	-2.6 (-8.6, 2.6)	-11.1, 4.3			3	-15.63 (4.544)	-17.1 (-19.3, -10.5)	-19.3, -10.5						
25 hours																
Absolute value	4	5.33 (0.532)	5.2 (5.0, 5.7)	4.9, 6.1			3	4.63 (0.252)	4.6 (4.4, 4.9)	4.4, 4.9						
Change from baseline	4	-0.14 (0.125)	-0.2 (-0.2, -0.1)	-0.3, 0.0			3	-1.05 (0.043)	-1.0 (-1.1, -1.0)	-1.1, -1.0						
Percent change from baseline	4	-2.76 (2.373)	-3.1 (-4.3, -1.2)	-5.3, 0.4			3	-18.50 (1.057)	-18.9 (-19.3, -17.3)	-19.3, -17.3						
28 hours																
Absolute value	4	5.35 (0.520)	5.2 (5.0, 5.7)	5.0, 6.1			3	4.37 (0.416)	4.5 (3.9, 4.7)	3.9, 4.7						
Change from baseline	4	-0.12 (0.181)	-0.1 (-0.3, 0.0)	-0.3, 0.0			3	-1.32 (0.181)	-1.2 (-1.5, -1.2)	-1.5, -1.2						
Percent change from baseline	4	-2.26 (3.377)	-1.5 (-5.0, 0.4)	-6.5, 0.5			3	-23.28 (4.188)	-21.1 (-28.1, -20.7)	-28.1, -20.7						
48 hours																
Absolute value	4	5.35 (0.545)	5.5 (5.0, 5.7)	4.6, 5.9			3	4.40 (0.721)	4.2 (3.8, 5.2)	3.8, 5.2						
Change from baseline	4	-0.12 (0.345)	-0.1 (-0.4, 0.1)	-0.6, 0.2			3	-1.28 (0.488)	-1.5 (-1.6, -0.7)	-1.6, -0.7						
Percent change from baseline	4	-2.20 (6.621)	-1.0 (-7.0, 2.6)	-11.1, 4.3			3	-22.84 (9.358)	-26.3 (-30.0, -12.2)	-30.0, -12.2						
No																
Baseline																
Absolute value	29	5.67 (0.426)	5.5 (5.4, 5.8)	5.2, 6.6			33	5.44 (0.374)	5.4 (5.2, 5.6)	5.0, 6.8						
1 hour																
Absolute value	29	5.53 (0.559)	5.3 (5.1, 5.9)	4.7, 6.8			33	5.05 (0.405)	5.0 (4.8, 5.4)	4.2, 5.8						
Change from baseline	29	-0.14 (0.316)	-0.2 (-0.3, 0.1)	-0.8, 0.5	-0.10 (0.064)	(-0.23, 0.02)	33	-0.38 (0.353)	-0.5 (-0.6, -0.1)	-1.0, 0.6	-0.41 (0.059)	(-0.53, -0.29)	-0.30 (-0.48, -0.13)	0.0011	-0.72 (-1.23, -0.20)	
Percent change from baseline	29	-2.56 (5.528)	-3.2 (-6.2, 1.9)	-13.8, 8.4			33	-6.94 (6.445)	-8.3 (-10.7, -2.3)	-18.4, 12.3						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

Lokelma

Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Congestive Heart Disease *(contd.)*																
No *(contd.)*																
2 hours																
Absolute value	28	5.30 (0.559)	5.1 (5.0, 5.6)	4.4, 6.5			33	4.93 (0.392)	4.9 (4.7, 5.2)	4.2, 5.9						
Change from baseline	28	-0.34 (0.311)	-0.4 (-0.6, -0.2)	-0.9, 0.5	-0.31 (0.069)	(-0.44, -0.17)	33	-0.51 (0.409)	-0.5 (-0.8, -0.3)	-1.4, 0.4	-0.53 (0.063)	(-0.66, -0.41)	-0.23 (-0.42, -0.04)	0.0192	-0.46 (-0.98, 0.05)	
Percent change from baseline	28	-6.13 (5.559)	-6.5 (-9.9, -3.9)	-16.6, 7.4			33	-9.19 (7.068)	-8.7 (-14.7, -4.6)	-23.4, 6.8						
4 hours																
Absolute value	28	5.17 (0.525)	5.2 (4.9, 5.5)	4.4, 6.1			33	4.90 (0.456)	5.0 (4.7, 5.1)	4.0, 5.9						
Change from baseline	28	-0.47 (0.308)	-0.4 (-0.7, -0.2)	-1.1, 0.0	-0.44 (0.067)	(-0.57, -0.31)	33	-0.54 (0.369)	-0.5 (-0.9, -0.2)	-1.2, 0.2	-0.56 (0.061)	(-0.68, -0.44)	-0.12 (-0.30, 0.06)	0.1904	-0.19 (-0.70, 0.31)	
Percent change from baseline	28	-8.43 (5.642)	-7.3 (-13.2, -3.7)	-19.6, 0.0			33	-9.82 (6.682)	-10.5 (-14.9, -3.4)	-22.3, 3.2						
24 hours																
Absolute value	27	5.39 (0.477)	5.3 (5.0, 5.7)	4.6, 6.6			33	4.76 (0.326)	4.8 (4.6, 5.0)	4.1, 5.4						
Change from baseline	27	-0.22 (0.356)	-0.3 (-0.5, 0.0)	-0.9, 0.5	-0.19 (0.067)	(-0.32, -0.05)	33	-0.68 (0.388)	-0.7 (-0.9, -0.4)	-1.9, 0.0	-0.70 (0.061)	(-0.82, -0.58)	-0.51 (-0.70, -0.33)	<.0001	-1.21 (-1.77, -0.66)	
Percent change from baseline	27	-3.93 (6.263)	-5.0 (-9.1, 0.5)	-15.6, 9.1			33	-12.23 (6.408)	-12.9 (-16.9, -7.2)	-28.2, 1.0						
25 hours																
Absolute value	27	5.33 (0.470)	5.3 (5.1, 5.6)	4.1, 6.3			33	4.44 (0.338)	4.5 (4.2, 4.7)	3.7, 5.2						
Change from baseline	27	-0.29 (0.328)	-0.3 (-0.5, -0.2)	-1.2, 0.4	-0.24 (0.073)	(-0.39, -0.10)	33	-0.99 (0.468)	-1.0 (-1.1, -0.7)	-2.6, -0.3	-1.02 (0.066)	(-1.15, -0.88)	-0.78 (-0.98, -0.58)	<.0001	-1.72 (-2.32, -1.13)	
Percent change from baseline	27	-5.07 (5.972)	-5.3 (-9.2, -2.7)	-22.3, 7.5			33	-18.02 (7.362)	-18.3 (-21.6, -12.6)	-38.5, -5.8						
28 hours																
Absolute value	27	5.17 (0.524)	5.2 (4.7, 5.5)	4.2, 6.3			33	4.33 (0.377)	4.4 (4.0, 4.6)	3.7, 5.2						
Change from baseline	27	-0.45 (0.439)	-0.5 (-0.8, -0.1)	-1.1, 0.5	-0.41 (0.076)	(-0.56, -0.25)	33	-1.11 (0.397)	-1.1 (-1.3, -0.9)	-2.0, -0.3	-1.13 (0.069)	(-1.27, -0.99)	-0.72 (-0.93, -0.51)	<.0001	-1.58 (-2.16, -1.00)	
Percent change from baseline	27	-7.94 (7.821)	-8.8 (-14.2, -1.9)	-20.4, 9.8			33	-20.22 (6.528)	-20.0 (-23.6, -16.1)	-33.9, -5.9						
48 hours																
Absolute value	27	5.36 (0.366)	5.4 (5.1, 5.6)	4.6, 6.1			33	4.14 (0.446)	4.2 (4.0, 4.4)	2.9, 4.9						
Change from baseline	27	-0.25 (0.341)	-0.2 (-0.5, -0.0)	-1.0, 0.5	-0.22 (0.076)	(-0.37, -0.07)	33	-1.30 (0.483)	-1.3 (-1.6, -1.1)	-2.5, -0.2	-1.32 (0.068)	(-1.46, -1.18)	-1.10 (-1.31, -0.90)	<.0001	-2.46 (-3.13, -1.78)	
Percent change from baseline	27	-4.34 (5.913)	-3.2 (-8.0, -0.5)	-15.6, 9.4			33	-23.72 (8.327)	-24.1 (-27.1, -19.6)	-44.0, -3.4						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Diabetes mellitus																0.4172
Yes																
Baseline																
Absolute value	16	5.58 (0.303)	5.5 (5.4, 5.7)	5.2, 6.3			24	5.49 (0.428)	5.4 (5.2, 5.8)	5.0, 6.8						
1 hour																
Absolute value	16	5.53 (0.619)	5.4 (5.1, 5.8)	4.7, 6.8			24	5.11 (0.435)	5.2 (4.8, 5.4)	4.2, 5.8						
Change from baseline	16	-0.05 (0.399)	-0.1 (-0.3, 0.3)	-0.8, 0.5	-0.03 (0.099)	(-0.23, 0.17)	24	-0.39 (0.377)	-0.5 (-0.6, -0.1)	-1.0, 0.6	-0.40 (0.081)	(-0.56, -0.23)	-0.36 (-0.62, -0.10)	0.0077	-0.87 (-1.53, -0.21)	
Percent change from baseline	16	-1.14 (7.027)	-1.8 (-5.8, 4.7)	-13.8, 8.4			24	-6.90 (6.800)	-9.2 (-10.5, -2.1)	-18.4, 12.3						
2 hours																
Absolute value	16	5.32 (0.586)	5.1 (5.0, 5.6)	4.7, 6.5			24	4.93 (0.388)	5.0 (4.8, 5.2)	4.2, 5.6						
Change from baseline	16	-0.26 (0.364)	-0.3 (-0.6, -0.0)	-0.7, 0.5	-0.24 (0.098)	(-0.44, -0.04)	24	-0.57 (0.427)	-0.6 (-0.9, -0.2)	-1.4, 0.1	-0.57 (0.080)	(-0.73, -0.41)	-0.33 (-0.59, -0.08)	0.0124	-0.76 (-1.41, -0.11)	
Percent change from baseline	16	-4.83 (6.500)	-6.0 (-10.3, -0.7)	-13.4, 7.4			24	-10.04 (7.268)	-10.4 (-15.3, -3.6)	-23.4, 2.5						
4 hours																
Absolute value	16	5.18 (0.496)	5.2 (4.9, 5.4)	4.4, 6.1			24	4.93 (0.462)	5.0 (4.7, 5.3)	4.0, 5.9						
Change from baseline	16	-0.40 (0.346)	-0.2 (-0.6, -0.1)	-1.1, -0.1	-0.38 (0.091)	(-0.56, -0.19)	24	-0.57 (0.372)	-0.6 (-0.9, -0.2)	-1.2, -0.0	-0.57 (0.074)	(-0.72, -0.42)	-0.20 (-0.43, 0.04)	0.1052	-0.47 (-1.11, 0.18)	
Percent change from baseline	16	-7.17 (6.284)	-3.9 (-10.7, -2.4)	-19.6, -1.2			24	-10.19 (6.643)	-10.9 (-14.3, -3.2)	-22.3, -0.4						
24 hours																
Absolute value	15	5.34 (0.476)	5.3 (5.0, 5.6)	4.6, 6.6			24	4.78 (0.344)	4.8 (4.5, 5.0)	4.1, 5.4						
Change from baseline	15	-0.19 (0.391)	-0.3 (-0.5, 0.2)	-0.9, 0.5	-0.17 (0.095)	(-0.36, 0.02)	24	-0.72 (0.412)	-0.7 (-1.0, -0.4)	-1.9, 0.0	-0.73 (0.075)	(-0.88, -0.57)	-0.55 (-0.80, -0.31)	<.0001	-1.31 (-2.01, -0.60)	
Percent change from baseline	15	-3.48 (7.035)	-5.4 (-9.1, 4.2)	-15.6, 9.1			24	-12.83 (6.629)	-12.9 (-17.9, -7.9)	-28.2, 1.0						
25 hours																
Absolute value	15	5.36 (0.383)	5.3 (5.1, 5.5)	4.9, 6.3			24	4.48 (0.323)	4.5 (4.3, 4.7)	3.8, 5.2						
Change from baseline	15	-0.17 (0.241)	-0.2 (-0.3, 0.0)	-0.5, 0.3	-0.14 (0.093)	(-0.33, 0.05)	24	-1.02 (0.494)	-1.0 (-1.2, -0.7)	-2.6, -0.4	-1.02 (0.074)	(-1.17, -0.87)	-0.88 (-1.13, -0.64)	<.0001	-2.02 (-2.81, -1.24)	
Percent change from baseline	15	-3.14 (4.382)	-3.6 (-6.0, 0.4)	-10.1, 5.3			24	-18.13 (7.398)	-17.6 (-21.8, -13.1)	-38.5, -7.1						
28 hours																
Absolute value	15	5.26 (0.500)	5.1 (4.9, 5.5)	4.7, 6.3			24	4.27 (0.351)	4.4 (3.9, 4.6)	3.8, 5.0						
Change from baseline	15	-0.27 (0.401)	-0.3 (-0.5, 0.0)	-0.8, 0.5	-0.25 (0.094)	(-0.44, -0.06)	24	-1.22 (0.387)	-1.2 (-1.4, -1.0)	-2.0, -0.4	-1.23 (0.074)	(-1.38, -1.08)	-0.98 (-1.22, -0.74)	<.0001	-2.43 (-3.27, -1.59)	
Percent change from baseline	15	-4.95 (7.311)	-6.5 (-10.1, 0.5)	-14.2, 9.8			24	-22.09 (6.053)	-21.3 (-26.0, -18.6)	-33.9, -7.4						
48 hours																
Absolute value	15	5.35 (0.381)	5.4 (5.2, 5.5)	4.6, 6.1			24	4.19 (0.490)	4.3 (3.9, 4.5)	2.9, 5.2						
Change from baseline	15	-0.18 (0.308)	-0.1 (-0.4, 0.0)	-0.9, 0.2	-0.16 (0.111)	(-0.38, 0.07)	24	-1.30 (0.535)	-1.4 (-1.6, -1.0)	-2.5, -0.2	-1.31 (0.088)	(-1.49, -1.13)	-1.15 (-1.44, -0.87)	<.0001	-2.43 (-3.27, -1.59)	
Percent change from baseline	15	-3.21 (5.654)	-1.8 (-7.1, 0.8)	-15.6, 4.3			24	-23.51 (9.048)	-25.2 (-28.2, -18.7)	-44.0, -3.4						
No																
Baseline																
Absolute value	17	5.71 (0.512)	5.5 (5.3, 6.3)	5.2, 6.6			12	5.38 (0.201)	5.4 (5.2, 5.5)	5.1, 5.8						
1 hour																
Absolute value	17	5.52 (0.539)	5.3 (5.1, 5.9)	4.9, 6.6			12	5.04 (0.340)	5.1 (4.8, 5.3)	4.3, 5.4						
Change from baseline	17	-0.20 (0.211)	-0.2 (-0.3, -0.1)	-0.5, 0.3	-0.19 (0.061)	(-0.31, -0.06)	12	-0.34 (0.284)	-0.3 (-0.5, -0.1)	-1.0, 0.1	-0.35 (0.072)	(-0.50, -0.20)	-0.17 (-0.36, 0.03)	0.0959	-0.60 (-1.35, 0.16)	
Percent change from baseline	17	-3.44 (3.709)	-3.4 (-6.2, -1.9)	-9.7, 5.0			12	-6.34 (5.384)	-5.7 (-9.5, -2.7)	-18.1, 1.9						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Diabetes mellitus *(contd.)*																
No *(contd.)*																
2 hours																
Absolute value	16	5.25 (0.550)	5.1 (4.9, 5.5)	4.4, 6.4			12	5.00 (0.388)	5.0 (4.8, 5.2)	4.5, 5.9						
Change from baseline	16	-0.41 (0.207)	-0.3 (-0.6, -0.2)	-0.9, -0.1	-0.40 (0.067)	(-0.54, -0.26)	12	-0.38 (0.315)	-0.4 (-0.5, -0.3)	-0.9, 0.4	-0.39 (0.077)	(-0.55, -0.24)	0.01 (-0.21, 0.22)	0.9585	0.09 (-0.66, 0.84)	
Percent change from baseline	16	-7.29 (3.835)	-6.5 (-9.7, -4.3)	-16.6, -1.9			12	-7.15 (5.826)	-7.1 (-10.2, -5.3)	-16.3, 6.8						
4 hours																
Absolute value	16	5.19 (0.552)	5.1 (4.8, 5.5)	4.4, 6.1			12	4.92 (0.430)	5.0 (4.6, 5.2)	4.2, 5.7						
Change from baseline	16	-0.47 (0.271)	-0.4 (-0.7, -0.3)	-0.9, 0.0	-0.46 (0.078)	(-0.62, -0.30)	12	-0.47 (0.342)	-0.4 (-0.7, -0.2)	-1.0, 0.2	-0.48 (0.090)	(-0.66, -0.29)	-0.01 (-0.26, 0.23)	0.9023	0.01 (-0.74, 0.76)	
Percent change from baseline	16	-8.37 (5.005)	-7.4 (-13.2, -5.1)	-16.6, 0.0			12	-8.73 (6.461)	-8.1 (-13.1, -4.4)	-19.2, 3.2						
24 hours																
Absolute value	16	5.42 (0.478)	5.4 (5.1, 5.8)	4.6, 6.2			12	4.74 (0.309)	4.8 (4.6, 5.0)	4.1, 5.3						
Change from baseline	16	-0.24 (0.323)	-0.2 (-0.5, 0.0)	-0.8, 0.4	-0.23 (0.079)	(-0.39, -0.07)	12	-0.64 (0.316)	-0.7 (-0.9, -0.4)	-1.2, -0.1	-0.65 (0.092)	(-0.84, -0.46)	-0.42 (-0.67, -0.17)	0.0019	-1.26 (-2.08, -0.44)	
Percent change from baseline	16	-4.12 (5.602)	-4.3 (-8.5, 0.2)	-12.6, 6.8			12	-11.86 (5.789)	-13.0 (-15.8, -7.6)	-21.9, -1.9						
25 hours																
Absolute value	16	5.30 (0.548)	5.4 (4.9, 5.7)	4.1, 6.3			12	4.42 (0.364)	4.5 (4.2, 4.7)	3.7, 4.9						
Change from baseline	16	-0.36 (0.349)	-0.3 (-0.6, -0.2)	-1.2, 0.4	-0.35 (0.088)	(-0.53, -0.17)	12	-0.97 (0.357)	-1.0 (-1.1, -0.8)	-1.6, -0.3	-0.98 (0.102)	(-1.19, -0.77)	-0.63 (-0.91, -0.35)	<.0001	-1.73 (-2.60, -0.85)	
Percent change from baseline	16	-6.30 (6.411)	-4.7 (-9.6, -2.7)	-22.3, 7.5			12	-17.92 (6.592)	-18.7 (-20.0, -14.3)	-29.5, -5.8						
28 hours																
Absolute value	16	5.13 (0.543)	5.3 (4.7, 5.5)	4.2, 6.1			12	4.46 (0.403)	4.5 (4.2, 4.7)	3.7, 5.2						
Change from baseline	16	-0.53 (0.424)	-0.5 (-1.0, -0.3)	-1.1, 0.2	-0.52 (0.095)	(-0.72, -0.33)	12	-0.93 (0.314)	-0.9 (-1.1, -0.7)	-1.6, -0.3	-0.94 (0.110)	(-1.16, -0.71)	-0.41 (-0.71, -0.11)	0.0089	-1.03 (-1.82, -0.23)	
Percent change from baseline	16	-9.32 (7.487)	-7.7 (-15.8, -4.6)	-20.4, 3.2			12	-17.24 (5.988)	-18.4 (-20.2, -13.2)	-29.5, -5.9						
48 hours																
Absolute value	16	5.37 (0.394)	5.4 (5.1, 5.8)	4.6, 5.9			12	4.10 (0.426)	4.2 (4.0, 4.3)	3.1, 4.8						
Change from baseline	16	-0.29 (0.368)	-0.3 (-0.5, -0.1)	-1.0, 0.5	-0.28 (0.089)	(-0.46, -0.10)	12	-1.28 (0.350)	-1.2 (-1.5, -1.1)	-2.0, -0.7	-1.29 (0.103)	(-1.50, -1.08)	-1.01 (-1.29, -0.73)	<.0001	-2.76 (-3.80, -1.72)	
Percent change from baseline	16	-4.86 (6.260)	-6.0 (-9.1, -1.2)	-15.1, 9.4			12	-23.90 (6.825)	-23.4 (-26.0, -20.0)	-39.5, -11.9						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
RAASi Medications																0.1879
Yes																
Baseline																
Absolute value	27	5.66 (0.417)	5.5 (5.4, 6.1)	5.2, 6.6			26	5.53 (0.398)	5.5 (5.4, 5.8)	5.0, 6.8						
1 hour																
Absolute value	27	5.57 (0.579)	5.4 (5.1, 5.9)	4.7, 6.8			26	5.14 (0.404)	5.3 (4.8, 5.4)	4.2, 5.8						
Change from baseline	27	-0.10 (0.328)	-0.1 (-0.3, 0.1)	-0.8, 0.5	-0.07 (0.067)	(-0.21, 0.06)	26	-0.39 (0.355)	-0.5 (-0.6, -0.1)	-1.0, 0.6	-0.40 (0.068)	(-0.54, -0.27)	-0.33 (-0.52, -0.13)	0.0013	-0.87 (-1.43, -0.31)	
Percent change from baseline	27	-1.77 (5.704)	-2.4 (-4.6, 2.3)	-13.8, 8.4			26	-6.94 (6.387)	-8.6 (-10.4, -2.3)	-18.4, 12.3						
2 hours																
Absolute value	26	5.32 (0.545)	5.1 (5.0, 5.7)	4.4, 6.5			26	4.97 (0.375)	5.1 (4.8, 5.2)	4.2, 5.6						
Change from baseline	26	-0.30 (0.312)	-0.3 (-0.5, -0.2)	-0.9, 0.5	-0.29 (0.069)	(-0.43, -0.15)	26	-0.56 (0.410)	-0.5 (-0.9, -0.3)	-1.4, 0.1	-0.57 (0.070)	(-0.71, -0.43)	-0.28 (-0.48, -0.08)	0.0060	-0.71 (-1.27, -0.15)	
Percent change from baseline	26	-5.47 (5.551)	-4.6 (-9.5, -3.7)	-16.6, 7.4			26	-9.89 (6.964)	-9.7 (-15.2, -4.6)	-23.4, 2.5						
4 hours																
Absolute value	26	5.23 (0.488)	5.2 (4.9, 5.5)	4.4, 6.1			26	4.97 (0.437)	5.0 (4.8, 5.3)	4.0, 5.9						
Change from baseline	26	-0.39 (0.296)	-0.4 (-0.6, -0.1)	-1.1, 0.0	-0.38 (0.065)	(-0.51, -0.25)	26	-0.56 (0.368)	-0.6 (-0.9, -0.2)	-1.2, -0.0	-0.57 (0.065)	(-0.70, -0.44)	-0.20 (-0.38, -0.01)	0.0375	-0.52 (-1.07, 0.03)	
Percent change from baseline	26	-6.98 (5.334)	-6.0 (-10.5, -2.8)	-19.6, 0.0			26	-10.08 (6.557)	-10.6 (-14.9, -3.0)	-22.3, -0.4						
24 hours																
Absolute value	25	5.41 (0.499)	5.3 (5.2, 5.7)	4.6, 6.6			26	4.83 (0.297)	4.8 (4.6, 5.0)	4.1, 5.4						
Change from baseline	25	-0.19 (0.353)	-0.3 (-0.4, 0.0)	-0.9, 0.5	-0.17 (0.070)	(-0.31, -0.03)	26	-0.71 (0.397)	-0.7 (-0.9, -0.5)	-1.9, 0.0	-0.72 (0.069)	(-0.85, -0.58)	-0.54 (-0.74, -0.35)	<.0001	-1.38 (-1.99, -0.77)	
Percent change from baseline	25	-3.34 (6.345)	-5.0 (-7.4, 0.9)	-15.6, 9.1			26	-12.49 (6.331)	-12.1 (-17.1, -8.5)	-28.2, 1.0						
25 hours																
Absolute value	25	5.34 (0.493)	5.3 (5.1, 5.6)	4.1, 6.3			26	4.49 (0.325)	4.6 (4.3, 4.7)	3.8, 5.2						
Change from baseline	25	-0.25 (0.338)	-0.2 (-0.4, -0.1)	-1.2, 0.4	-0.23 (0.078)	(-0.39, -0.07)	26	-1.04 (0.482)	-1.0 (-1.3, -0.7)	-2.6, -0.4	-1.05 (0.077)	(-1.20, -0.90)	-0.82 (-1.04, -0.60)	<.0001	-1.88 (-2.54, -1.22)	
Percent change from baseline	25	-4.57 (6.202)	-3.7 (-7.3, -2.6)	-22.3, 7.5			26	-18.49 (7.334)	-18.4 (-22.0, -12.6)	-38.5, -7.1						
28 hours																
Absolute value	25	5.26 (0.522)	5.2 (5.0, 5.5)	4.2, 6.3			26	4.35 (0.329)	4.4 (4.0, 4.6)	3.8, 5.0						
Change from baseline	25	-0.34 (0.405)	-0.4 (-0.5, -0.1)	-1.1, 0.5	-0.32 (0.073)	(-0.47, -0.17)	26	-1.18 (0.367)	-1.1 (-1.3, -0.9)	-2.0, -0.7	-1.19 (0.072)	(-1.34, -1.05)	-0.87 (-1.08, -0.67)	<.0001	-2.19 (-2.88, -1.49)	
Percent change from baseline	25	-6.04 (7.319)	-6.4 (-10.1, -1.8)	-20.4, 9.8			26	-21.21 (5.623)	-20.9 (-23.6, -16.3)	-33.9, -12.6						
48 hours																
Absolute value	25	5.38 (0.398)	5.4 (5.2, 5.6)	4.6, 6.1			26	4.21 (0.432)	4.2 (4.0, 4.5)	3.1, 5.2						
Change from baseline	25	-0.22 (0.343)	-0.2 (-0.4, -0.0)	-1.0, 0.5	-0.21 (0.076)	(-0.36, -0.06)	26	-1.32 (0.462)	-1.4 (-1.6, -1.0)	-2.5, -0.6	-1.33 (0.074)	(-1.48, -1.18)	-1.13 (-1.34, -0.91)	<.0001	-2.70 (-3.46, -1.94)	
Percent change from baseline	25	-3.87 (6.055)	-2.8 (-7.9, -0.5)	-15.6, 9.4			26	-23.80 (7.588)	-25.1 (-27.1, -19.2)	-39.5, -11.3						
No																
Baseline																
Absolute value	6	5.59 (0.487)	5.4 (5.3, 5.7)	5.2, 6.5			10	5.26 (0.171)	5.2 (5.1, 5.4)	5.1, 5.5						
1 hour																
Absolute value	6	5.32 (0.523)	5.2 (4.9, 5.4)	4.9, 6.3			10	4.94 (0.378)	5.0 (4.6, 5.3)	4.3, 5.4						
Change from baseline	6	-0.27 (0.256)	-0.3 (-0.5, -0.1)	-0.5, 0.1	-0.29 (0.131)	(-0.57, -0.01)	10	-0.32 (0.330)	-0.2 (-0.6, -0.1)	-1.0, 0.1	-0.31 (0.100)	(-0.52, -0.09)	-0.01 (-0.37, 0.35)	0.9309	-0.17 (-1.18, 0.84)	
Percent change from baseline	6	-4.83 (4.740)	-5.0 (-9.7, -1.9)	-9.7, 2.4			10	-6.14 (6.328)	-3.5 (-10.7, -2.0)	-18.1, 1.9						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
RAASi Medications *(contd.)*																
No *(contd.)*																
2 hours																
Absolute value	6	5.12 (0.646)	4.9 (4.7, 5.1)	4.7, 6.4			10	4.90 (0.424)	4.9 (4.7, 5.0)	4.3, 5.9						
Change from baseline	6	-0.47 (0.218)	-0.5 (-0.6, -0.3)	-0.7, -0.1	-0.49 (0.125)	(-0.76, -0.23)	10	-0.36 (0.345)	-0.4 (-0.5, -0.2)	-0.9, 0.4	-0.35 (0.096)	(-0.55, -0.14)	0.15 (-0.20, 0.49)	0.3838	0.35 (-0.67, 1.37)	
Percent change from baseline	6	-8.63 (4.103)	-9.9 (-10.9, -5.8)	-13.4, -1.9			10	-6.94 (6.497)	-7.1 (-9.6, -3.9)	-16.9, 6.8						
4 hours																
Absolute value	6	4.97 (0.625)	4.8 (4.5, 5.2)	4.4, 6.1			10	4.81 (0.470)	4.7 (4.4, 5.1)	4.2, 5.7						
Change from baseline	6	-0.62 (0.315)	-0.7 (-0.8, -0.4)	-0.9, -0.1	-0.64 (0.138)	(-0.94, -0.35)	10	-0.45 (0.347)	-0.5 (-0.7, -0.2)	-1.0, 0.2	-0.44 (0.106)	(-0.67, -0.21)	0.21 (-0.17, 0.58)	0.2657	0.50 (-0.53, 1.53)	
Percent change from baseline	6	-11.23 (6.000)	-13.5 (-15.4, -6.5)	-17.1, -1.4			10	-8.72 (6.692)	-8.9 (-13.7, -3.4)	-19.2, 3.2						
24 hours																
Absolute value	6	5.25 (0.327)	5.2 (5.0, 5.5)	4.9, 5.7			10	4.60 (0.365)	4.6 (4.4, 4.8)	4.1, 5.3						
Change from baseline	6	-0.34 (0.352)	-0.3 (-0.5, -0.2)	-0.8, 0.2	-0.36 (0.154)	(-0.69, -0.03)	10	-0.66 (0.349)	-0.7 (-0.9, -0.4)	-1.2, -0.1	-0.65 (0.118)	(-0.91, -0.39)	-0.29 (-0.71, 0.14)	0.1680	-0.93 (-1.99, 0.13)	
Percent change from baseline	6	-5.76 (5.866)	-6.3 (-9.7, -3.8)	-12.6, 4.3			10	-12.57 (6.539)	-13.5 (-17.6, -7.2)	-21.9, -1.9						
25 hours																
Absolute value	6	5.27 (0.383)	5.2 (5.1, 5.5)	4.8, 5.9			10	4.37 (0.356)	4.4 (4.2, 4.5)	3.7, 4.9						
Change from baseline	6	-0.32 (0.174)	-0.3 (-0.4, -0.2)	-0.6, -0.2	-0.34 (0.130)	(-0.62, -0.06)	10	-0.89 (0.344)	-0.9 (-1.1, -0.7)	-1.6, -0.3	-0.88 (0.100)	(-1.09, -0.66)	-0.53 (-0.90, -0.17)	0.0068	-1.94 (-3.16, -0.73)	
Percent change from baseline	6	-5.64 (2.608)	-5.1 (-7.7, -3.3)	-9.6, -3.1			10	-16.94 (6.457)	-17.9 (-19.6, -13.7)	-29.5, -5.8						
28 hours																
Absolute value	6	4.90 (0.424)	4.8 (4.6, 5.3)	4.4, 5.5			10	4.29 (0.491)	4.2 (3.8, 4.7)	3.7, 5.2						
Change from baseline	6	-0.69 (0.435)	-0.8 (-1.0, -0.5)	-1.1, 0.0	-0.71 (0.180)	(-1.10, -0.32)	10	-0.97 (0.416)	-1.1 (-1.3, -0.6)	-1.6, -0.3	-0.96 (0.139)	(-1.26, -0.66)	-0.25 (-0.74, 0.24)	0.2983	-0.67 (-1.71, 0.36)	
Percent change from baseline	6	-12.06 (7.432)	-12.7 (-18.9, -9.6)	-18.9, 0.5			10	-18.56 (8.051)	-19.8 (-25.5, -11.1)	-29.5, -5.9						
48 hours																
Absolute value	6	5.30 (0.329)	5.3 (5.1, 5.5)	4.9, 5.8			10	4.04 (0.550)	4.2 (3.7, 4.4)	2.9, 4.9						
Change from baseline	6	-0.29 (0.348)	-0.3 (-0.6, -0.0)	-0.7, 0.2	-0.31 (0.202)	(-0.74, 0.12)	10	-1.22 (0.531)	-1.1 (-1.4, -1.1)	-2.3, -0.2	-1.21 (0.155)	(-1.54, -0.87)	-0.90 (-1.45, -0.35)	0.0036	-1.97 (-3.20, -0.75)	
Percent change from baseline	6	-4.87 (5.858)	-5.9 (-10.1, -0.5)	-11.1, 4.3			10	-23.24 (10.299)	-21.6 (-27.5, -19.6)	-44.0, -3.4						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline eGFR																
<15																
Baseline																
Absolute value	11	5.64 (0.407)	5.4 (5.4, 6.1)	5.2, 6.3			9	5.45 (0.237)	5.4 (5.4, 5.6)	5.2, 5.9						
1 hour																
Absolute value	11	5.46 (0.482)	5.3 (5.1, 5.9)	4.9, 6.5			9	5.09 (0.341)	5.1 (4.8, 5.4)	4.5, 5.5						
Change from baseline	11	-0.17 (0.274)	-0.2 (-0.4, -0.1)	-0.5, 0.5	-0.18 (0.095)	(-0.38, 0.02)	9	-0.36 (0.346)	-0.5 (-0.6, -0.0)	-0.9, 0.1	-0.36 (0.105)	(-0.58, -0.14)	-0.19 (-0.49, 0.12)	0.2108	-0.62 (-1.52, 0.28)	
Percent change from baseline	11	-3.07 (4.706)	-4.3 (-6.6, -1.9)	-8.4, 7.4			9	-6.60 (6.252)	-9.3 (-10.7, -0.5)	-14.9, 1.9						
2 hours																
Absolute value	11	5.39 (0.513)	5.1 (5.0, 5.7)	4.9, 6.5			9	4.80 (0.357)	4.7 (4.5, 5.2)	4.3, 5.3						
Change from baseline	11	-0.25 (0.352)	-0.3 (-0.6, -0.2)	-0.7, 0.5	-0.25 (0.116)	(-0.49, -0.00)	9	-0.65 (0.411)	-0.5 (-0.9, -0.5)	-1.4, -0.1	-0.65 (0.129)	(-0.92, -0.38)	-0.40 (-0.77, -0.03)	0.0338	-1.07 (-2.02, -0.13)	
Percent change from baseline	11	-4.34 (6.062)	-4.7 (-9.5, -3.7)	-11.3, 7.4			9	-11.85 (7.165)	-9.6 (-16.3, -8.7)	-23.4, -2.3						
4 hours																
Absolute value	11	5.21 (0.485)	5.2 (4.9, 5.6)	4.4, 6.0			9	4.83 (0.415)	5.0 (4.6, 5.0)	4.2, 5.3						
Change from baseline	11	-0.43 (0.294)	-0.4 (-0.8, -0.1)	-0.8, 0.0	-0.43 (0.101)	(-0.64, -0.22)	9	-0.62 (0.365)	-0.6 (-0.9, -0.5)	-1.1, -0.1	-0.62 (0.111)	(-0.85, -0.38)	-0.19 (-0.50, 0.13)	0.2329	-0.59 (-1.49, 0.31)	
Percent change from baseline	11	-7.59 (5.277)	-8.1 (-13.0, -2.8)	-15.4, 0.0			9	-11.36 (6.766)	-11.1 (-14.9, -8.8)	-21.5, -1.4						
24 hours																
Absolute value	11	5.51 (0.566)	5.4 (5.0, 5.8)	4.6, 6.6			9	4.77 (0.278)	4.8 (4.6, 4.9)	4.4, 5.3						
Change from baseline	11	-0.13 (0.346)	-0.1 (-0.4, 0.1)	-0.6, 0.5	-0.13 (0.103)	(-0.35, 0.09)	9	-0.69 (0.320)	-0.8 (-0.9, -0.5)	-1.1, -0.2	-0.68 (0.114)	(-0.92, -0.44)	-0.55 (-0.88, -0.23)	0.0021	-1.67 (-2.69, -0.65)	
Percent change from baseline	11	-2.33 (6.070)	-1.9 (-7.4, 0.9)	-12.0, 9.1			9	-12.49 (5.555)	-14.4 (-17.1, -8.8)	-19.3, -3.8						
25 hours																
Absolute value	11	5.38 (0.471)	5.5 (5.1, 5.7)	4.6, 6.3			9	4.60 (0.400)	4.7 (4.4, 4.8)	3.8, 5.2						
Change from baseline	11	-0.25 (0.285)	-0.2 (-0.6, -0.1)	-0.6, 0.3	-0.26 (0.110)	(-0.49, -0.02)	9	-0.85 (0.433)	-0.7 (-1.1, -0.5)	-1.6, -0.3	-0.85 (0.122)	(-1.11, -0.59)	-0.59 (-0.94, -0.24)	0.0022	-1.67 (-2.69, -0.65)	
Percent change from baseline	11	-4.51 (4.941)	-3.7 (-9.2, -2.6)	-12.0, 4.1			9	-15.55 (7.673)	-12.6 (-19.3, -10.3)	-26.8, -5.8						
28 hours																
Absolute value	11	5.25 (0.580)	5.3 (4.7, 5.8)	4.4, 6.3			9	4.31 (0.289)	4.4 (4.1, 4.5)	3.9, 4.7						
Change from baseline	11	-0.39 (0.489)	-0.5 (-0.8, -0.1)	-1.1, 0.5	-0.39 (0.124)	(-0.66, -0.13)	9	-1.14 (0.269)	-1.2 (-1.3, -1.0)	-1.5, -0.7	-1.14 (0.138)	(-1.43, -0.85)	-0.75 (-1.14, -0.35)	0.0009	-1.85 (-2.90, -0.80)	
Percent change from baseline	11	-6.88 (8.603)	-7.6 (-15.8, -1.9)	-18.9, 9.8			9	-20.91 (4.690)	-21.2 (-23.4, -18.2)	-28.1, -12.6						
48 hours																
Absolute value	11	5.38 (0.464)	5.3 (4.9, 5.8)	4.7, 6.1			9	4.08 (0.338)	4.2 (3.8, 4.2)	3.5, 4.6						
Change from baseline	11	-0.25 (0.268)	-0.3 (-0.5, 0.0)	-0.7, 0.1	-0.26 (0.087)	(-0.44, -0.07)	9	-1.38 (0.297)	-1.5 (-1.6, -1.2)	-1.9, -1.0	-1.37 (0.097)	(-1.58, -1.17)	-1.12 (-1.39, -0.84)	<.0001	-3.98 (-5.50, -2.47)	
Percent change from baseline	11	-4.51 (4.746)	-5.8 (-7.9, 0.8)	-13.0, 0.9			9	-25.21 (5.389)	-25.1 (-29.3, -21.9)	-34.6, -18.2						
15-29+																
Baseline																
Absolute value	11	5.82 (0.542)	5.5 (5.5, 6.5)	5.2, 6.6			13	5.59 (0.453)	5.5 (5.4, 5.7)	5.1, 6.8						
1 hour																
Absolute value	11	5.85 (0.614)	5.8 (5.2, 6.4)	5.0, 6.8			13	5.17 (0.403)	5.3 (5.0, 5.4)	4.3, 5.8						
Change from baseline	11	0.03 (0.286)	0.1 (-0.2, 0.3)	-0.3, 0.5	0.06 (0.092)	(-0.13, 0.25)	13	-0.42 (0.310)	-0.4 (-0.6, -0.1)	-1.0, -0.1	-0.43 (0.082)	(-0.60, -0.26)	-0.49 (-0.75, -0.23)	0.0007	-1.50 (-2.40, -0.59)	
Percent change from baseline	11	0.51 (4.890)	1.9 (-3.4, 5.0)	-6.2, 8.4			13	-7.34 (5.199)	-6.5 (-10.4, -2.3)	-18.1, -2.0						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline eGFR *(contd.)*																
15-29+ *(contd.)*																
2 hours																
Absolute value	10	5.46 (0.654)	5.3 (5.0, 6.2)	4.8, 6.5			13	5.11 (0.359)	5.0 (4.9, 5.2)	4.5, 5.9						
Change from baseline	10	-0.27 (0.228)	-0.3 (-0.5, -0.2)	-0.5, 0.2	-0.26 (0.112)	(-0.50, -0.03)	13	-0.48 (0.446)	-0.4 (-0.8, -0.3)	-1.4, 0.4	-0.49 (0.098)	(-0.69, -0.28)	-0.22 (-0.54, 0.09)	0.1479	-0.55 (-1.39, 0.29)	
Percent change from baseline	10	-4.98 (4.100)	-4.4 (-8.9, -3.2)	-9.8, 3.6			13	-8.26 (7.102)	-7.4 (-14.3, -4.6)	-20.9, 6.8						
4 hours																
Absolute value	10	5.38 (0.590)	5.4 (4.9, 6.1)	4.4, 6.1			13	5.12 (0.462)	5.1 (4.8, 5.3)	4.4, 5.9						
Change from baseline	10	-0.35 (0.286)	-0.4 (-0.4, -0.2)	-1.1, -0.0	-0.34 (0.112)	(-0.57, -0.11)	13	-0.46 (0.404)	-0.4 (-0.7, -0.1)	-1.2, 0.2	-0.47 (0.097)	(-0.68, -0.27)	-0.13 (-0.44, 0.18)	0.3825	-0.30 (-1.13, 0.52)	
Percent change from baseline	10	-6.25 (5.241)	-6.0 (-7.2, -2.8)	-19.6, -0.9			13	-8.14 (6.849)	-7.4 (-13.6, -2.4)	-20.3, 3.2						
24 hours																
Absolute value	9	5.40 (0.477)	5.3 (5.2, 5.7)	4.6, 6.1			13	4.75 (0.326)	4.8 (4.6, 4.9)	4.1, 5.3						
Change from baseline	9	-0.27 (0.383)	-0.3 (-0.6, -0.0)	-0.8, 0.4	-0.23 (0.128)	(-0.50, 0.04)	13	-0.84 (0.448)	-0.9 (-1.0, -0.6)	-1.9, -0.1	-0.85 (0.107)	(-1.08, -0.62)	-0.62 (-0.97, -0.26)	0.0019	-1.34 (-2.28, -0.40)	
Percent change from baseline	9	-4.67 (6.627)	-5.8 (-10.5, -0.0)	-12.6, 6.8			13	-14.74 (6.817)	-16.1 (-17.6, -10.9)	-28.2, -1.9						
25 hours																
Absolute value	9	5.43 (0.466)	5.4 (5.1, 5.7)	4.9, 6.3			13	4.36 (0.304)	4.4 (4.2, 4.5)	3.7, 4.9						
Change from baseline	9	-0.24 (0.310)	-0.2 (-0.4, -0.2)	-0.6, 0.4	-0.18 (0.139)	(-0.47, 0.11)	13	-1.22 (0.539)	-1.1 (-1.5, -0.9)	-2.6, -0.5	-1.24 (0.118)	(-1.49, -0.98)	-1.06 (-1.44, -0.67)	<.0001	-2.13 (-3.19, -1.07)	
Percent change from baseline	9	-4.12 (5.460)	-3.6 (-6.8, -2.7)	-11.6, 7.5			13	-21.52 (7.701)	-19.6 (-26.6, -17.1)	-38.5, -9.3						
28 hours																
Absolute value	9	5.31 (0.417)	5.2 (5.1, 5.5)	4.7, 6.1			13	4.42 (0.460)	4.4 (4.2, 4.7)	3.7, 5.2						
Change from baseline	9	-0.36 (0.382)	-0.4 (-0.5, -0.2)	-1.0, 0.2	-0.32 (0.139)	(-0.61, -0.02)	13	-1.17 (0.491)	-1.1 (-1.6, -0.9)	-1.9, -0.3	-1.18 (0.117)	(-1.43, -0.94)	-0.87 (-1.25, -0.48)	0.0002	-1.79 (-2.79, -0.79)	
Percent change from baseline	9	-6.17 (6.349)	-6.2 (-8.9, -3.4)	-15.7, 3.2			13	-20.77 (7.956)	-20.4 (-26.7, -16.1)	-32.5, -5.9						
48 hours																
Absolute value	9	5.33 (0.377)	5.3 (5.1, 5.5)	4.6, 5.8			13	4.11 (0.444)	4.1 (4.0, 4.4)	3.1, 4.8						
Change from baseline	9	-0.34 (0.435)	-0.4 (-0.6, -0.2)	-1.0, 0.5	-0.30 (0.136)	(-0.59, -0.01)	13	-1.48 (0.449)	-1.4 (-1.7, -1.3)	-2.5, -0.7	-1.49 (0.113)	(-1.73, -1.25)	-1.19 (-1.56, -0.81)	<.0001	-2.57 (-3.71, -1.43)	
Percent change from baseline	9	-5.69 (7.360)	-8.0 (-11.1, -2.8)	-15.1, 9.4			13	-26.37 (7.085)	-25.3 (-29.0, -24.1)	-39.5, -11.9						
30-59+																
Baseline																
Absolute value	11	5.49 (0.239)	5.5 (5.3, 5.6)	5.2, 6.1			11	5.42 (0.331)	5.5 (5.1, 5.8)	5.0, 5.9						
1 hour																
Absolute value	11	5.25 (0.482)	5.1 (4.9, 5.4)	4.7, 6.5			11	5.12 (0.391)	5.3 (4.8, 5.4)	4.5, 5.7						
Change from baseline	11	-0.24 (0.356)	-0.2 (-0.5, -0.1)	-0.8, 0.4	-0.24 (0.113)	(-0.47, 0.00)	11	-0.30 (0.391)	-0.5 (-0.6, -0.0)	-0.7, 0.6	-0.30 (0.113)	(-0.54, -0.06)	-0.06 (-0.40, 0.27)	0.6919	-0.15 (-0.99, 0.68)	
Percent change from baseline	11	-4.41 (6.335)	-3.2 (-9.7, -1.8)	-13.8, 7.0			11	-5.32 (7.382)	-8.9 (-10.2, -0.2)	-13.0, 12.3						
2 hours																
Absolute value	11	5.02 (0.451)	4.9 (4.7, 5.1)	4.4, 6.1			11	4.96 (0.388)	5.1 (4.8, 5.2)	4.3, 5.4						
Change from baseline	11	-0.47 (0.276)	-0.5 (-0.7, -0.2)	-0.9, 0.0	-0.47 (0.090)	(-0.66, -0.28)	11	-0.46 (0.308)	-0.5 (-0.7, -0.3)	-0.9, 0.1	-0.46 (0.090)	(-0.65, -0.27)	0.01 (-0.26, 0.28)	0.9305	0.06 (-0.77, 0.90)	
Percent change from baseline	11	-8.76 (5.098)	-10.1 (-12.3, -4.3)	-16.6, 0.4			11	-8.38 (5.737)	-8.8 (-12.2, -5.4)	-16.9, 2.5						
4 hours																
Absolute value	11	4.98 (0.440)	4.9 (4.7, 5.2)	4.4, 6.0			11	4.92 (0.340)	5.0 (4.7, 5.1)	4.1, 5.3						
Change from baseline	11	-0.51 (0.348)	-0.6 (-0.9, -0.1)	-1.0, -0.1	-0.51 (0.097)	(-0.71, -0.31)	11	-0.50 (0.287)	-0.6 (-0.7, -0.2)	-0.9, -0.1	-0.51 (0.097)	(-0.71, -0.30)	0.00 (-0.28, 0.29)	0.9870	0.03 (-0.81, 0.86)	

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline eGFR *(contd.)*																
30-59+ *(contd.)*																
4 hours *(contd.)*																
Percent change from baseline	11	-9.34 (6.351)	-10.5 (-16.6, -2.4)	-17.5, -1.2			11	-9.19 (5.220)	-10.5 (-12.6, -3.4)	-17.6, -1.5						
24 hours																
Absolute value	11	5.24 (0.347)	5.2 (5.0, 5.5)	4.6, 5.7			11	4.77 (0.405)	4.8 (4.4, 5.1)	4.1, 5.4						
Change from baseline	11	-0.26 (0.347)	-0.4 (-0.5, 0.0)	-0.9, 0.3	-0.25 (0.093)	(-0.45, -0.06)	11	-0.65 (0.260)	-0.6 (-0.9, -0.4)	-1.1, -0.3	-0.65 (0.093)	(-0.85, -0.46)	-0.40 (-0.67, -0.12)	0.0069	-1.27 (-2.19, -0.36)	
Percent change from baseline	11	-4.59 (6.397)	-6.2 (-9.1, 0.5)	-15.6, 5.3			11	-11.97 (4.893)	-11.3 (-17.6, -7.2)	-19.3, -5.4						
25 hours																
Absolute value	11	5.19 (0.478)	5.2 (5.1, 5.4)	4.1, 6.1			11	4.50 (0.310)	4.6 (4.3, 4.7)	3.9, 4.9						
Change from baseline	11	-0.30 (0.362)	-0.3 (-0.4, -0.2)	-1.2, 0.3	-0.30 (0.096)	(-0.50, -0.10)	11	-0.92 (0.262)	-1.0 (-1.1, -0.9)	-1.3, -0.4	-0.92 (0.096)	(-1.12, -0.72)	-0.63 (-0.91, -0.34)	0.0002	-1.96 (-2.97, -0.94)	
Percent change from baseline	11	-5.57 (6.845)	-5.3 (-7.3, -3.2)	-22.3, 5.3			11	-16.91 (4.541)	-17.3 (-20.0, -15.6)	-22.0, -7.4						
28 hours																
Absolute value	11	5.04 (0.537)	4.9 (4.7, 5.4)	4.2, 6.1			11	4.31 (0.367)	4.4 (3.9, 4.6)	3.8, 4.7						
Change from baseline	11	-0.46 (0.433)	-0.5 (-0.8, 0.0)	-1.1, 0.2	-0.45 (0.125)	(-0.71, -0.19)	11	-1.11 (0.395)	-1.1 (-1.2, -0.9)	-2.0, -0.4	-1.11 (0.125)	(-1.38, -0.85)	-0.66 (-1.03, -0.29)	0.0013	-1.58 (-2.54, -0.62)	
Percent change from baseline	11	-8.39 (8.052)	-9.7 (-14.2, 0.4)	-20.4, 3.3			11	-20.38 (6.691)	-20.0 (-23.6, -15.6)	-33.9, -7.4						
48 hours																
Absolute value	11	5.36 (0.326)	5.4 (5.2, 5.5)	4.6, 5.9			11	4.30 (0.615)	4.3 (4.0, 4.8)	2.9, 5.2						
Change from baseline	11	-0.13 (0.315)	-0.1 (-0.3, 0.2)	-0.9, 0.2	-0.13 (0.141)	(-0.42, 0.17)	11	-1.12 (0.586)	-1.1 (-1.6, -0.7)	-2.3, -0.2	-1.12 (0.141)	(-1.42, -0.83)	-1.00 (-1.42, -0.58)	<.0001	-2.11 (-3.15, -1.06)	
Percent change from baseline	11	-2.28 (5.806)	-1.8 (-6.0, 3.3)	-15.6, 4.3			11	-20.62 (10.956)	-20.0 (-27.0, -11.9)	-44.0, -3.4						
>=60																
Baseline																
Absolute value							3	5.05 (0.100)	5.1 (5.0, 5.2)	5.0, 5.2						
1 hour																
Absolute value							3	4.57 (0.404)	4.5 (4.2, 5.0)	4.2, 5.0						
Change from baseline							3	-0.48 (0.451)	-0.5 (-1.0, -0.1)	-1.0, -0.1						
Percent change from baseline							3	-9.51 (8.736)	-9.1 (-18.4, -1.0)	-18.4, -1.0						
2 hours																
Absolute value							3	4.70 (0.436)	4.9 (4.2, 5.0)	4.2, 5.0						
Change from baseline							3	-0.35 (0.529)	-0.2 (-1.0, 0.0)	-1.0, 0.0						
Percent change from baseline							3	-6.80 (10.279)	-3.0 (-18.4, 1.0)	-18.4, 1.0						
4 hours																
Absolute value							3	4.37 (0.404)	4.3 (4.0, 4.8)	4.0, 4.8						
Change from baseline							3	-0.68 (0.503)	-0.8 (-1.2, -0.2)	-1.2, -0.2						
Percent change from baseline							3	-13.40 (9.731)	-14.9 (-22.3, -3.0)	-22.3, -3.0						
24 hours																
Absolute value							3	4.80 (0.346)	5.0 (4.4, 5.0)	4.4, 5.0						
Change from baseline							3	-0.25 (0.361)	-0.2 (-0.7, 0.0)	-0.7, 0.0						
Percent change from baseline							3	-4.92 (7.156)	-2.9 (-12.9, 1.0)	-12.9, 1.0						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline eGFR *(contd.)*																
>=60 *(contd.)*																
25 hours																
Absolute value							3	4.30 (0.265)	4.2 (4.1, 4.6)	4.1, 4.6						
Change from baseline							3	-0.75 (0.346)	-1.0 (-1.0, -0.4)	-1.0, -0.4						
Percent change from baseline							3	-14.78 (6.676)	-18.4 (-18.8, -7.1)	-18.8, -7.1						
28 hours																
Absolute value							3	4.13 (0.252)	4.1 (3.9, 4.4)	3.9, 4.4						
Change from baseline							3	-0.92 (0.153)	-1.0 (-1.1, -0.8)	-1.1, -0.8						
Percent change from baseline							3	-18.20 (3.367)	-18.8 (-21.2, -14.6)	-21.2, -14.6						
48 hours																
Absolute value							3	4.13 (0.321)	4.0 (3.9, 4.5)	3.9, 4.5						
Change from baseline							3	-0.92 (0.252)	-1.0 (-1.2, -0.7)	-1.2, -0.7						
Percent change from baseline							3	-18.20 (5.148)	-19.2 (-22.8, -12.6)	-22.8, -12.6						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Sex																0.1128
Male																
Baseline																
Absolute value	23	5.65 (0.432)	5.5 (5.4, 5.8)	5.2, 6.6			28	5.46 (0.387)	5.4 (5.2, 5.6)	5.0, 6.8						
1 hour																
Absolute value	23	5.55 (0.600)	5.3 (5.1, 5.9)	4.7, 6.8			28	5.11 (0.425)	5.3 (4.8, 5.4)	4.2, 5.8						
Change from baseline	23	-0.11 (0.318)	-0.1 (-0.3, 0.1)	-0.8, 0.5	-0.07 (0.075)	(-0.22, 0.08)	28	-0.34 (0.368)	-0.4 (-0.6, -0.1)	-1.0, 0.6	-0.36 (0.068)	(-0.50, -0.23)	-0.29 (-0.50, -0.09)	0.0064	-0.69 (-1.26, -0.12)	
Percent change from baseline	23	-2.00 (5.601)	-2.4 (-4.6, 1.9)	-13.8, 8.4			28	-6.20 (6.725)	-7.1 (-10.5, -2.1)	-18.4, 12.3						
2 hours																
Absolute value	22	5.28 (0.531)	5.1 (4.9, 5.3)	4.7, 6.5			28	4.98 (0.394)	5.0 (4.8, 5.2)	4.2, 5.9						
Change from baseline	22	-0.33 (0.234)	-0.3 (-0.5, -0.2)	-0.7, 0.2	-0.30 (0.071)	(-0.45, -0.16)	28	-0.48 (0.395)	-0.5 (-0.7, -0.2)	-1.4, 0.4	-0.49 (0.063)	(-0.62, -0.37)	-0.19 (-0.38, 0.00)	0.0547	-0.43 (-0.99, 0.14)	
Percent change from baseline	22	-6.07 (4.200)	-5.9 (-9.7, -3.7)	-13.4, 3.6			28	-8.55 (6.836)	-8.8 (-13.9, -3.6)	-20.9, 6.8						
4 hours																
Absolute value	22	5.19 (0.509)	5.1 (4.9, 5.4)	4.4, 6.1			28	4.94 (0.478)	5.0 (4.7, 5.3)	4.0, 5.9						
Change from baseline	22	-0.42 (0.295)	-0.4 (-0.6, -0.2)	-1.1, 0.0	-0.40 (0.075)	(-0.55, -0.24)	28	-0.52 (0.380)	-0.5 (-0.8, -0.2)	-1.2, 0.2	-0.54 (0.067)	(-0.67, -0.40)	-0.14 (-0.34, 0.07)	0.1776	-0.27 (-0.84, 0.29)	
Percent change from baseline	22	-7.62 (5.387)	-7.2 (-10.9, -2.8)	-19.6, 0.0			28	-9.46 (6.869)	-9.7 (-13.6, -3.1)	-22.3, 3.2						
24 hours																
Absolute value	21	5.27 (0.434)	5.3 (5.0, 5.6)	4.6, 6.1			28	4.78 (0.356)	4.8 (4.6, 5.0)	4.1, 5.4						
Change from baseline	21	-0.31 (0.333)	-0.4 (-0.5, -0.1)	-0.9, 0.4	-0.29 (0.075)	(-0.44, -0.13)	28	-0.68 (0.405)	-0.6 (-0.9, -0.4)	-1.9, 0.0	-0.69 (0.065)	(-0.82, -0.56)	-0.41 (-0.61, -0.20)	0.0002	-0.97 (-1.57, -0.37)	
Percent change from baseline	21	-5.54 (5.973)	-6.2 (-9.7, -1.9)	-15.6, 6.8			28	-12.17 (6.694)	-11.2 (-17.3, -7.4)	-28.2, 1.0						
25 hours																
Absolute value	21	5.36 (0.404)	5.3 (5.1, 5.5)	4.6, 6.3			28	4.50 (0.349)	4.5 (4.3, 4.7)	3.7, 5.2						
Change from baseline	21	-0.22 (0.249)	-0.2 (-0.3, -0.2)	-0.6, 0.4	-0.18 (0.078)	(-0.34, -0.03)	28	-0.96 (0.473)	-1.0 (-1.1, -0.6)	-2.6, -0.3	-0.97 (0.067)	(-1.11, -0.84)	-0.79 (-1.00, -0.58)	<.0001	-1.87 (-2.55, -1.20)	
Percent change from baseline	21	-3.94 (4.522)	-3.7 (-6.0, -2.7)	-12.0, 7.5			28	-17.28 (7.388)	-18.2 (-20.2, -11.4)	-38.5, -5.8						
28 hours																
Absolute value	21	5.14 (0.481)	5.1 (4.8, 5.4)	4.4, 6.1			28	4.35 (0.388)	4.4 (4.0, 4.7)	3.7, 5.2						
Change from baseline	21	-0.44 (0.397)	-0.5 (-0.8, -0.1)	-1.1, 0.2	-0.41 (0.081)	(-0.57, -0.24)	28	-1.11 (0.394)	-1.1 (-1.2, -0.9)	-2.0, -0.3	-1.13 (0.070)	(-1.27, -0.99)	-0.72 (-0.94, -0.51)	<.0001	-1.71 (-2.37, -1.05)	
Percent change from baseline	21	-7.76 (7.059)	-7.8 (-14.2, -1.9)	-18.9, 3.3			28	-20.24 (6.506)	-20.9 (-23.5, -16.2)	-33.9, -5.9						
48 hours																
Absolute value	21	5.29 (0.378)	5.3 (5.1, 5.5)	4.6, 5.9			28	4.23 (0.393)	4.2 (4.0, 4.5)	3.5, 5.2						
Change from baseline	21	-0.29 (0.362)	-0.2 (-0.6, -0.1)	-1.0, 0.5	-0.26 (0.083)	(-0.43, -0.09)	28	-1.23 (0.457)	-1.2 (-1.5, -1.0)	-2.5, -0.2	-1.25 (0.072)	(-1.39, -1.10)	-0.99 (-1.21, -0.76)	<.0001	-2.25 (-2.97, -1.53)	
Percent change from baseline	21	-5.02 (6.325)	-3.2 (-10.1, -1.4)	-15.6, 9.4			28	-22.33 (7.441)	-23.0 (-26.7, -19.2)	-37.0, -3.4						
Female																
Baseline																
Absolute value	10	5.63 (0.426)	5.5 (5.3, 6.1)	5.2, 6.3			8	5.46 (0.320)	5.5 (5.2, 5.8)	5.1, 5.9						
1 hour																
Absolute value	10	5.46 (0.519)	5.3 (5.1, 5.9)	4.9, 6.5			8	4.99 (0.309)	5.0 (4.8, 5.2)	4.5, 5.4						
Change from baseline	10	-0.17 (0.336)	-0.2 (-0.4, 0.1)	-0.7, 0.5	-0.16 (0.095)	(-0.37, 0.04)	8	-0.47 (0.243)	-0.4 (-0.6, -0.4)	-0.9, -0.1	-0.48 (0.106)	(-0.70, -0.26)	-0.32 (-0.62, -0.01)	0.0423	-0.98 (-1.97, -0.00)	
Percent change from baseline	10	-3.07 (5.832)	-3.9 (-6.3, 2.3)	-12.3, 7.4			8	-8.52 (4.316)	-8.3 (-11.6, -6.3)	-14.9, -1.0						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Sex *(contd.)*																
Female *(contd.)*																
2 hours																
Absolute value	10	5.30 (0.650)	5.1 (4.9, 5.7)	4.4, 6.5			8	4.85 (0.351)	4.9 (4.7, 5.1)	4.3, 5.4						
Change from baseline	10	-0.33 (0.429)	-0.4 (-0.6, -0.3)	-0.9, 0.5	-0.32 (0.134)	(-0.61, -0.04)	8	-0.61 (0.417)	-0.5 (-0.9, -0.3)	-1.4, -0.2	-0.62 (0.150)	(-0.94, -0.30)	-0.29 (-0.72, 0.14)	0.1671	-0.64 (-1.59, 0.31)	
Percent change from baseline	10	-6.04 (7.692)	-7.6 (-10.9, -4.4)	-16.6, 7.4			8	-10.92 (7.154)	-9.1 (-16.0, -5.3)	-23.4, -3.0						
4 hours																
Absolute value	10	5.18 (0.559)	5.2 (4.7, 5.6)	4.4, 6.0			8	4.88 (0.328)	5.0 (4.7, 5.1)	4.3, 5.3						
Change from baseline	10	-0.45 (0.351)	-0.3 (-0.8, -0.1)	-1.0, -0.1	-0.44 (0.105)	(-0.67, -0.22)	8	-0.58 (0.303)	-0.7 (-0.8, -0.3)	-1.0, -0.1	-0.59 (0.118)	(-0.84, -0.34)	-0.15 (-0.48, 0.19)	0.3654	-0.38 (-1.32, 0.55)	
Percent change from baseline	10	-8.12 (6.399)	-5.3 (-15.4, -2.8)	-17.5, -1.4			8	-10.56 (5.474)	-11.6 (-14.9, -5.8)	-17.4, -2.4						
24 hours																
Absolute value	10	5.62 (0.476)	5.6 (5.3, 5.7)	5.0, 6.6			8	4.70 (0.214)	4.8 (4.5, 4.8)	4.4, 5.0						
Change from baseline	10	-0.01 (0.317)	0.0 (-0.2, 0.2)	-0.6, 0.5	-0.00 (0.093)	(-0.20, 0.19)	8	-0.76 (0.290)	-0.8 (-1.0, -0.5)	-1.1, -0.3	-0.77 (0.105)	(-0.99, -0.55)	-0.76 (-1.06, -0.46)	<.0001	-2.43 (-3.65, -1.21)	
Percent change from baseline	10	-0.18 (5.362)	0.2 (-3.8, 4.2)	-9.2, 9.1			8	-13.69 (4.822)	-14.3 (-17.6, -10.1)	-19.3, -6.3						
25 hours																
Absolute value	10	5.27 (0.602)	5.3 (4.9, 5.7)	4.1, 6.3			8	4.31 (0.236)	4.3 (4.2, 4.5)	4.0, 4.7						
Change from baseline	10	-0.36 (0.414)	-0.3 (-0.6, -0.1)	-1.2, 0.3	-0.35 (0.119)	(-0.61, -0.10)	8	-1.14 (0.332)	-1.0 (-1.5, -0.9)	-1.6, -0.8	-1.16 (0.133)	(-1.44, -0.87)	-0.80 (-1.18, -0.42)	0.0004	-2.05 (-3.20, -0.90)	
Percent change from baseline	10	-6.52 (7.519)	-6.5 (-9.5, -2.8)	-22.3, 4.1			8	-20.80 (5.161)	-18.5 (-26.7, -16.5)	-27.3, -15.6						
28 hours																
Absolute value	10	5.29 (0.605)	5.3 (5.0, 5.8)	4.2, 6.3			8	4.29 (0.340)	4.3 (4.0, 4.6)	3.8, 4.7						
Change from baseline	10	-0.34 (0.503)	-0.4 (-0.5, 0.0)	-1.1, 0.5	-0.33 (0.141)	(-0.63, -0.04)	8	-1.17 (0.382)	-1.1 (-1.4, -0.9)	-1.9, -0.8	-1.18 (0.158)	(-1.52, -0.85)	-0.85 (-1.30, -0.39)	0.0011	-1.82 (-2.92, -0.71)	
Percent change from baseline	10	-6.06 (8.950)	-7.1 (-9.6, 0.5)	-20.4, 9.8			8	-21.30 (6.265)	-19.4 (-25.8, -16.8)	-32.5, -13.8						
48 hours																
Absolute value	10	5.51 (0.363)	5.5 (5.3, 5.8)	4.9, 6.1			8	3.93 (0.636)	4.1 (3.5, 4.3)	2.9, 4.8						
Change from baseline	10	-0.12 (0.268)	-0.1 (-0.4, 0.1)	-0.5, 0.2	-0.11 (0.122)	(-0.37, 0.14)	8	-1.53 (0.500)	-1.5 (-1.9, -1.3)	-2.3, -0.7	-1.54 (0.137)	(-1.83, -1.25)	-1.43 (-1.82, -1.04)	<.0001	-3.64 (-5.15, -2.13)	
Percent change from baseline	10	-2.05 (4.676)	-1.6 (-6.0, 0.9)	-8.0, 4.3			8	-28.23 (9.892)	-26.8 (-34.3, -23.9)	-44.0, -11.9						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Age																
<65 years																
Baseline																
Absolute value	1	5.45 (NC)	5.5 (5.5, 5.5)	5.5, 5.5			5	5.95 (0.541)	5.9 (5.8, 5.9)	5.4, 6.8						
1 hour																
Absolute value	1	4.70 (NC)	4.7 (4.7, 4.7)	4.7, 4.7			5	5.28 (0.390)	5.4 (5.0, 5.4)	4.8, 5.8						
Change from baseline	1	-0.75 (NC)	-0.8 (-0.8, -0.8)	-0.8, -0.8			5	-0.66 (0.276)	-0.5 (-0.9, -0.5)	-1.0, -0.3						
Percent change from baseline	1	-13.76 (NC)	-13.8 (-13.8, -13.8)	-13.8, -13.8			5	-11.03 (3.890)	-10.3 (-14.9, -8.9)	-15.0, -6.1						
2 hours																
Absolute value	1	4.90 (NC)	4.9 (4.9, 4.9)	4.9, 4.9			5	4.96 (0.522)	5.2 (4.5, 5.4)	4.3, 5.4						
Change from baseline	1	-0.55 (NC)	-0.5 (-0.5, -0.5)	-0.5, -0.5			5	-0.98 (0.453)	-1.1 (-1.4, -0.7)	-1.4, -0.3						
Percent change from baseline	1	-10.09 (NC)	-10.1 (-10.1, -10.1)	-10.1, -10.1			5	-16.45 (7.128)	-19.6 (-20.9, -12.2)	-23.4, -6.1						
4 hours																
Absolute value	1	5.20 (NC)	5.2 (5.2, 5.2)	5.2, 5.2			5	5.10 (0.612)	5.1 (5.0, 5.3)	4.2, 5.9						
Change from baseline	1	-0.25 (NC)	-0.3 (-0.3, -0.3)	-0.3, -0.3			5	-0.84 (0.216)	-0.9 (-0.9, -0.7)	-1.1, -0.6						
Percent change from baseline	1	-4.59 (NC)	-4.6 (-4.6, -4.6)	-4.6, -4.6			5	-14.36 (4.351)	-13.6 (-14.9, -11.3)	-21.5, -10.5						
24 hours																
Absolute value	1	4.60 (NC)	4.6 (4.6, 4.6)	4.6, 4.6			5	4.96 (0.207)	4.9 (4.8, 5.0)	4.8, 5.3						
Change from baseline	1	-0.85 (NC)	-0.9 (-0.9, -0.9)	-0.9, -0.9			5	-0.98 (0.563)	-0.8 (-1.1, -0.6)	-1.9, -0.5						
Percent change from baseline	1	-15.60 (NC)	-15.6 (-15.6, -15.6)	-15.6, -15.6			5	-16.08 (7.507)	-13.0 (-18.3, -10.5)	-28.2, -10.3						
25 hours																
Absolute value	1	4.90 (NC)	4.9 (4.9, 4.9)	4.9, 4.9			5	4.58 (0.311)	4.7 (4.3, 4.8)	4.2, 4.9						
Change from baseline	1	-0.55 (NC)	-0.5 (-0.5, -0.5)	-0.5, -0.5			5	-1.36 (0.792)	-1.1 (-1.6, -1.0)	-2.6, -0.5						
Percent change from baseline	1	-10.09 (NC)	-10.1 (-10.1, -10.1)	-10.1, -10.1			5	-22.22 (10.808)	-18.3 (-26.8, -17.3)	-38.5, -10.3						
28 hours																
Absolute value	1	4.90 (NC)	4.9 (4.9, 4.9)	4.9, 4.9			5	4.56 (0.336)	4.6 (4.4, 4.7)	4.1, 5.0						
Change from baseline	1	-0.55 (NC)	-0.5 (-0.5, -0.5)	-0.5, -0.5			5	-1.38 (0.274)	-1.3 (-1.5, -1.2)	-1.8, -1.2						
Percent change from baseline	1	-10.09 (NC)	-10.1 (-10.1, -10.1)	-10.1, -10.1			5	-23.18 (2.864)	-23.4 (-25.1, -20.7)	-26.7, -20.0						
48 hours																
Absolute value	1	4.60 (NC)	4.6 (4.6, 4.6)	4.6, 4.6			5	4.32 (0.606)	4.3 (4.2, 4.4)	3.5, 5.2						
Change from baseline	1	-0.85 (NC)	-0.9 (-0.9, -0.9)	-0.9, -0.9			5	-1.62 (0.652)	-1.6 (-1.9, -1.5)	-2.5, -0.7						
Percent change from baseline	1	-15.60 (NC)	-15.6 (-15.6, -15.6)	-15.6, -15.6			5	-27.17 (9.731)	-27.0 (-34.6, -25.1)	-37.0, -12.2						
>= 65 years																
Baseline																
Absolute value	32	5.65 (0.429)	5.5 (5.4, 5.9)	5.2, 6.6			31	5.38 (0.271)	5.4 (5.2, 5.5)	5.0, 6.0						
1 hour																
Absolute value	32	5.55 (0.559)	5.4 (5.1, 5.9)	4.9, 6.8			31	5.05 (0.401)	5.1 (4.8, 5.4)	4.2, 5.7						
Change from baseline	32	-0.11 (0.304)	-0.1 (-0.3, 0.1)	-0.7, 0.5	-0.09 (0.059)	(-0.20, 0.03)	31	-0.33 (0.335)	-0.4 (-0.6, -0.1)	-1.0, 0.6	-0.34 (0.059)	(-0.46, -0.22)	-0.25 (-0.43, -0.08)	0.0041	-0.68 (-1.19, -0.17)	
Percent change from baseline	32	-1.97 (5.296)	-2.8 (-5.4, 2.1)	-12.3, 8.4			31	-6.02 (6.367)	-6.5 (-10.4, -2.0)	-18.4, 12.3						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
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Table 8.1.2.1 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint), ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)						Lokelma 10g QD (N=36)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Age *(contd.)*																
>= 65 years *(contd.)*																
2 hours																
Absolute value	31	5.30 (0.565)	5.1 (4.9, 5.7)	4.4, 6.5			31	4.95 (0.369)	5.0 (4.8, 5.2)	4.2, 5.9						
Change from baseline	31	-0.33 (0.303)	-0.3 (-0.6, -0.2)	-0.9, 0.5	-0.31 (0.059)	(-0.43, -0.19)	31	-0.43 (0.336)	-0.4 (-0.7, -0.2)	-1.0, 0.4	-0.44 (0.059)	(-0.56, -0.32)	-0.13 (-0.30, 0.04)	0.1220	-0.32 (-0.82, 0.19)	
Percent change from baseline	31	-5.93 (5.435)	-5.8 (-9.8, -3.7)	-16.6, 7.4			31	-7.88 (6.154)	-7.4 (-13.6, -3.3)	-18.4, 6.8						
4 hours																
Absolute value	31	5.18 (0.525)	5.2 (4.8, 5.5)	4.4, 6.1			31	4.90 (0.419)	5.0 (4.7, 5.2)	4.0, 5.7						
Change from baseline	31	-0.44 (0.311)	-0.4 (-0.7, -0.1)	-1.1, 0.0	-0.42 (0.062)	(-0.55, -0.30)	31	-0.48 (0.356)	-0.5 (-0.7, -0.2)	-1.2, 0.2	-0.50 (0.062)	(-0.62, -0.38)	-0.08 (-0.25, 0.10)	0.3949	-0.13 (-0.63, 0.37)	
Percent change from baseline	31	-7.88 (5.684)	-7.1 (-13.0, -2.8)	-19.6, 0.0			31	-8.95 (6.557)	-8.2 (-13.7, -3.0)	-22.3, 3.2						
24 hours																
Absolute value	30	5.41 (0.456)	5.4 (5.0, 5.7)	4.6, 6.6			31	4.73 (0.336)	4.8 (4.5, 5.0)	4.1, 5.4						
Change from baseline	30	-0.19 (0.337)	-0.3 (-0.4, 0.0)	-0.8, 0.5	-0.18 (0.060)	(-0.30, -0.06)	31	-0.65 (0.332)	-0.7 (-0.9, -0.4)	-1.2, 0.0	-0.66 (0.059)	(-0.78, -0.54)	-0.49 (-0.66, -0.31)	<.0001	-1.35 (-1.91, -0.80)	
Percent change from baseline	30	-3.42 (5.940)	-4.9 (-7.8, 0.9)	-12.6, 9.1			31	-11.94 (6.022)	-12.9 (-17.1, -6.4)	-21.9, 1.0						
25 hours																
Absolute value	30	5.34 (0.470)	5.3 (5.1, 5.6)	4.1, 6.3			31	4.44 (0.337)	4.5 (4.2, 4.7)	3.7, 5.2						
Change from baseline	30	-0.26 (0.312)	-0.2 (-0.4, -0.2)	-1.2, 0.4	-0.23 (0.061)	(-0.35, -0.11)	31	-0.94 (0.353)	-1.0 (-1.1, -0.7)	-1.6, -0.3	-0.96 (0.060)	(-1.08, -0.84)	-0.72 (-0.90, -0.55)	<.0001	-2.04 (-2.66, -1.42)	
Percent change from baseline	30	-4.60 (5.674)	-3.9 (-7.3, -2.7)	-22.3, 7.5			31	-17.39 (6.243)	-18.4 (-20.4, -12.6)	-29.5, -5.8						
28 hours																
Absolute value	30	5.20 (0.525)	5.2 (4.8, 5.5)	4.2, 6.3			31	4.30 (0.372)	4.3 (3.9, 4.6)	3.7, 5.2						
Change from baseline	30	-0.40 (0.434)	-0.4 (-0.8, -0.1)	-1.1, 0.5	-0.37 (0.074)	(-0.52, -0.23)	31	-1.08 (0.389)	-1.1 (-1.2, -0.9)	-2.0, -0.3	-1.10 (0.073)	(-1.24, -0.95)	-0.72 (-0.93, -0.51)	<.0001	-1.65 (-2.23, -1.07)	
Percent change from baseline	30	-7.11 (7.720)	-7.1 (-14.2, -1.8)	-20.4, 9.8			31	-20.04 (6.706)	-20.0 (-23.6, -15.6)	-33.9, -5.9						
48 hours																
Absolute value	30	5.39 (0.361)	5.4 (5.1, 5.6)	4.6, 6.1			31	4.14 (0.446)	4.2 (3.9, 4.5)	2.9, 4.9						
Change from baseline	30	-0.21 (0.325)	-0.2 (-0.4, -0.0)	-1.0, 0.5	-0.20 (0.068)	(-0.33, -0.06)	31	-1.24 (0.433)	-1.2 (-1.5, -1.0)	-2.3, -0.2	-1.26 (0.067)	(-1.39, -1.12)	-1.06 (-1.26, -0.87)	<.0001	-2.68 (-3.37, -1.99)	
Percent change from baseline	30	-3.68 (5.629)	-2.8 (-7.9, -0.5)	-15.1, 9.4			31	-23.07 (8.052)	-23.6 (-27.1, -19.2)	-44.0, -3.4						

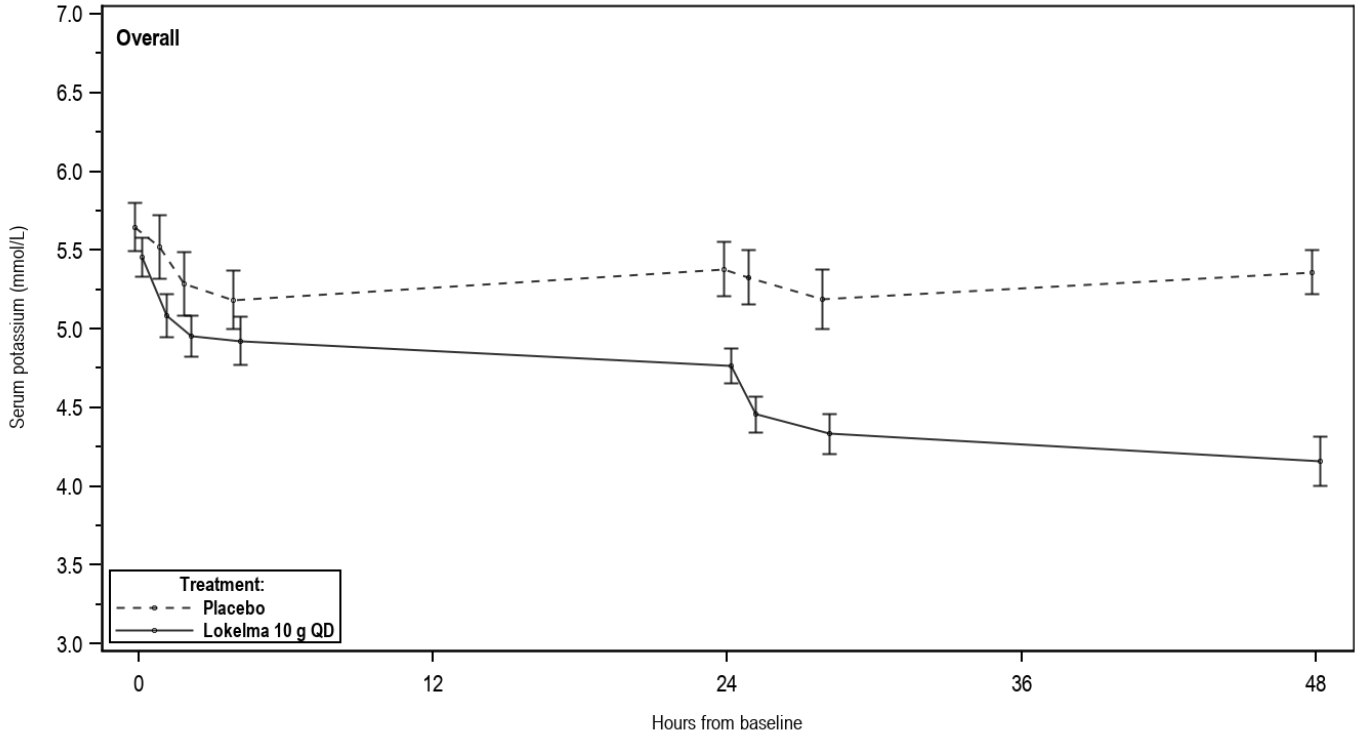
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Figure 8.1.2.2 - Study ZS-002 Japan: Serum potassium (mmol/L) over time up to 48 hours (Day 4 0hr pre-dose timepoint): absolute values, ZS 10g TID vs. combined placebo, overall and by subgroups (intent-to-treat population)



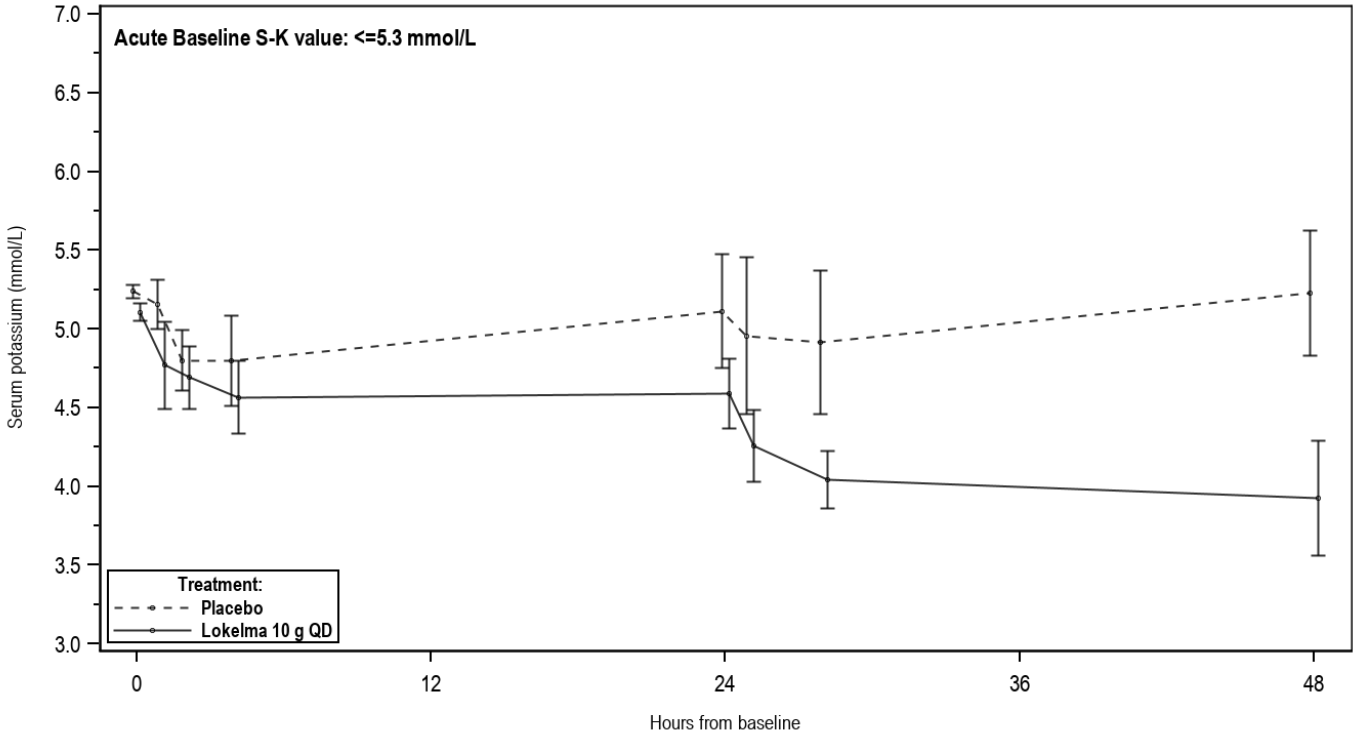
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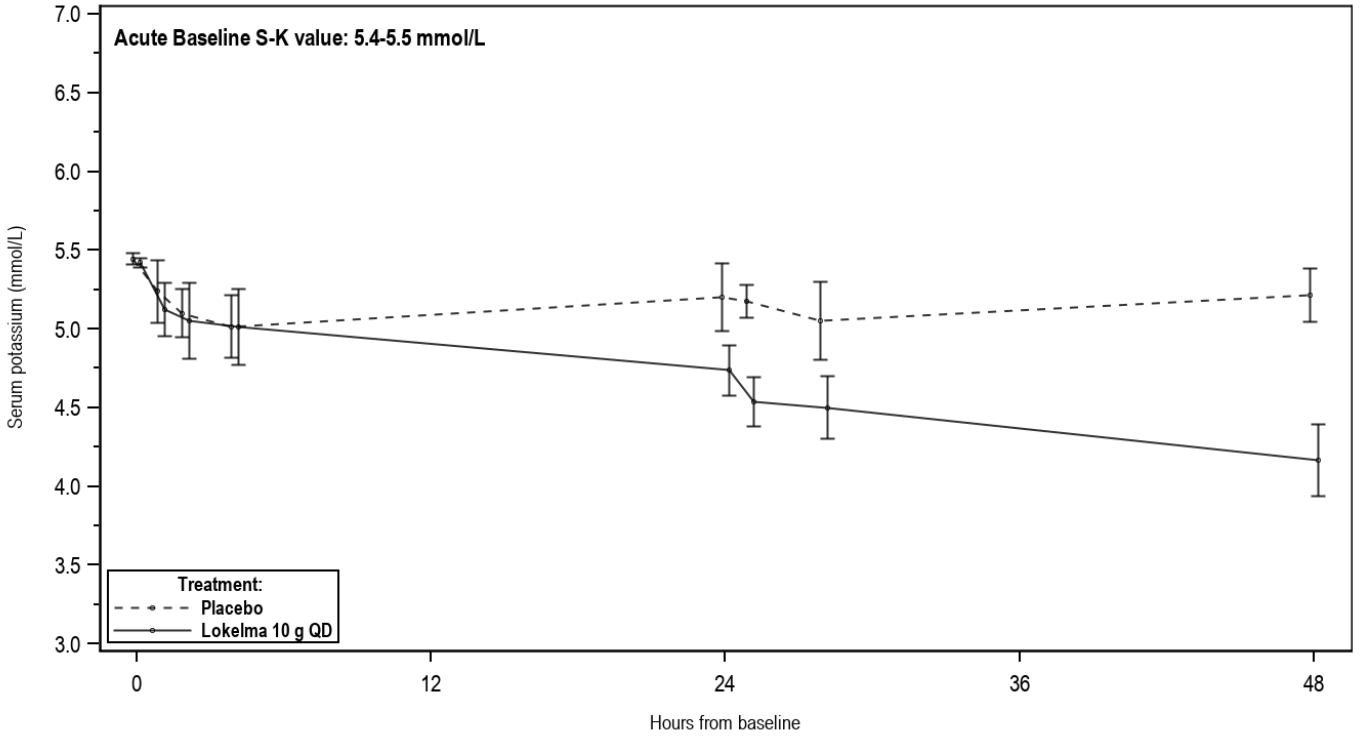
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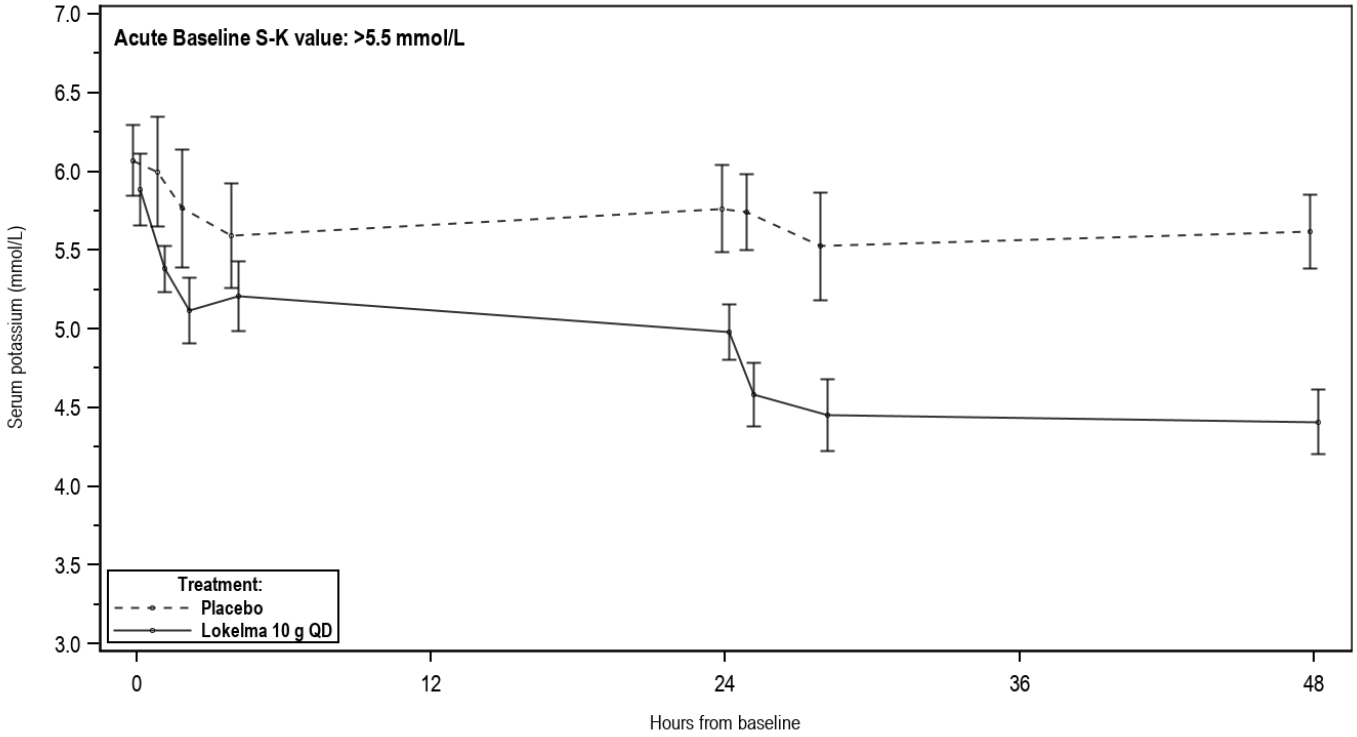
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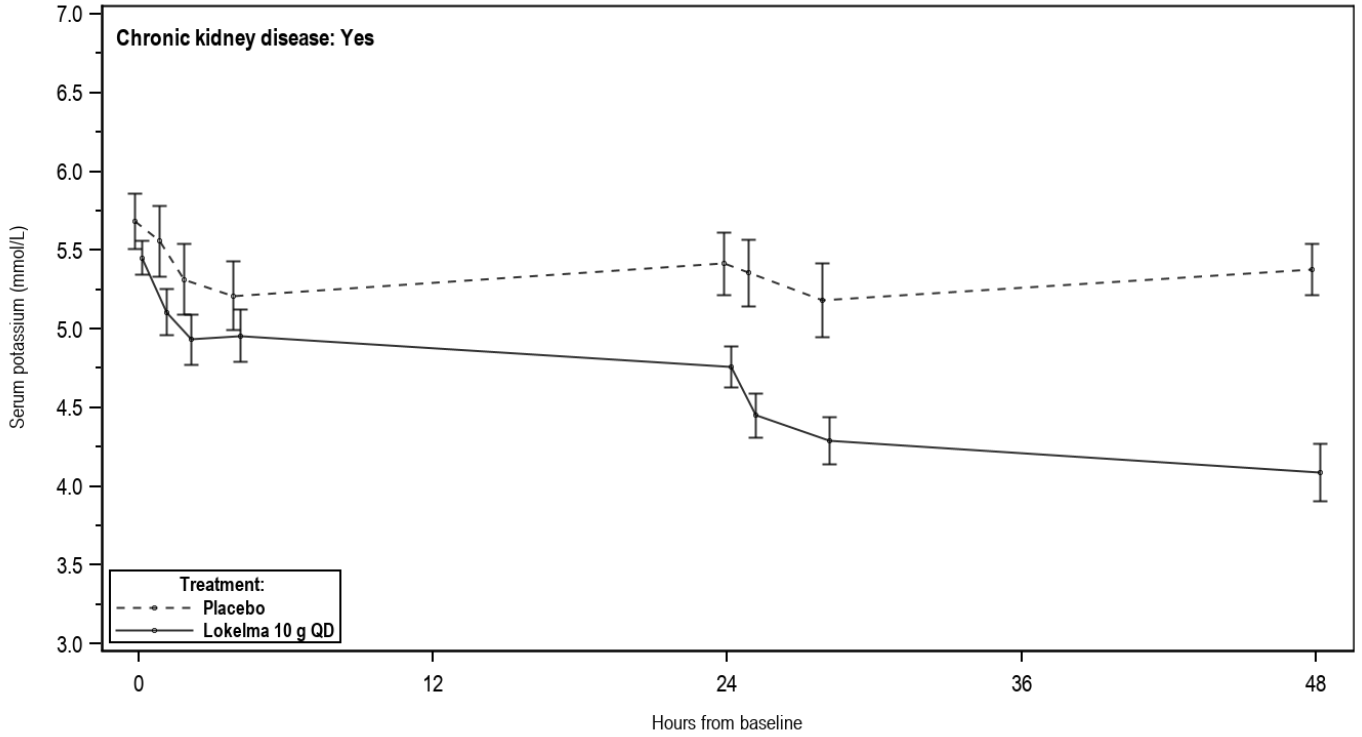
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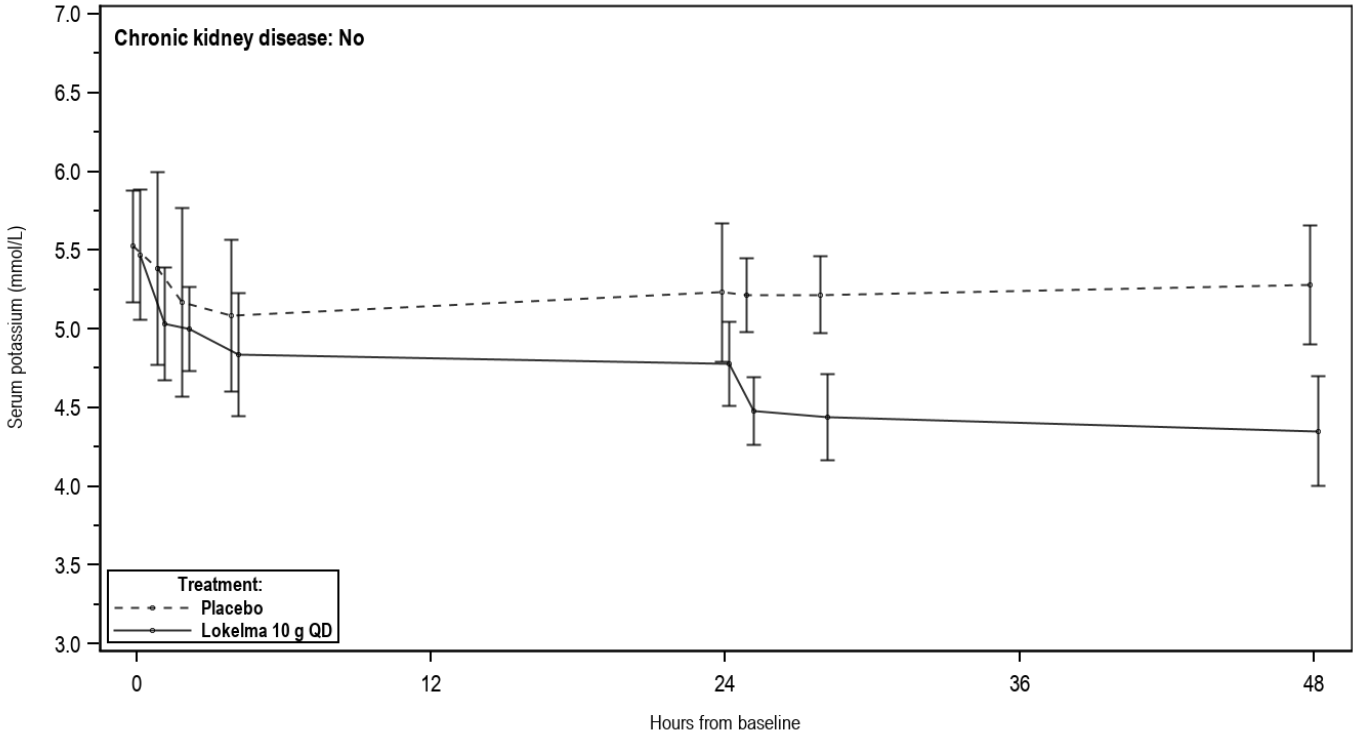
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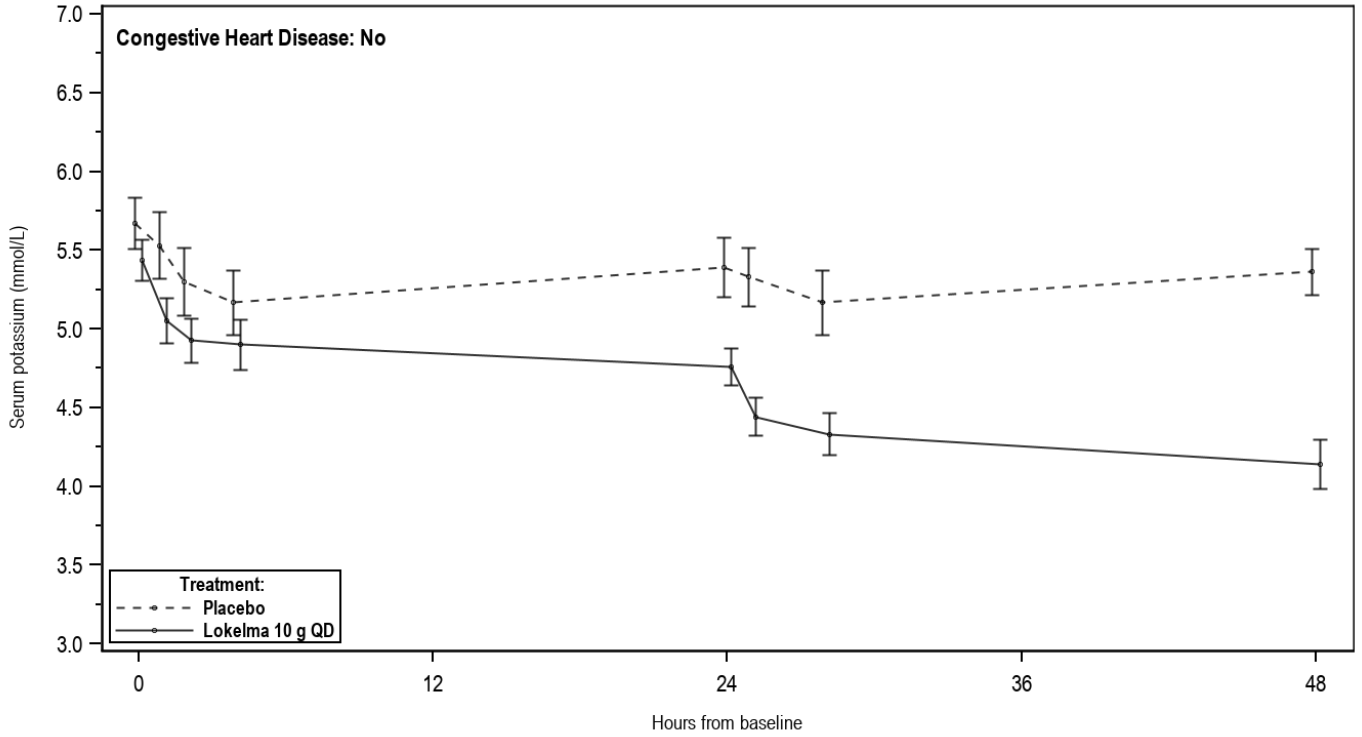
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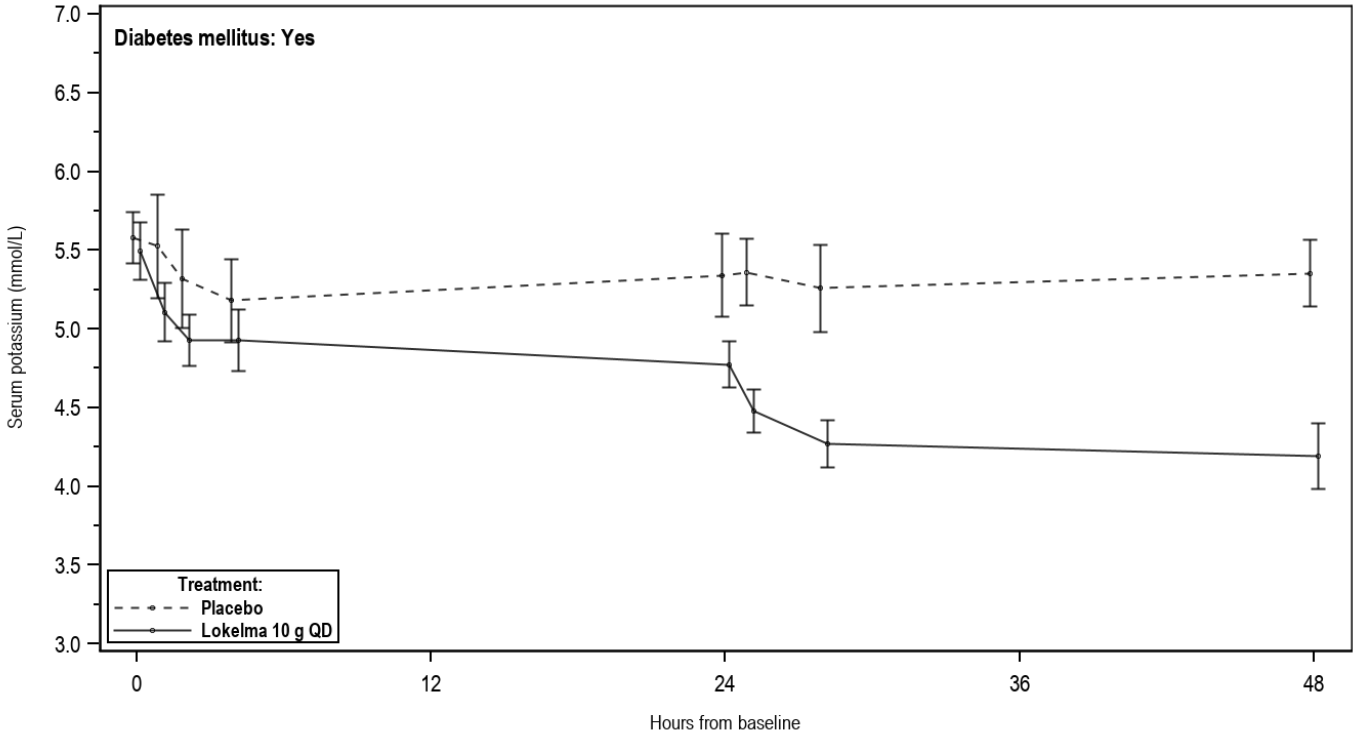
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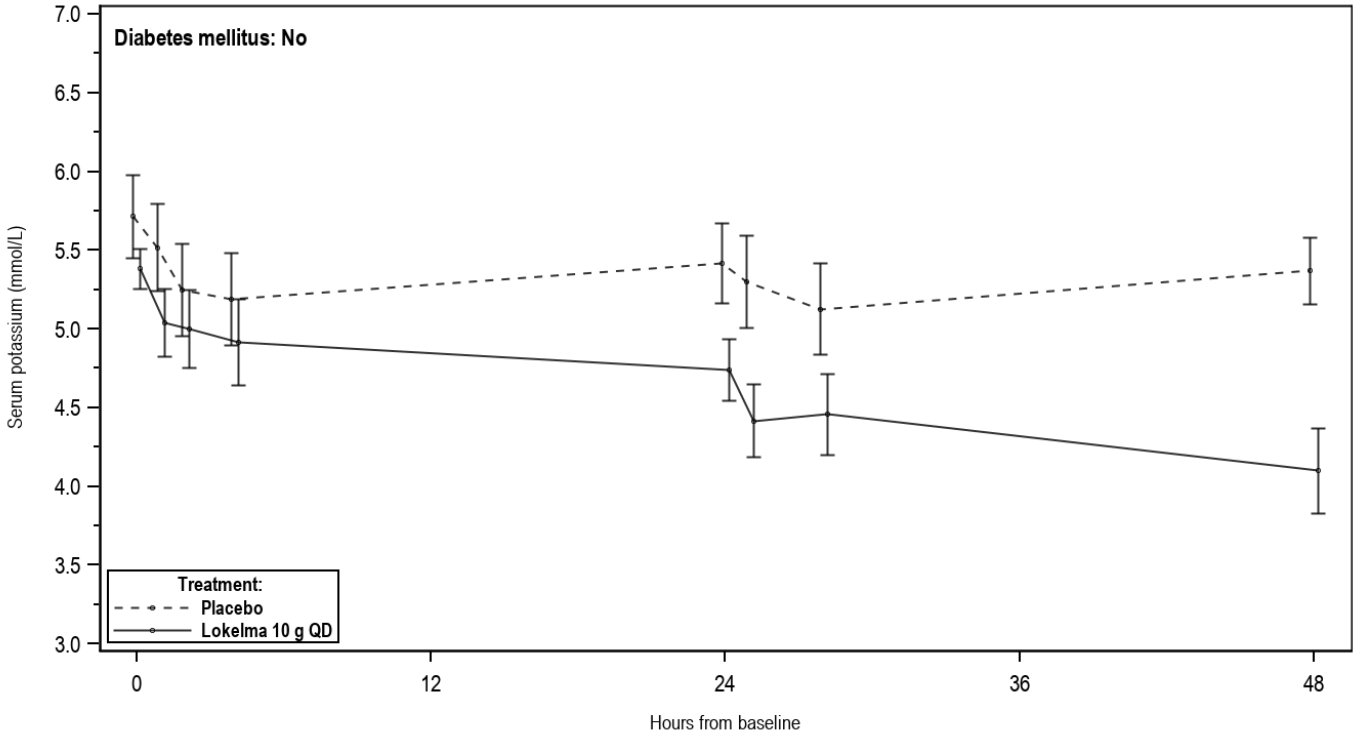
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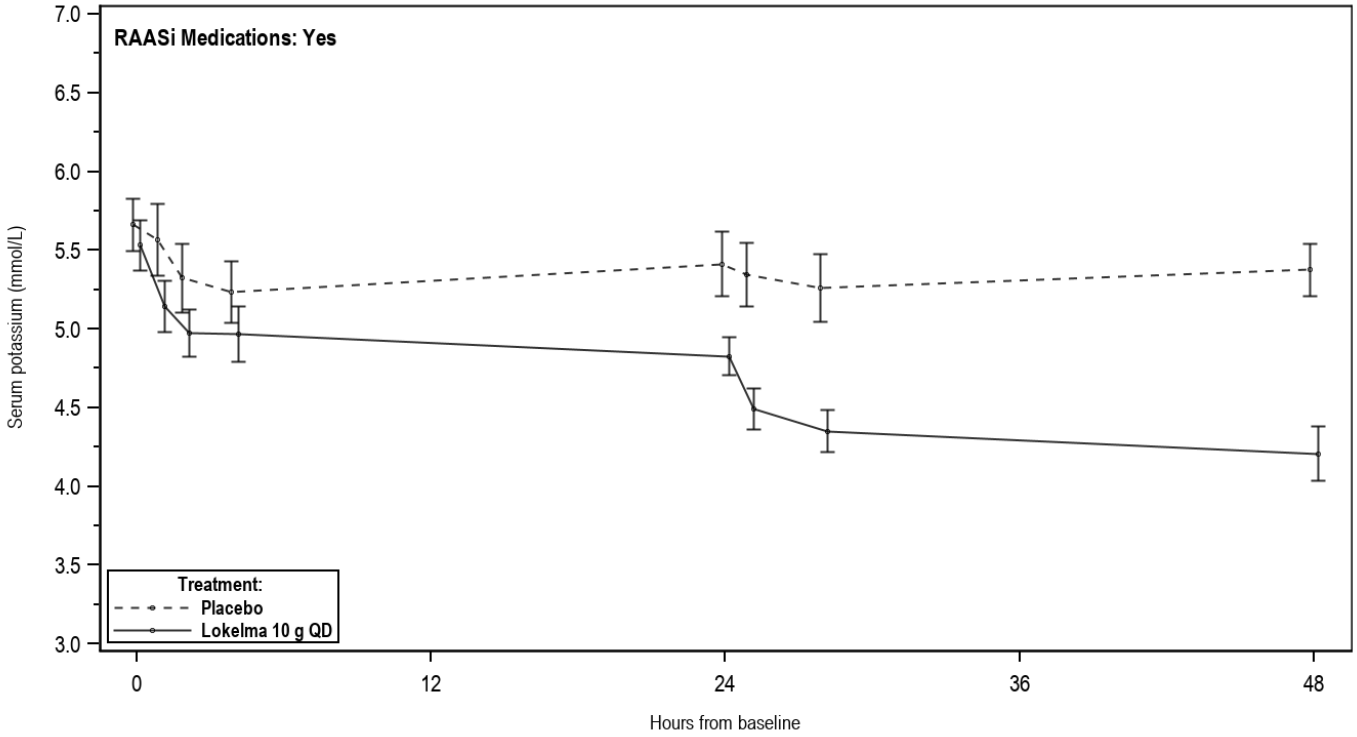
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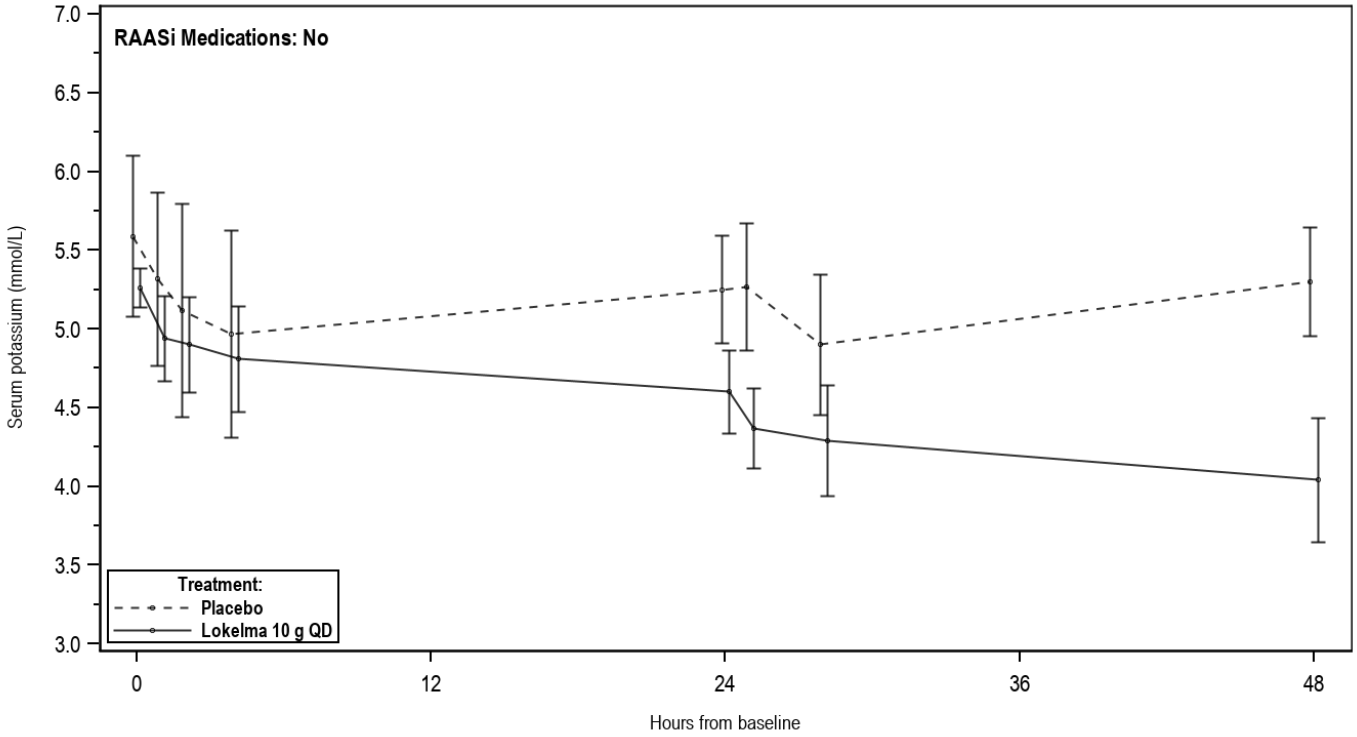
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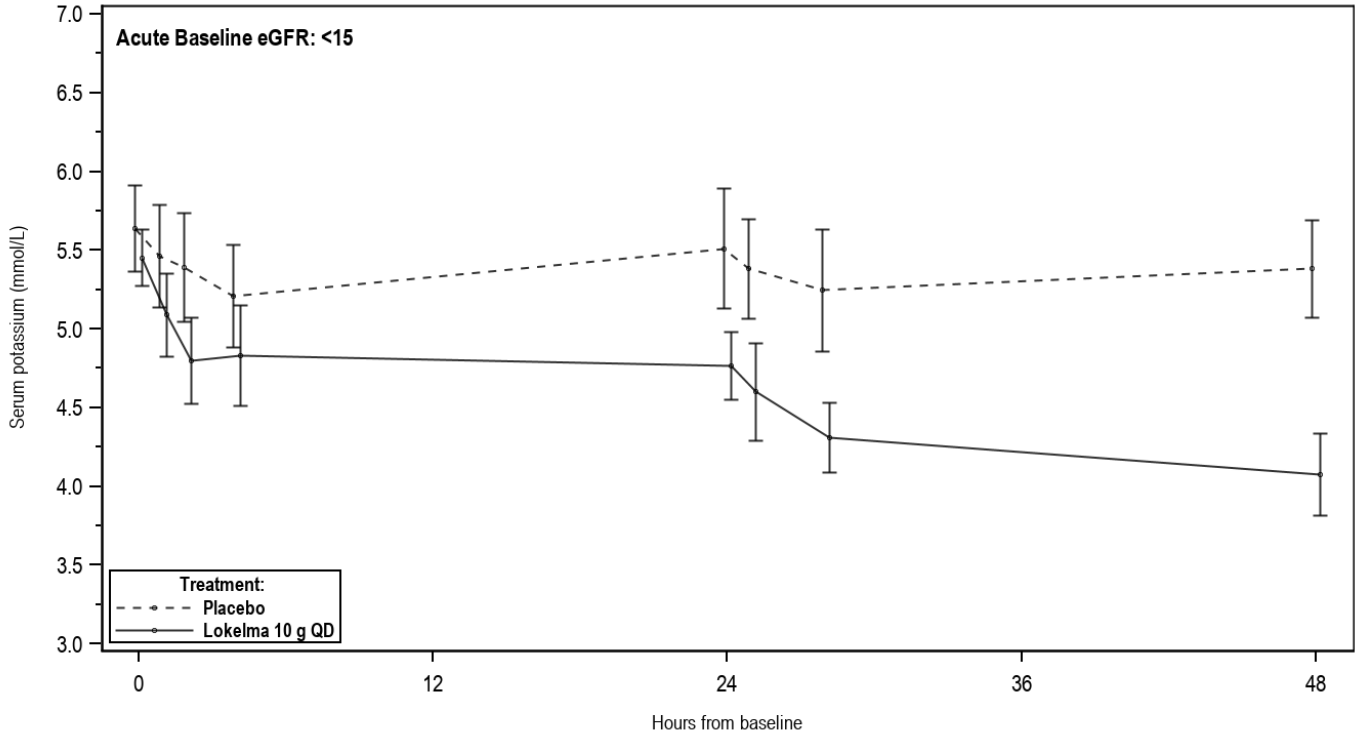
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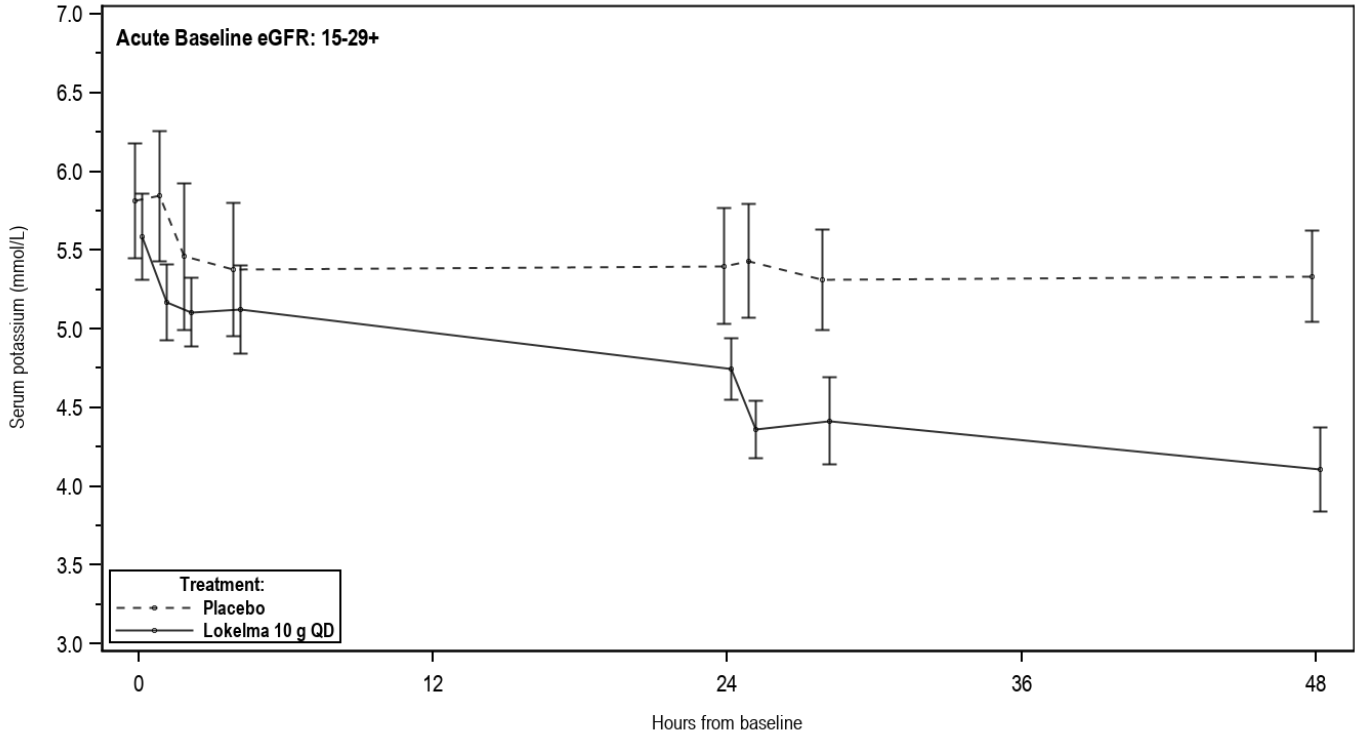
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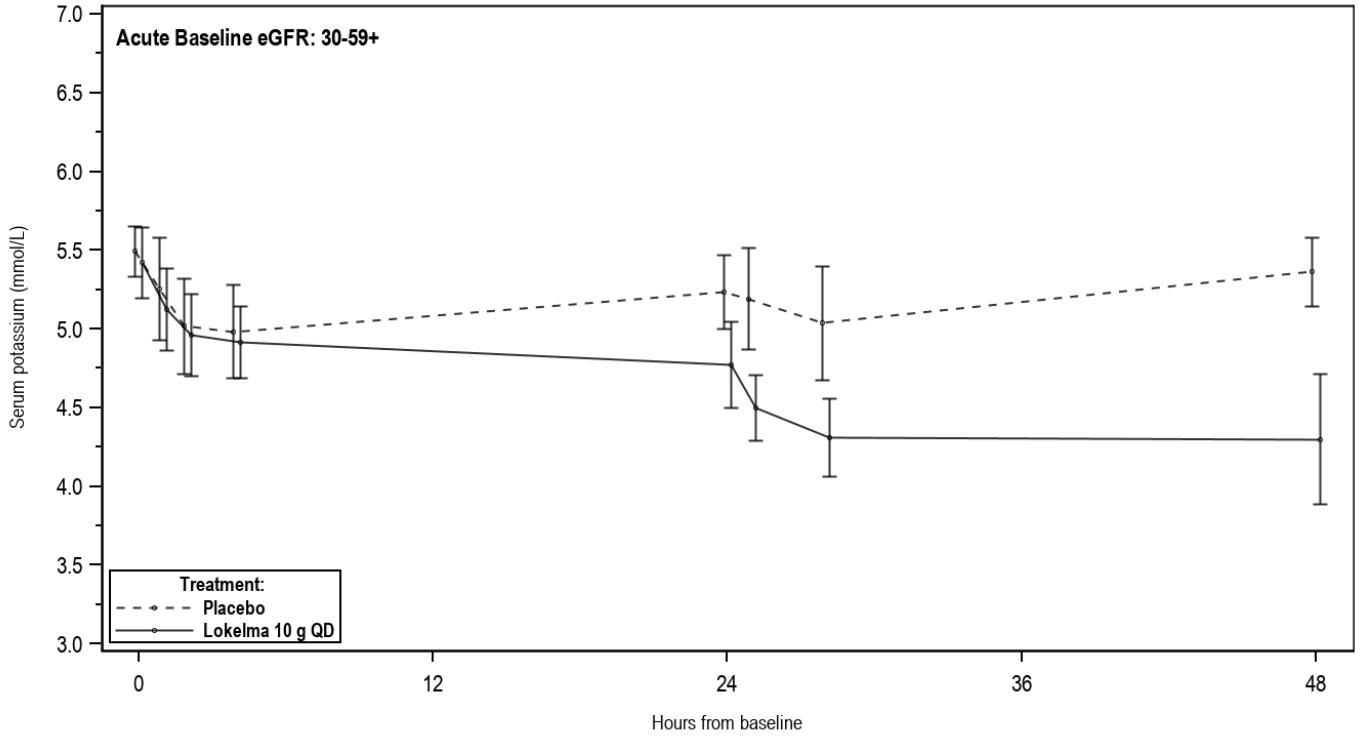
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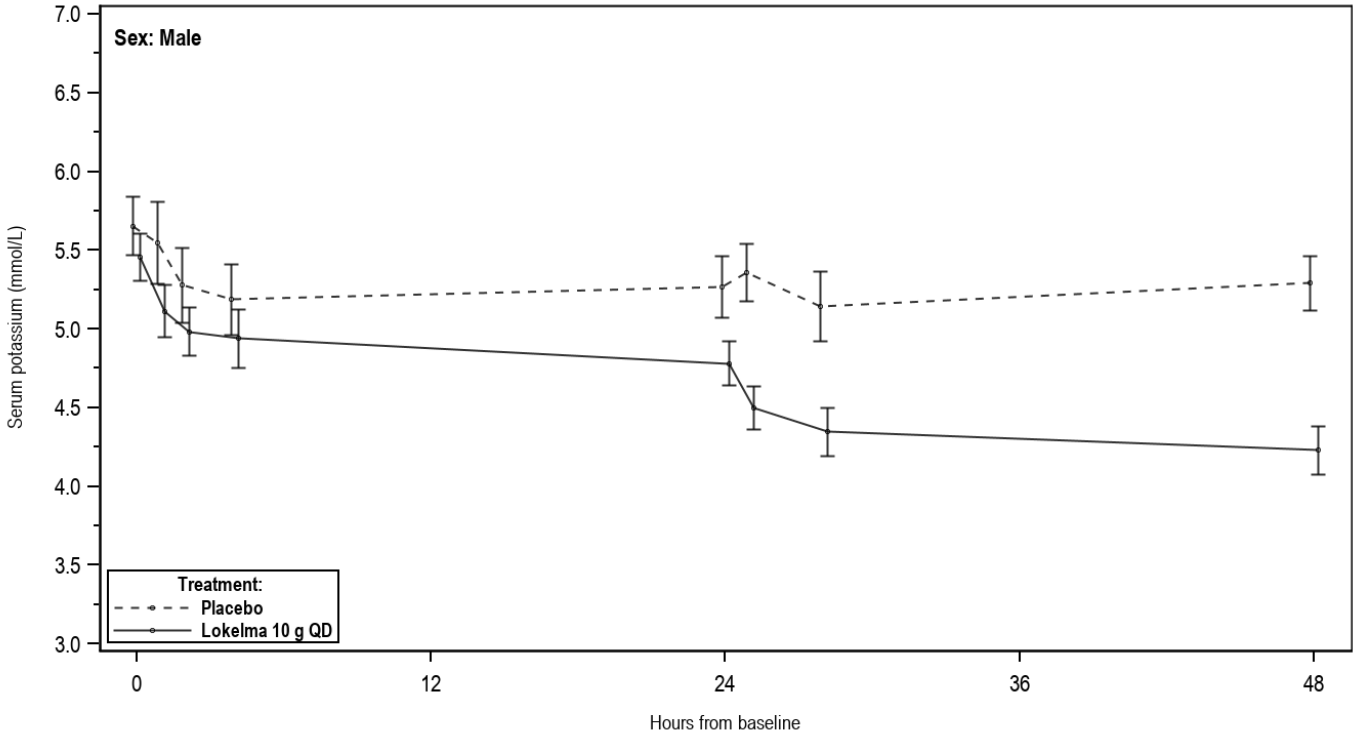
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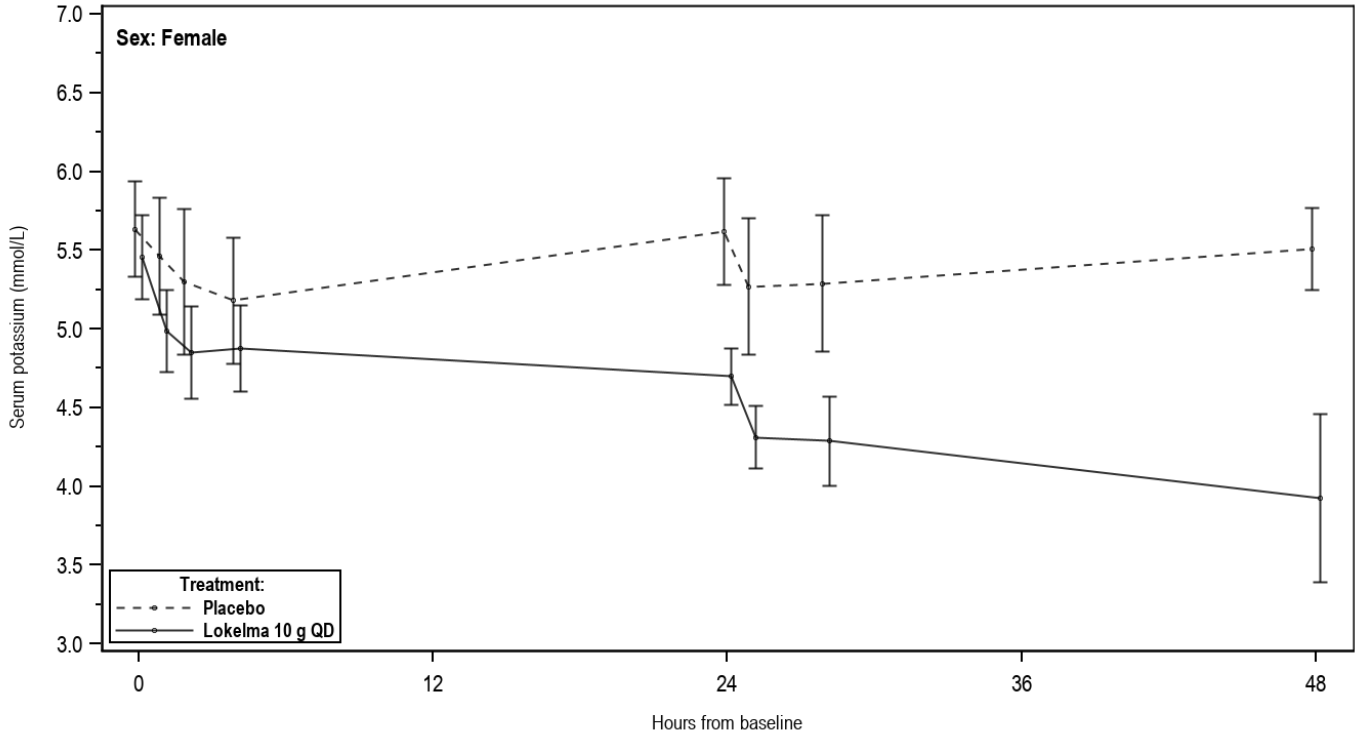
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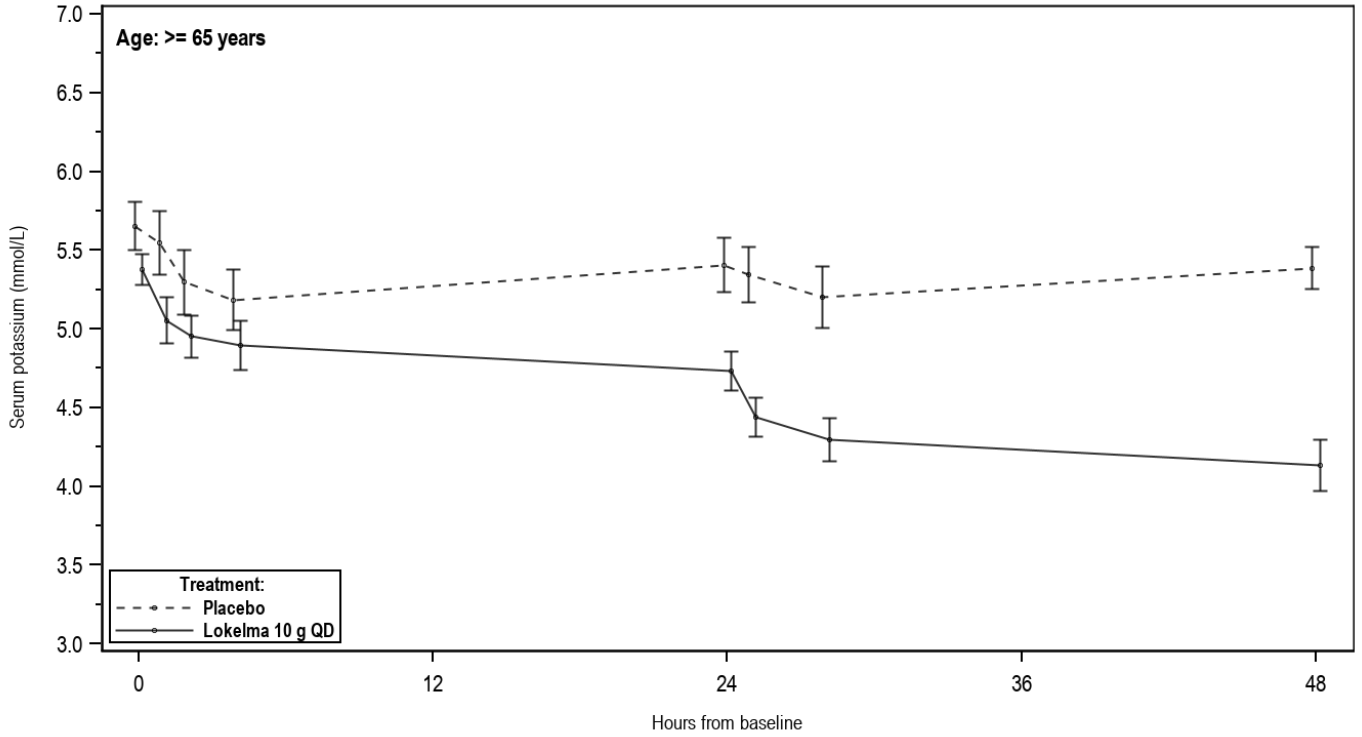
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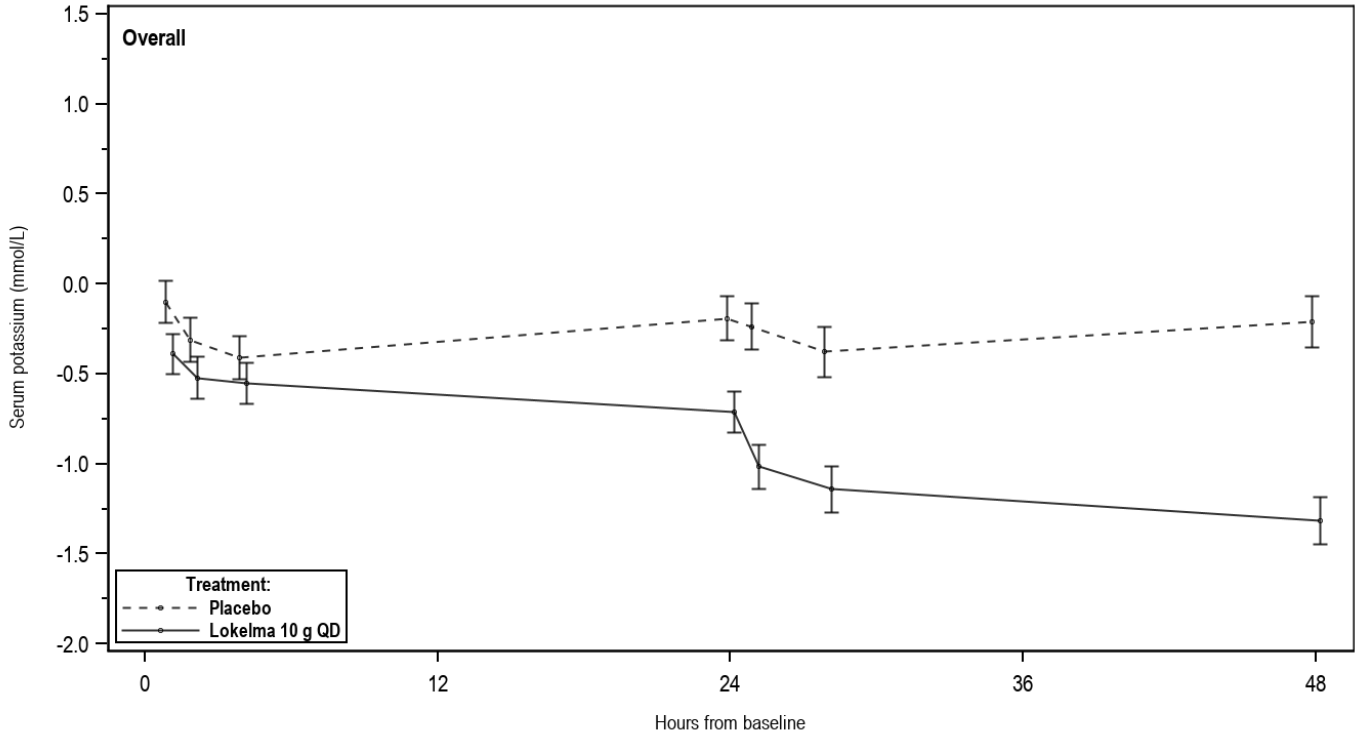
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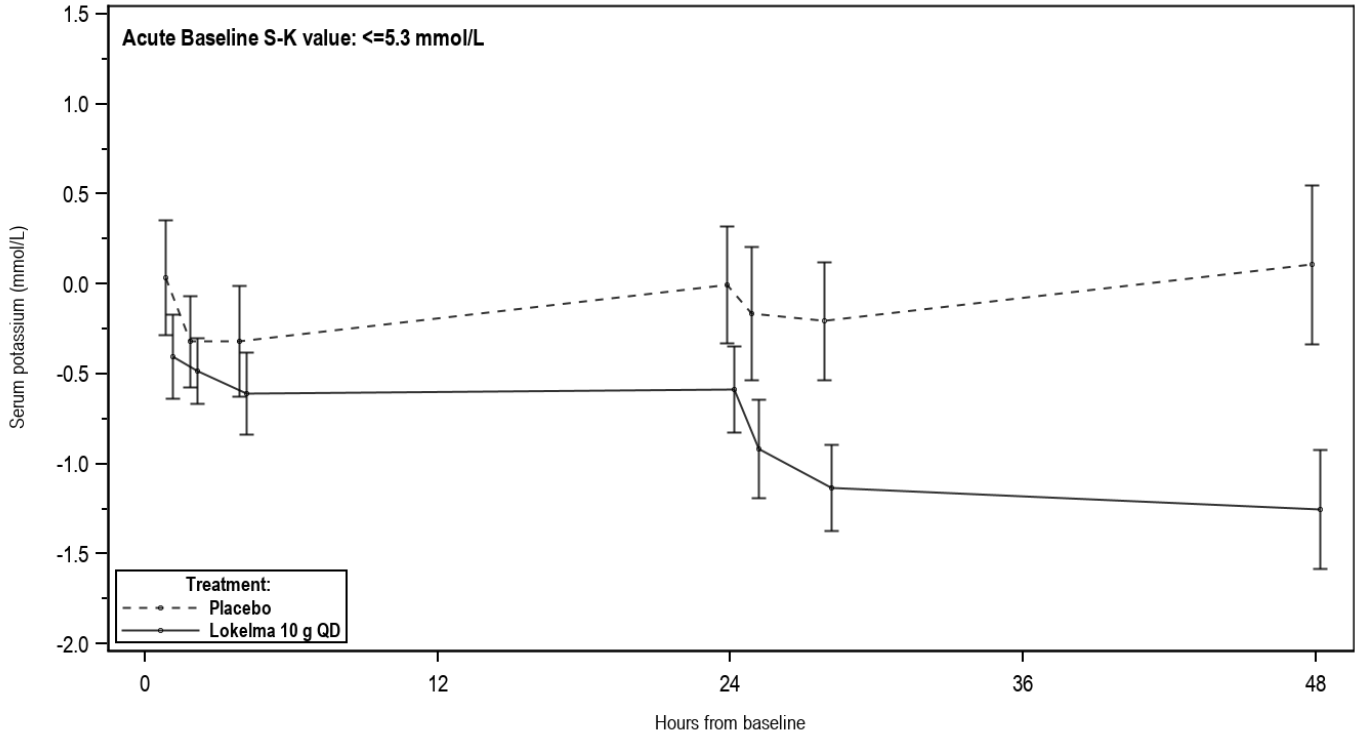
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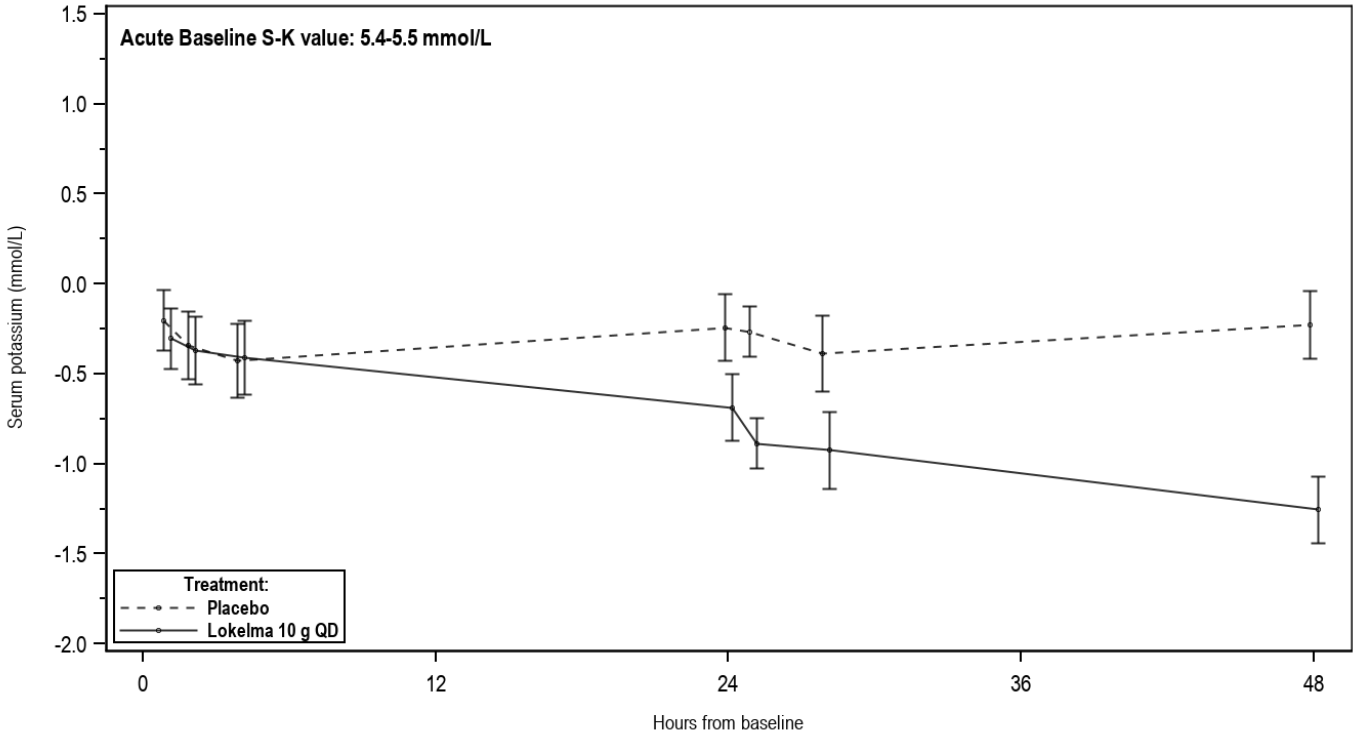
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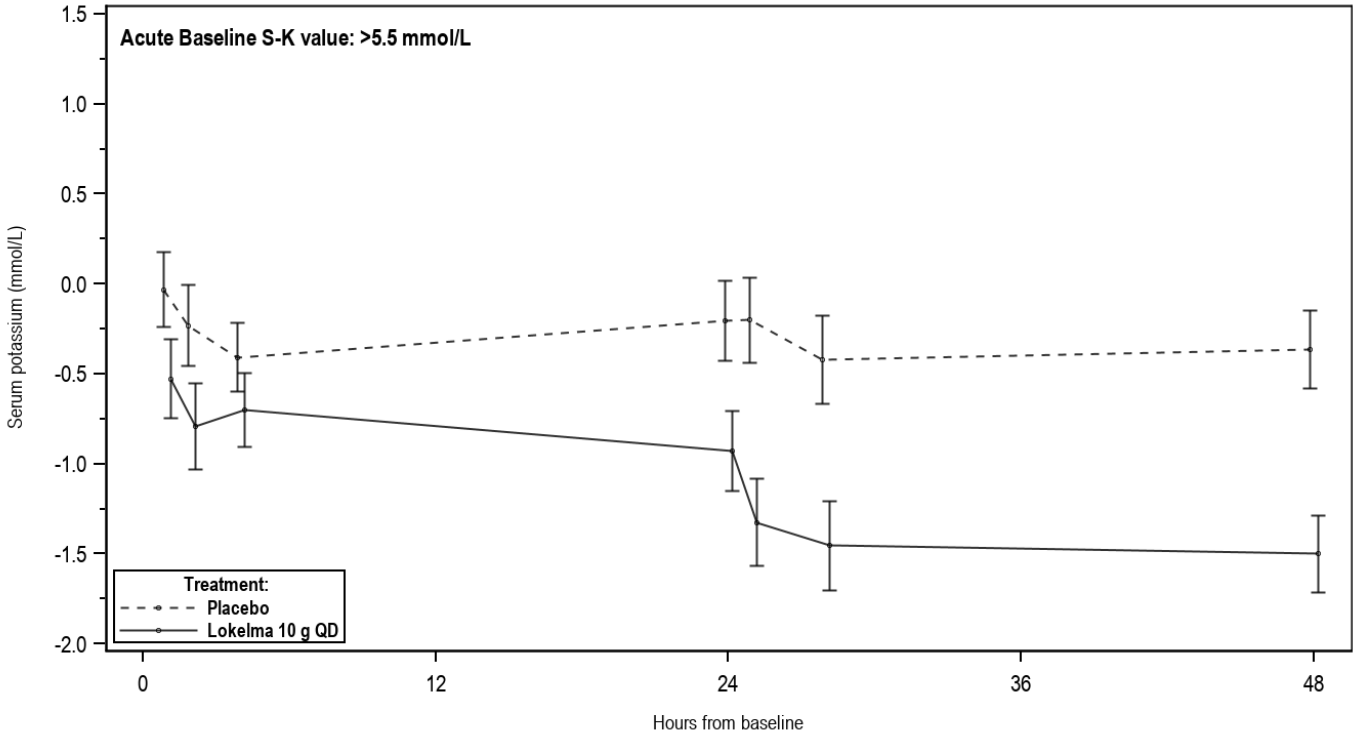
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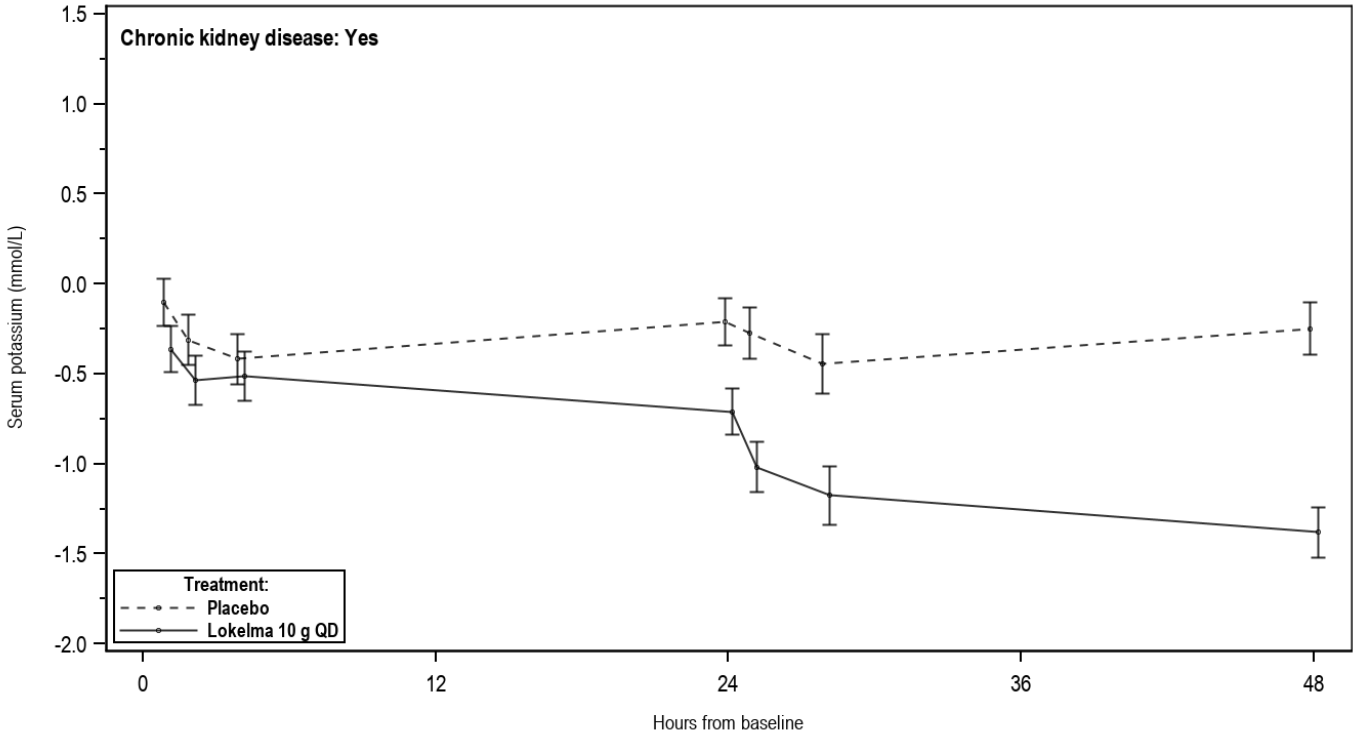
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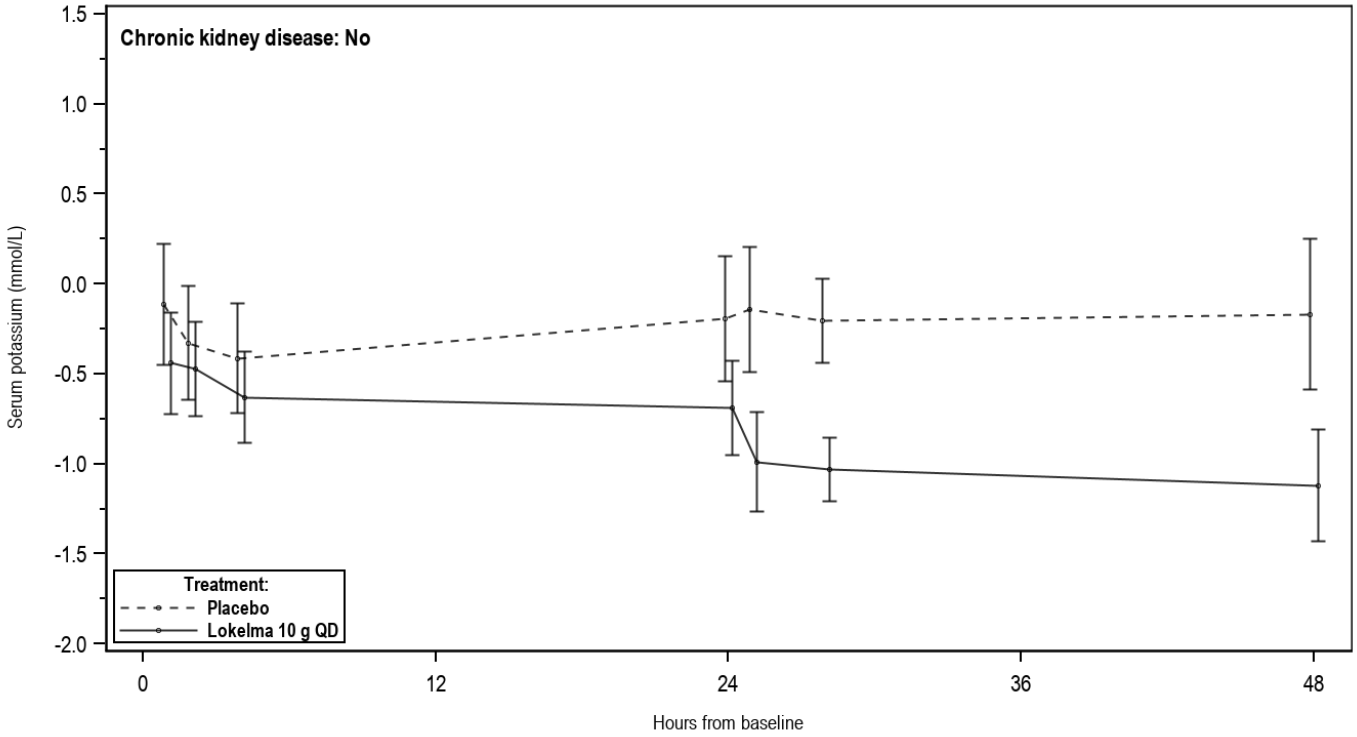
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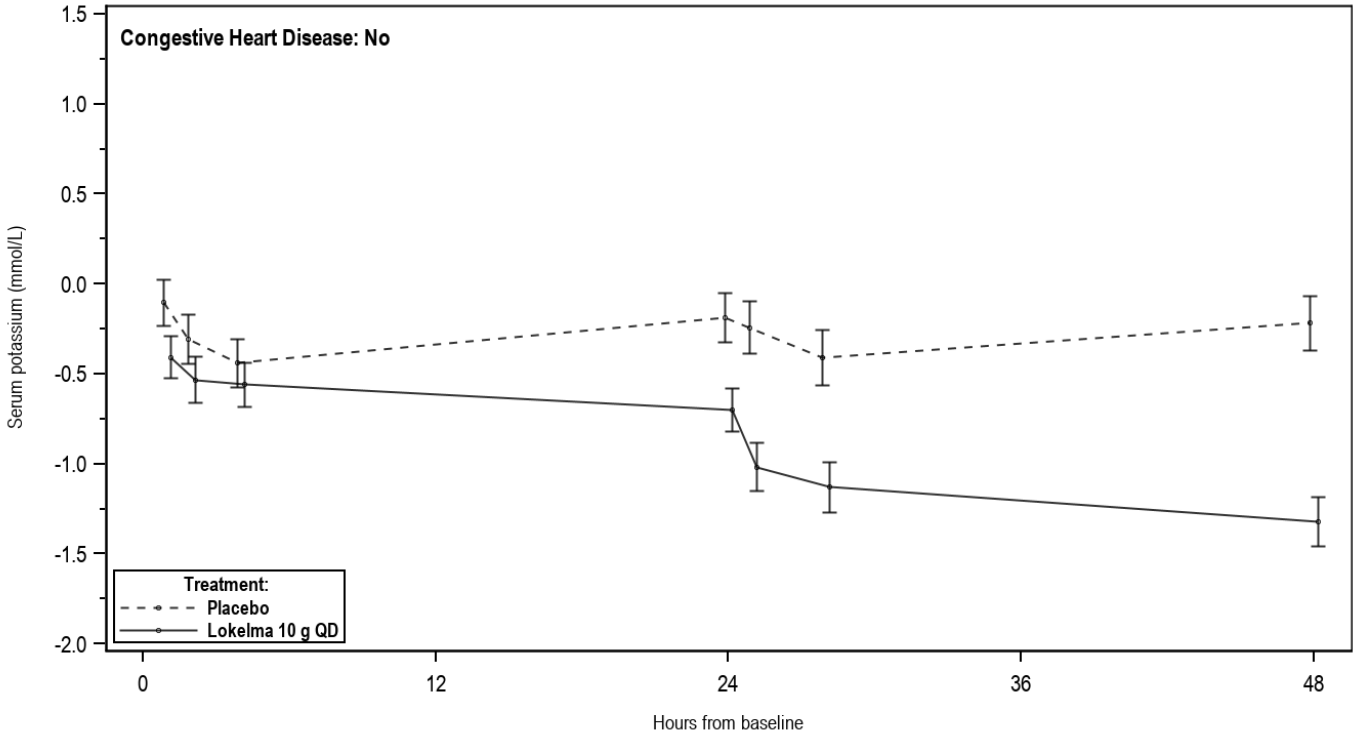
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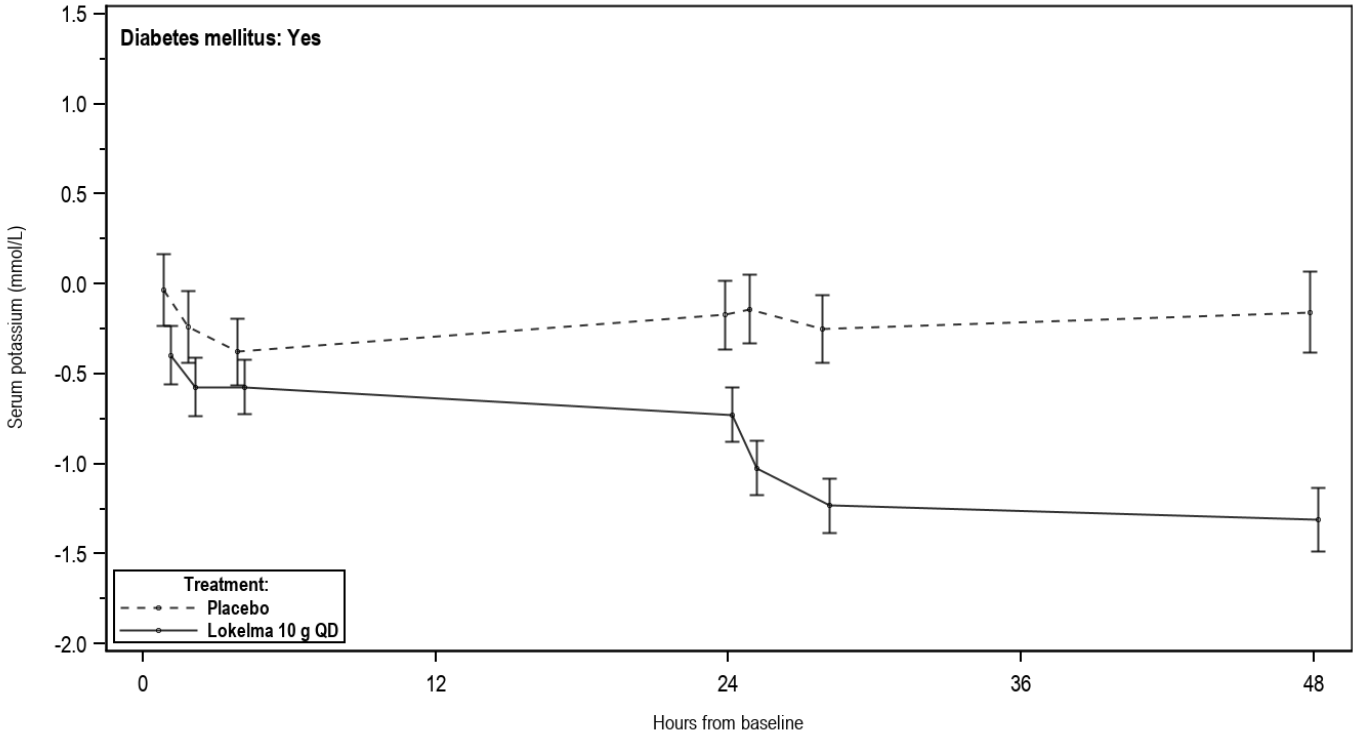
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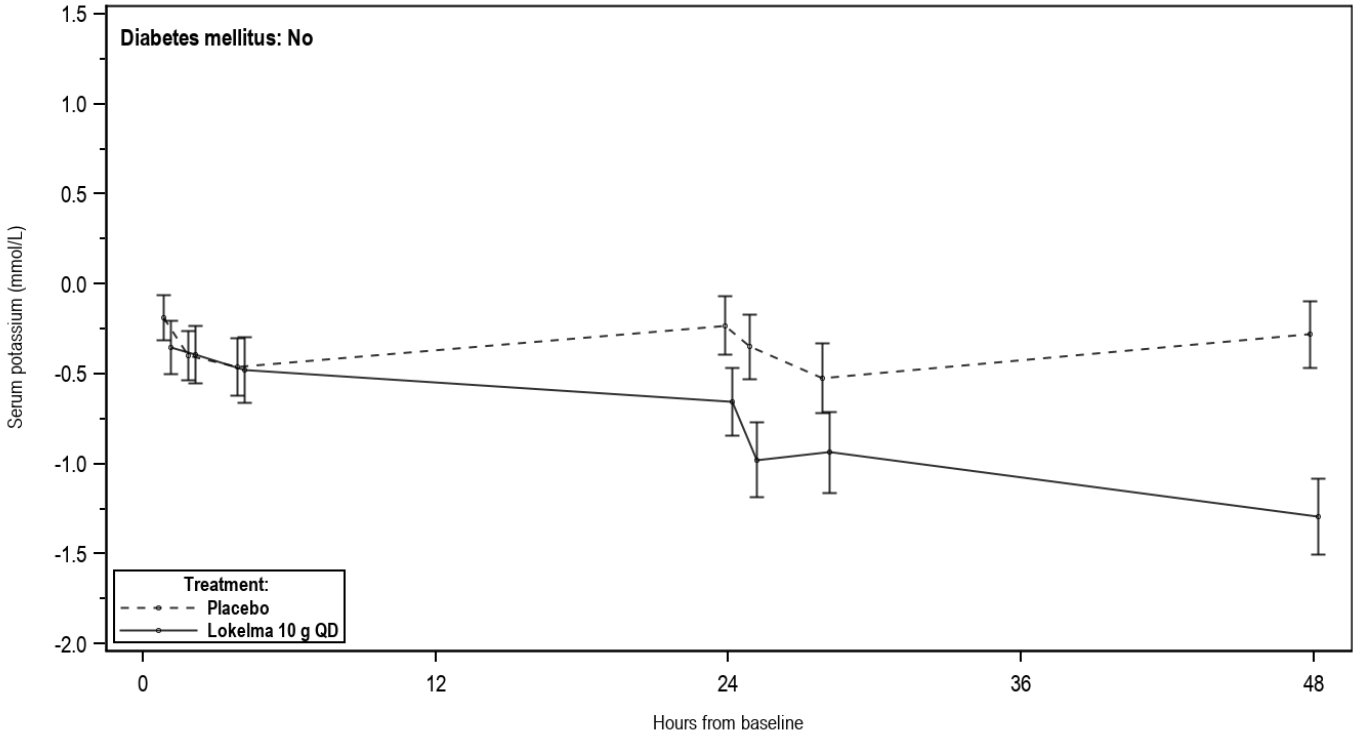
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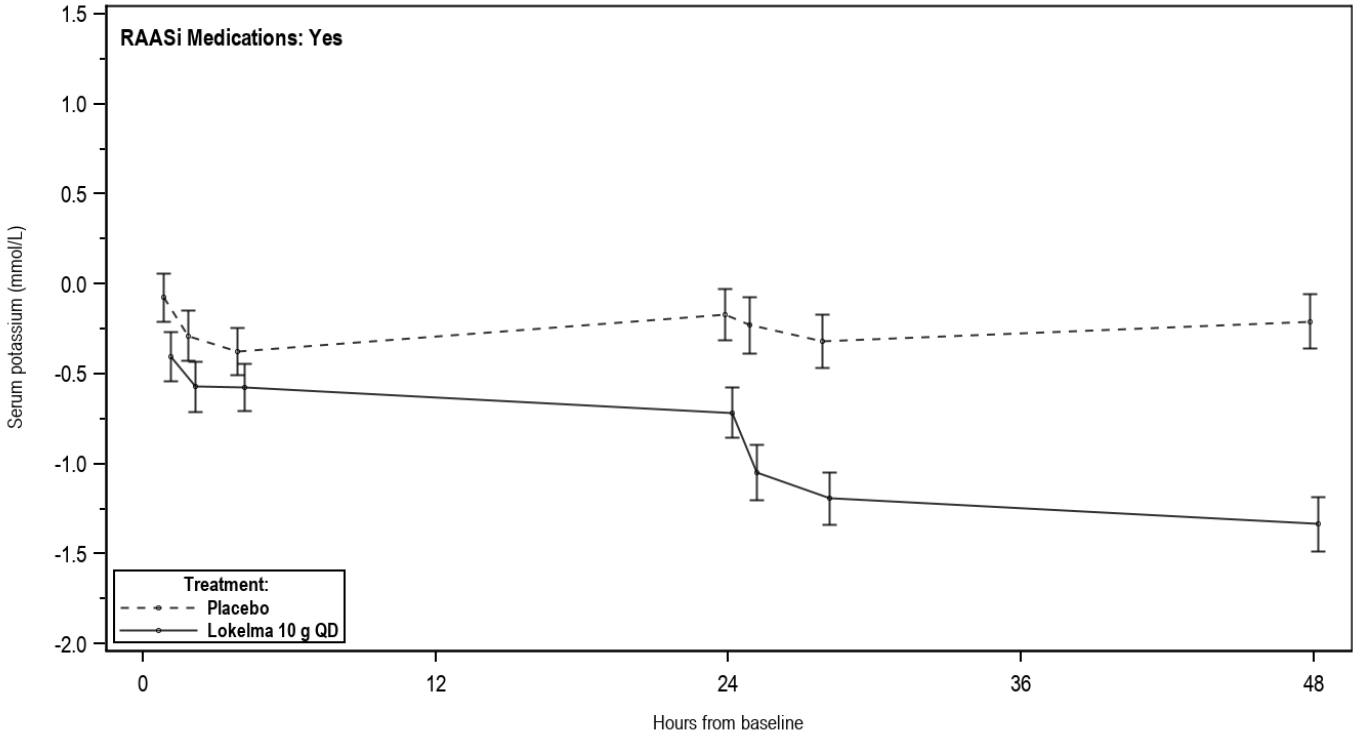
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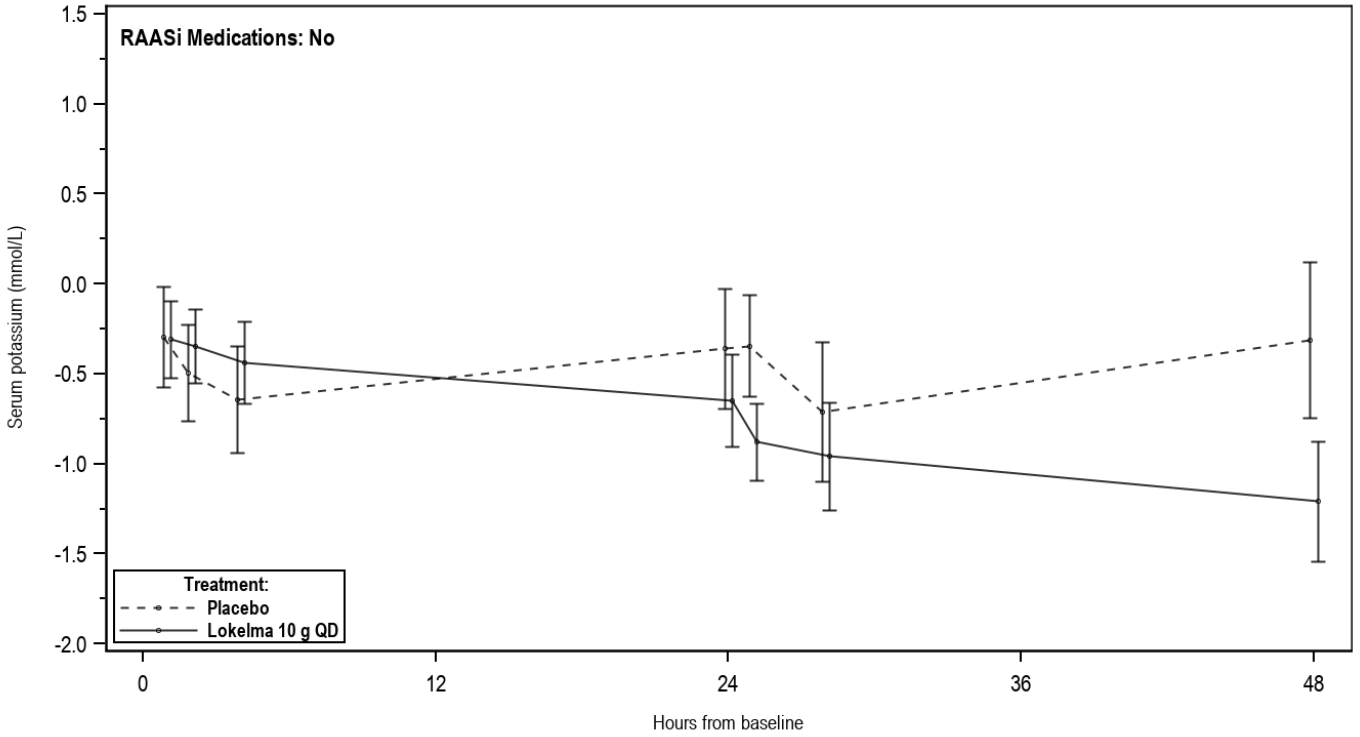
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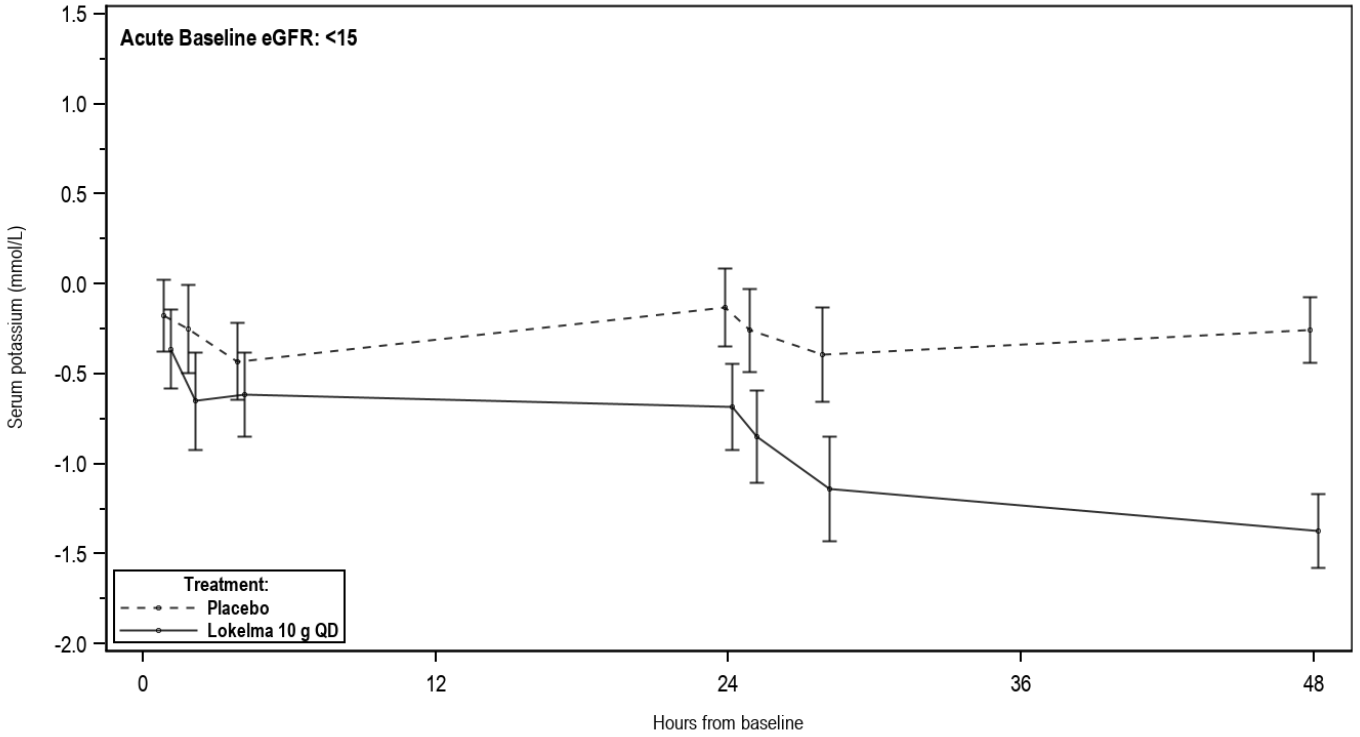
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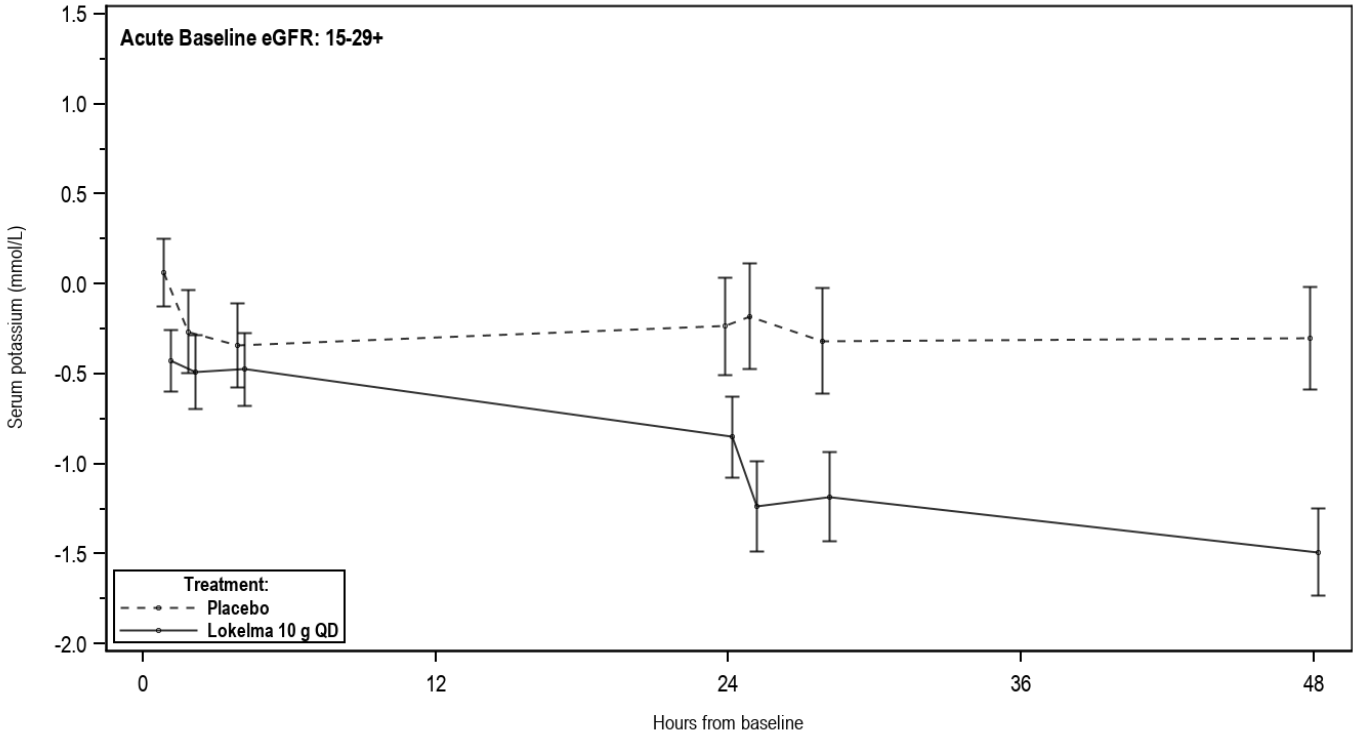
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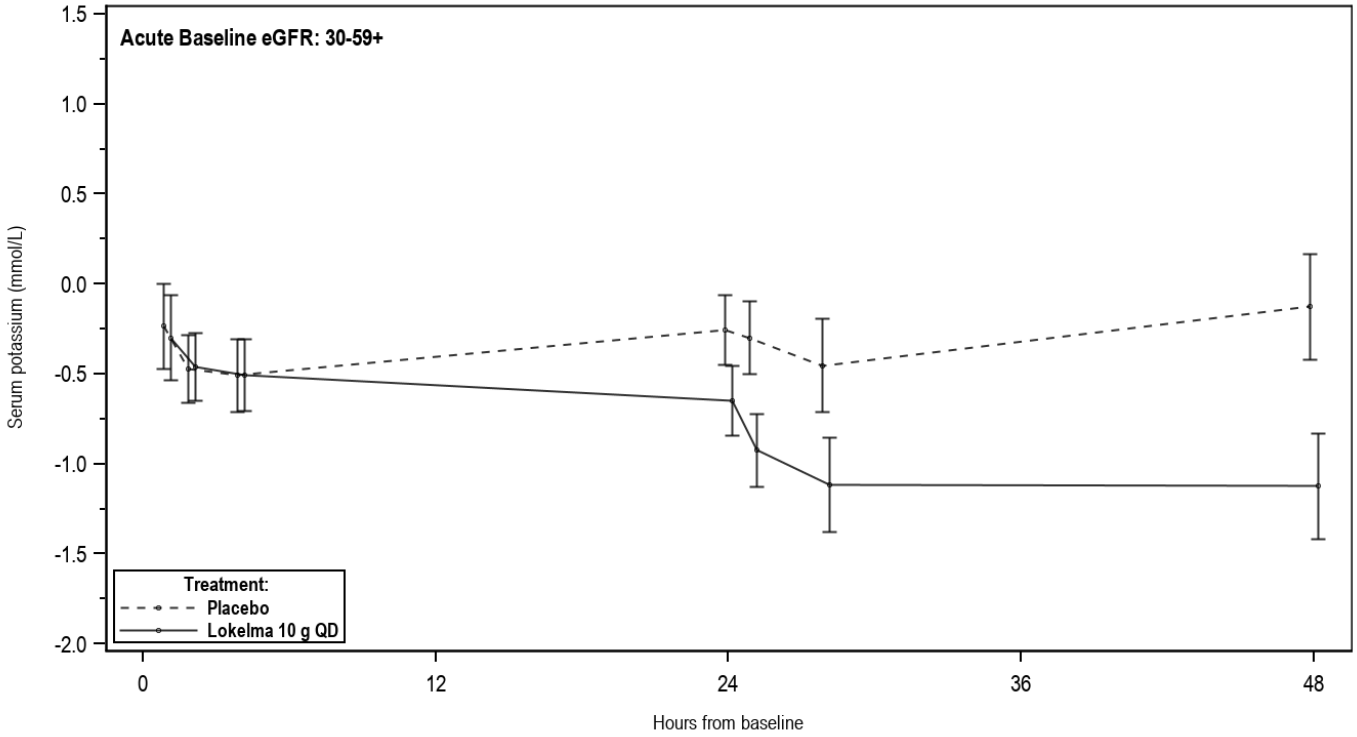
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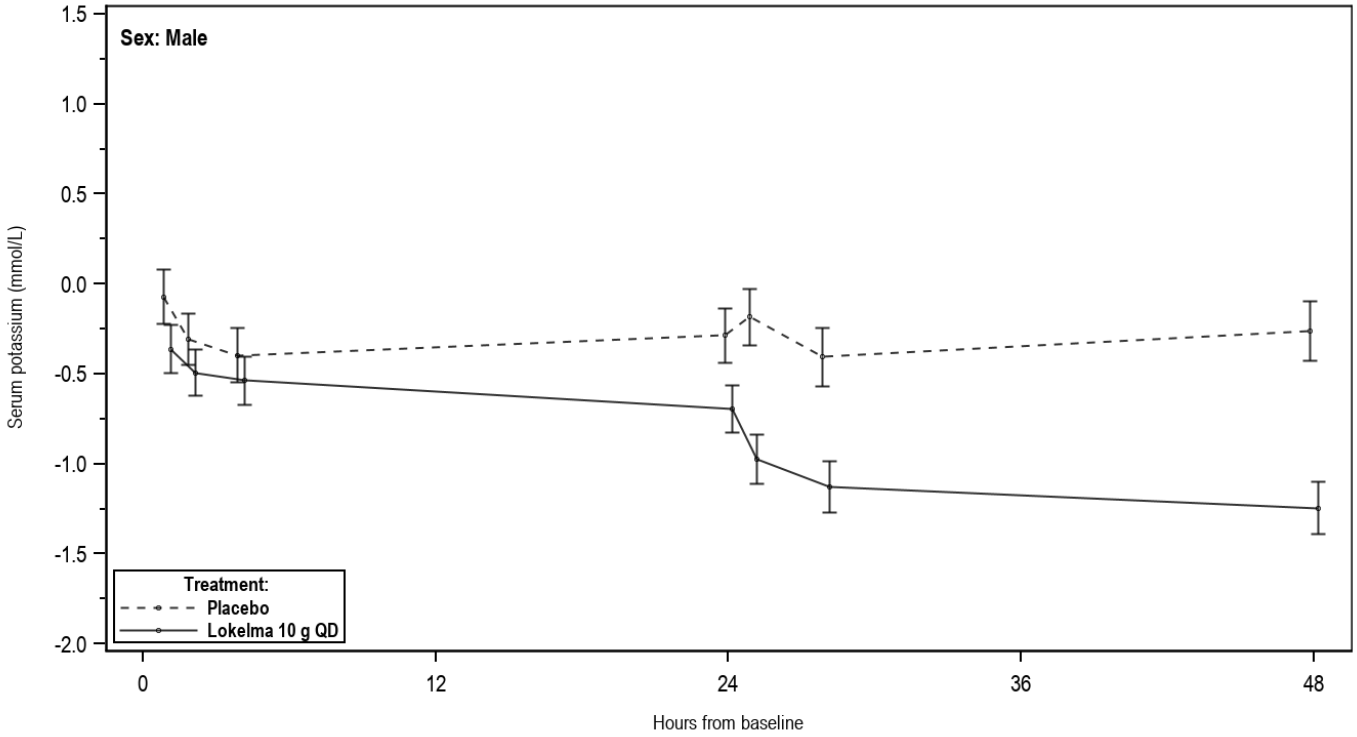
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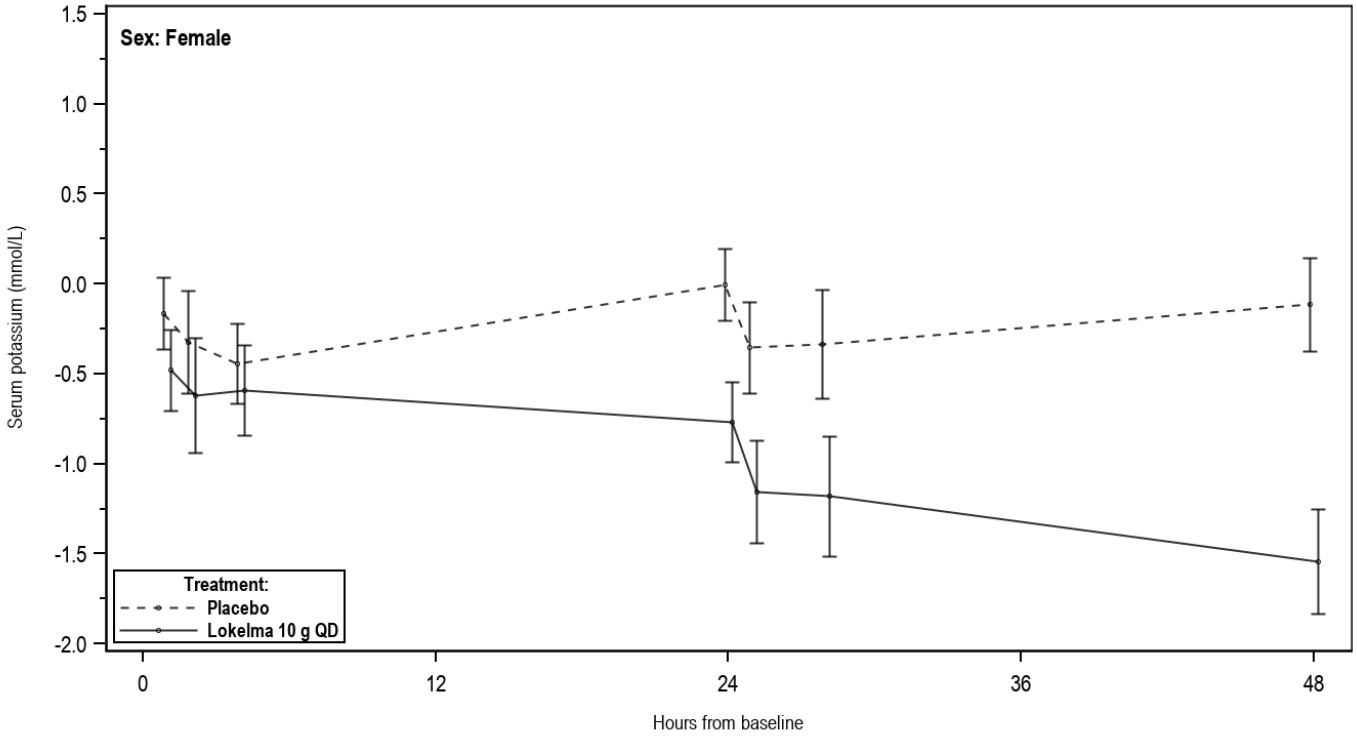
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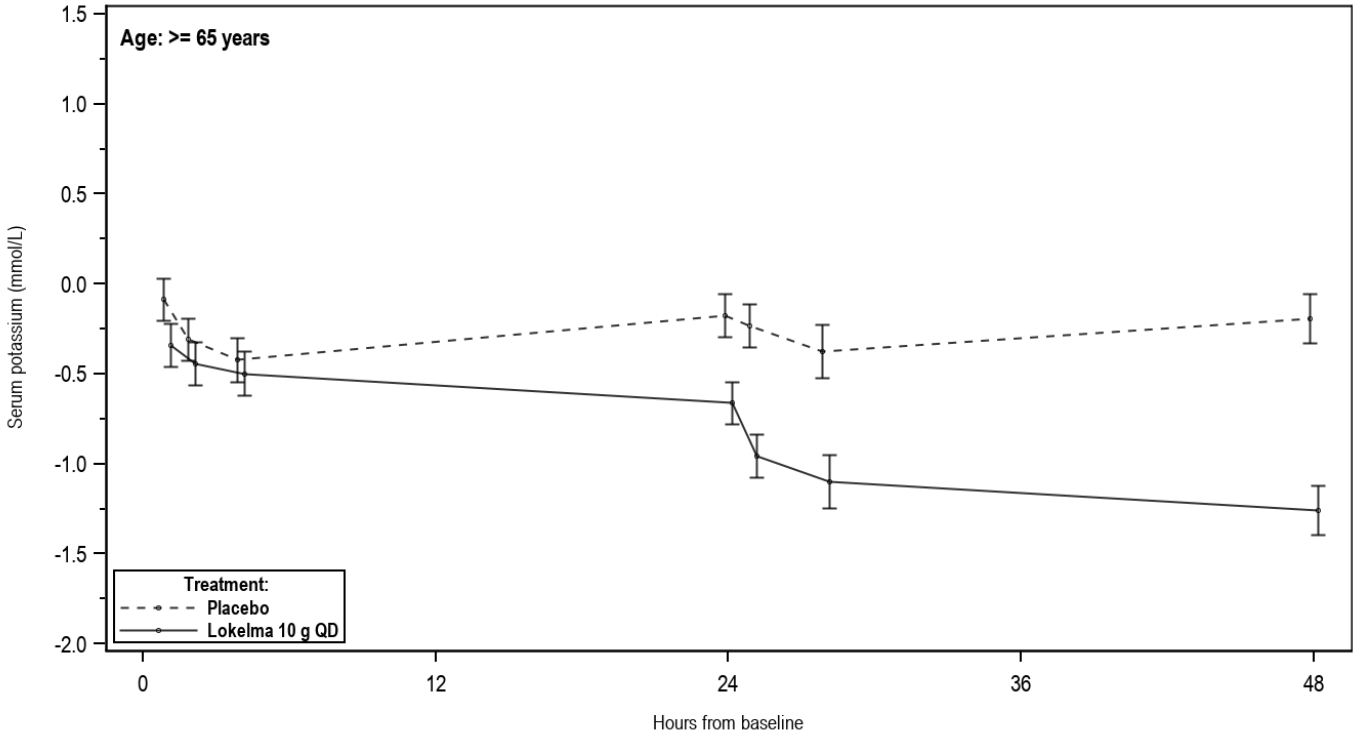
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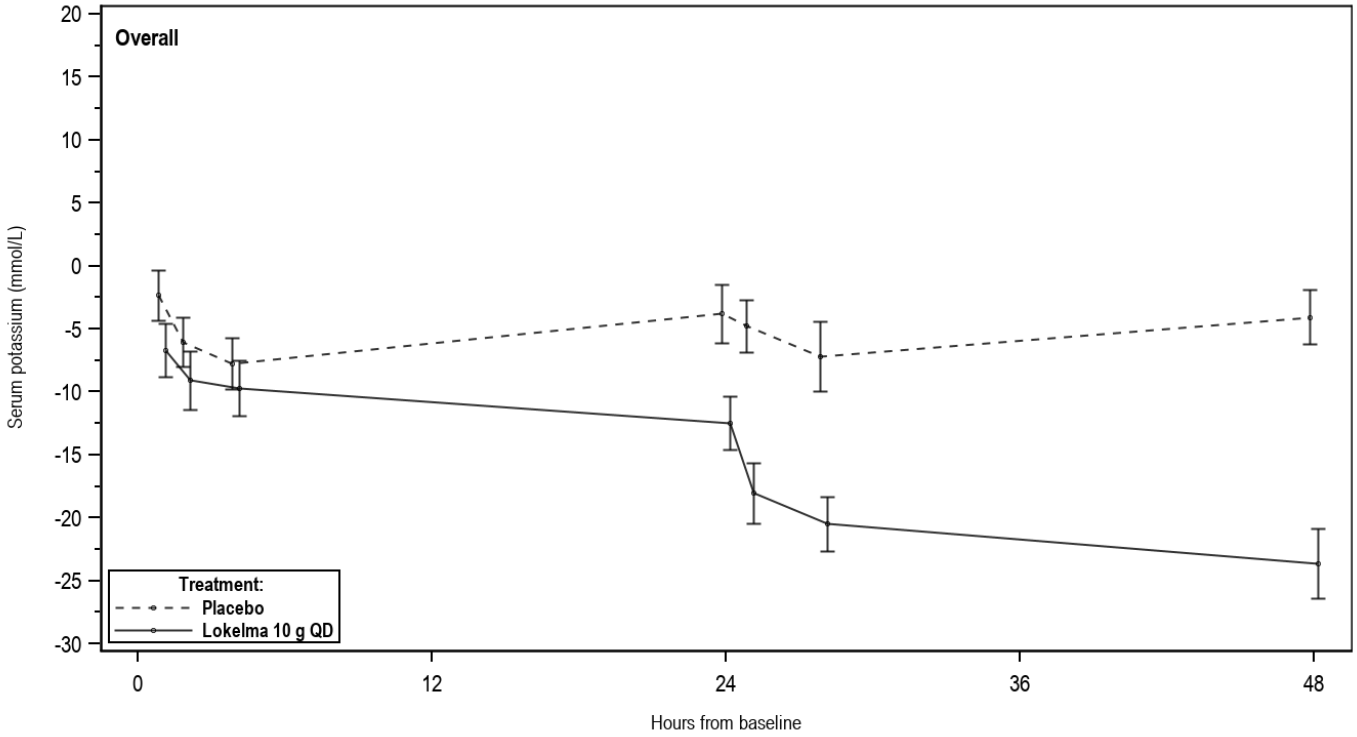
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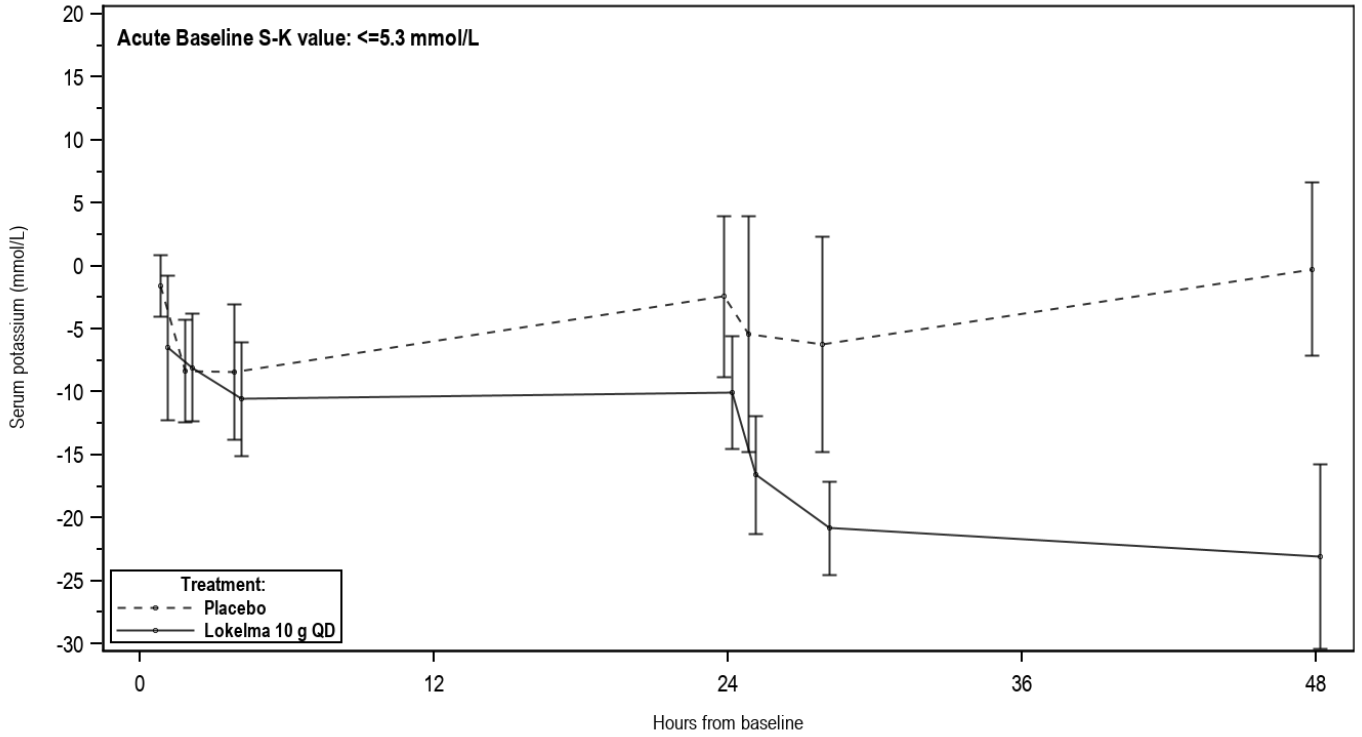
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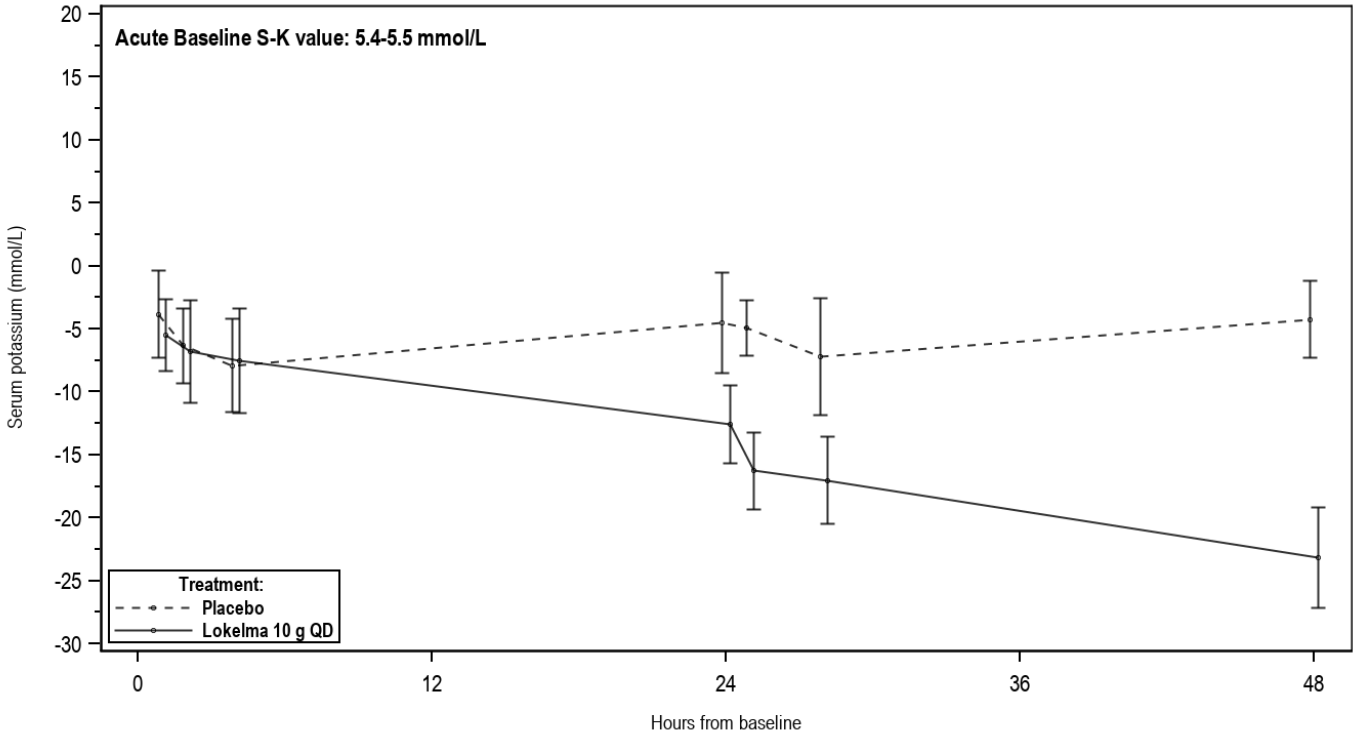
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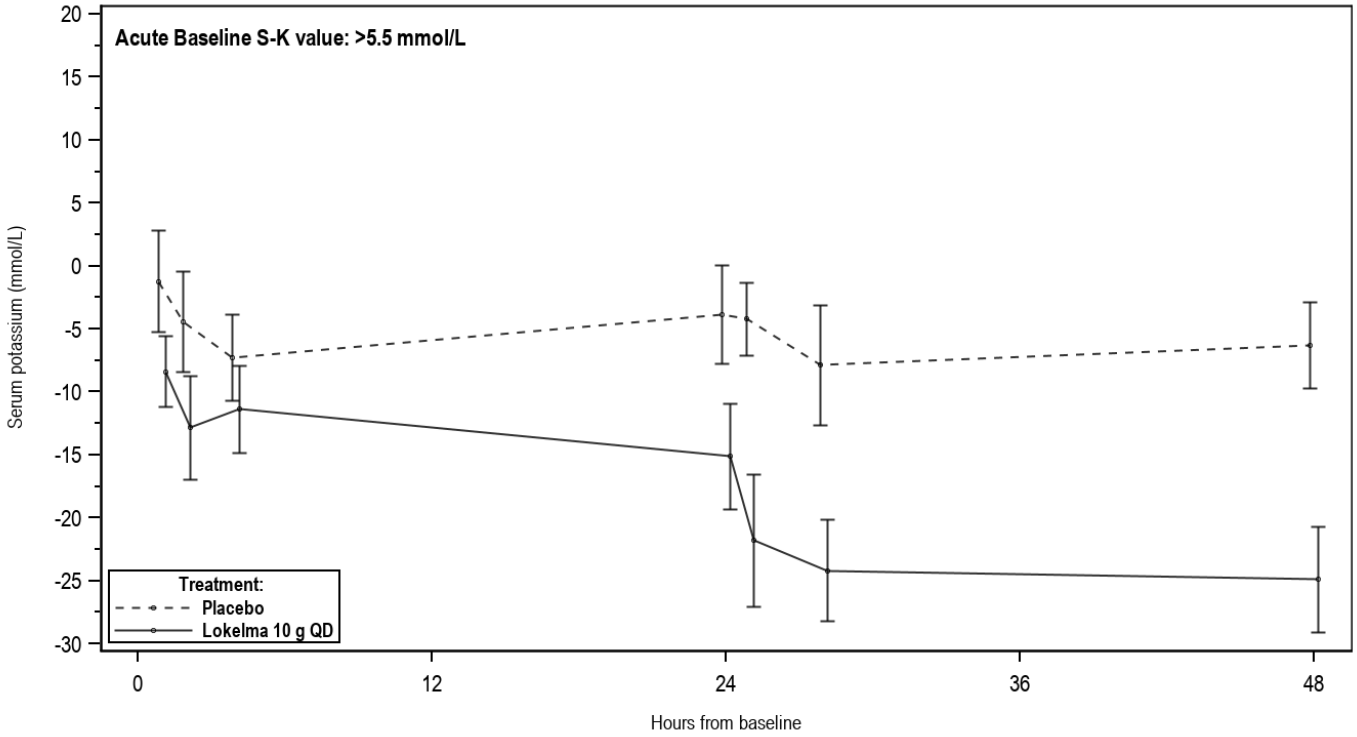
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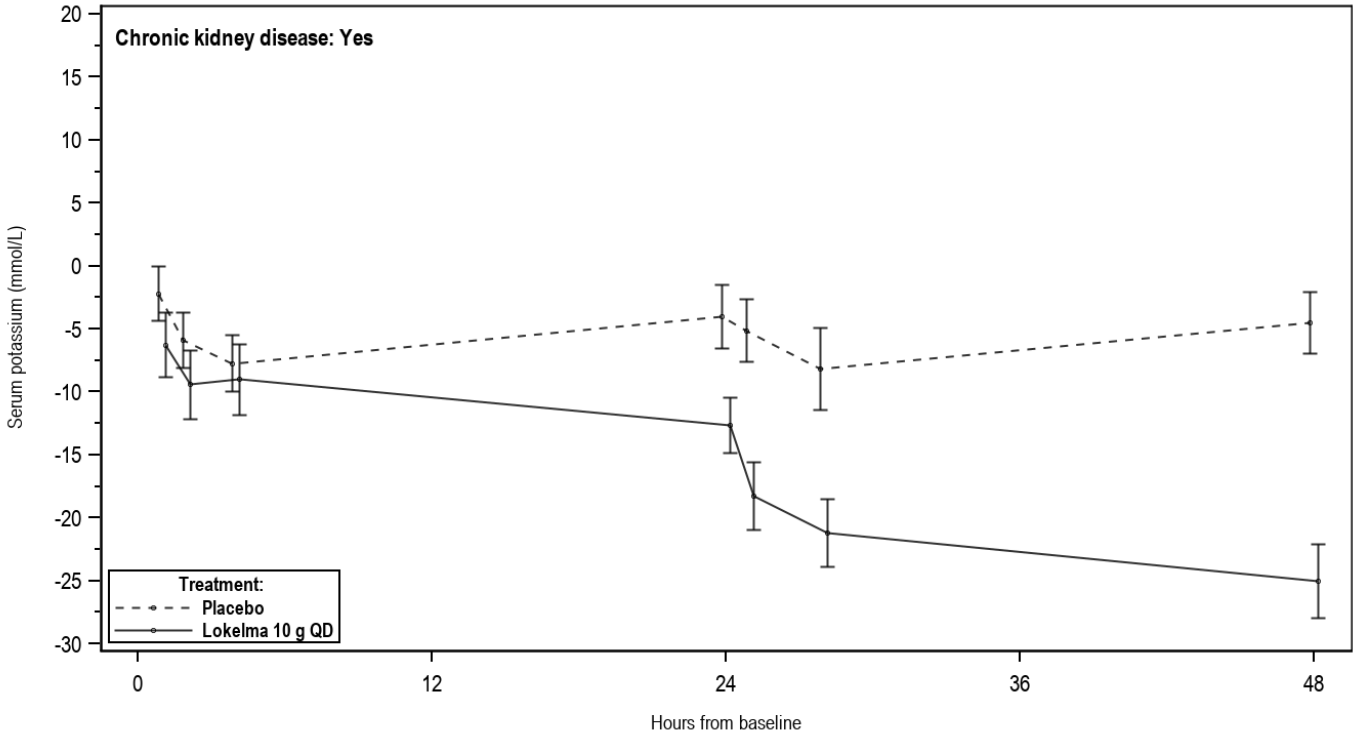
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.

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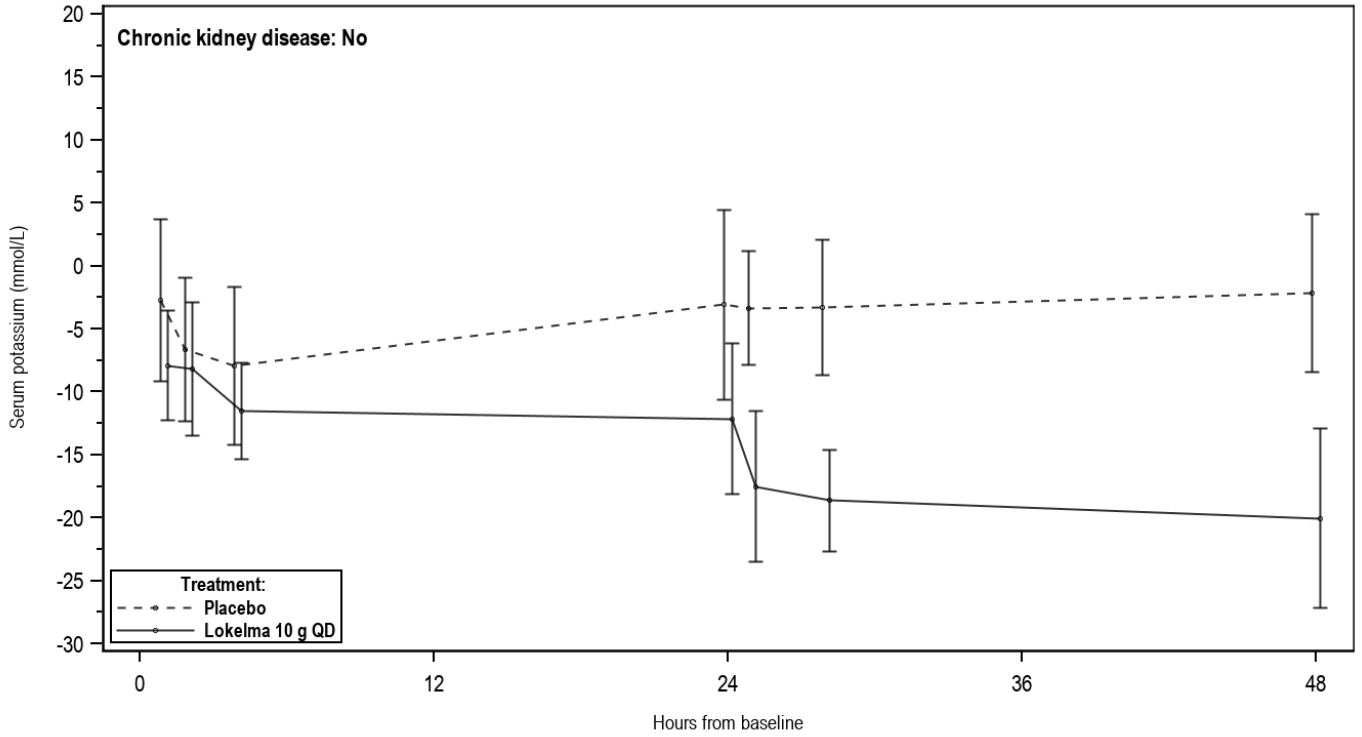
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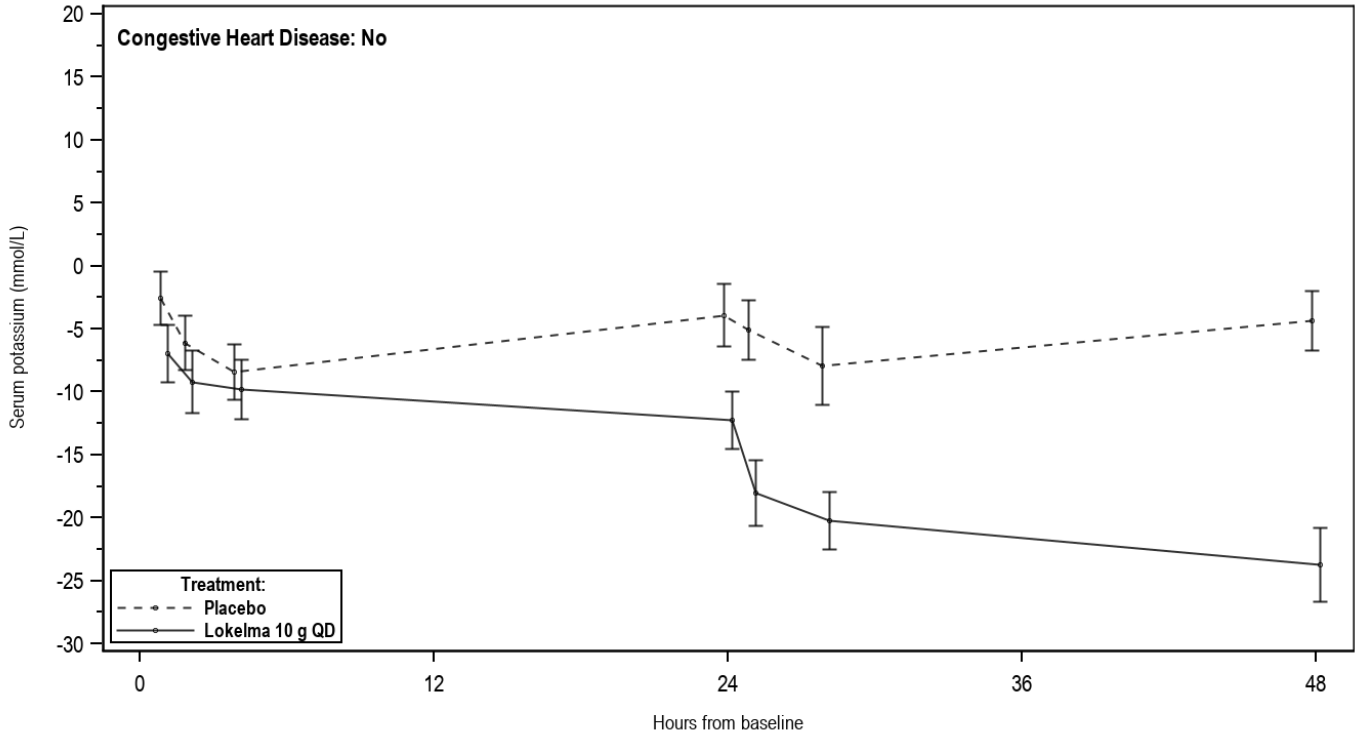
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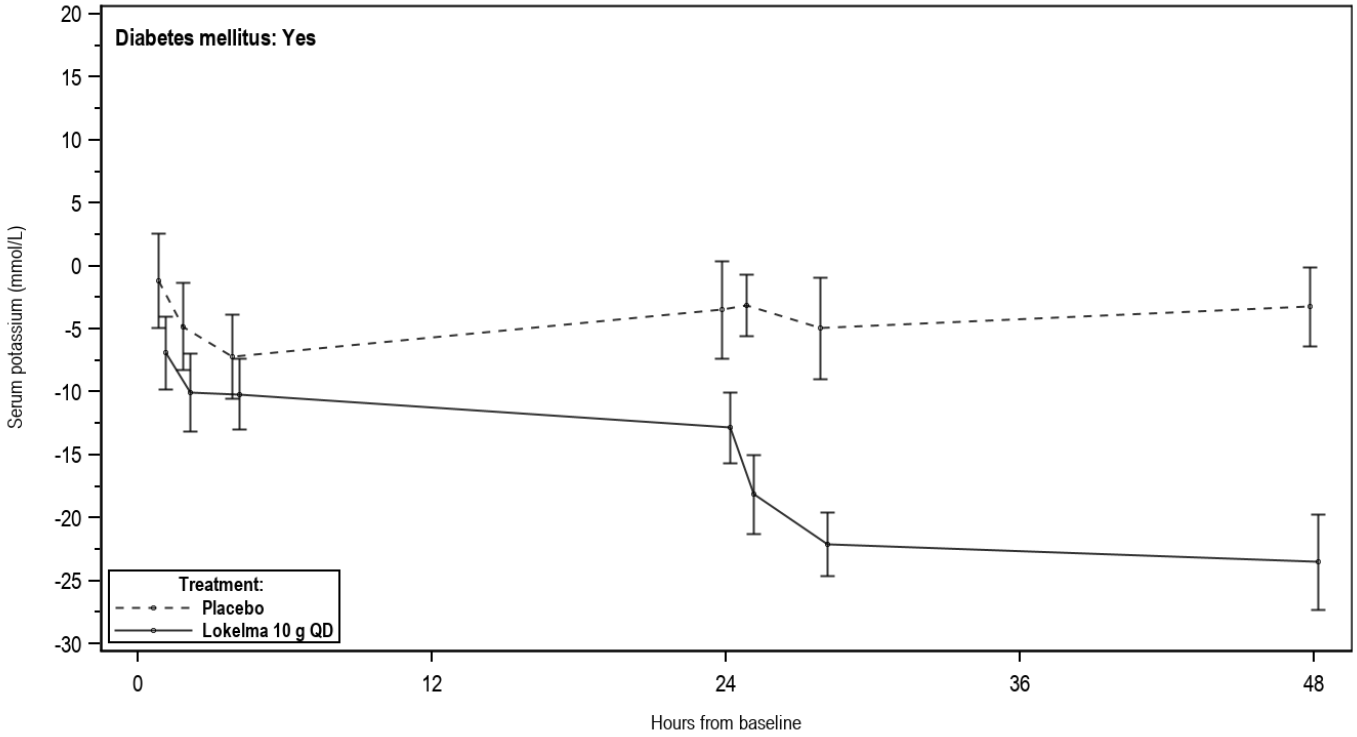
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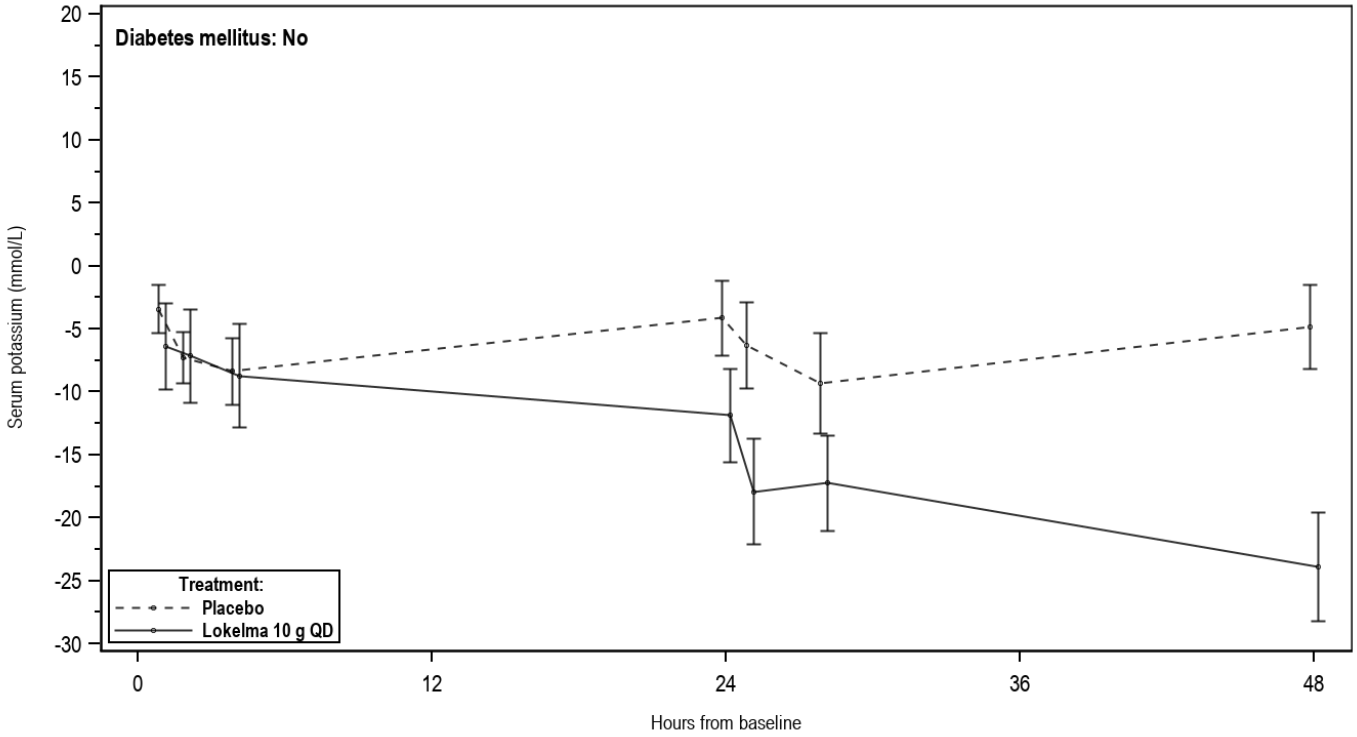
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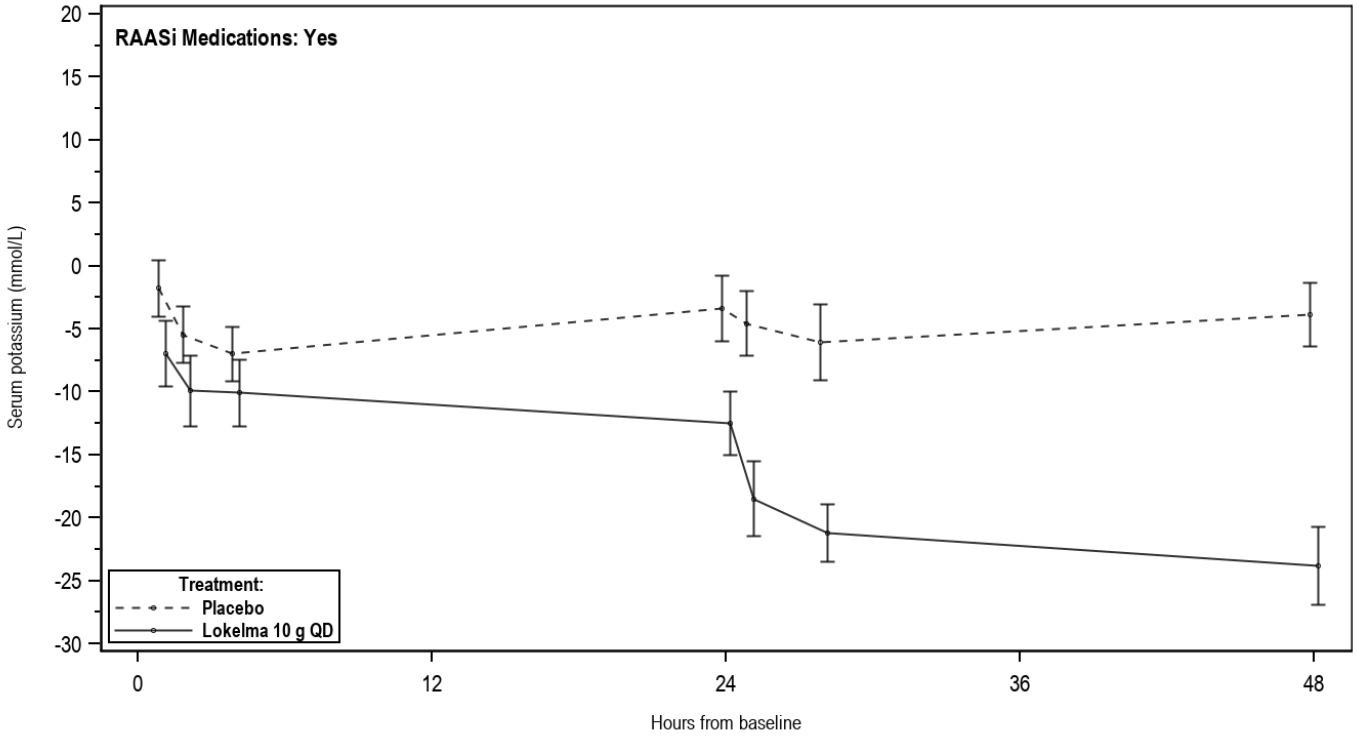
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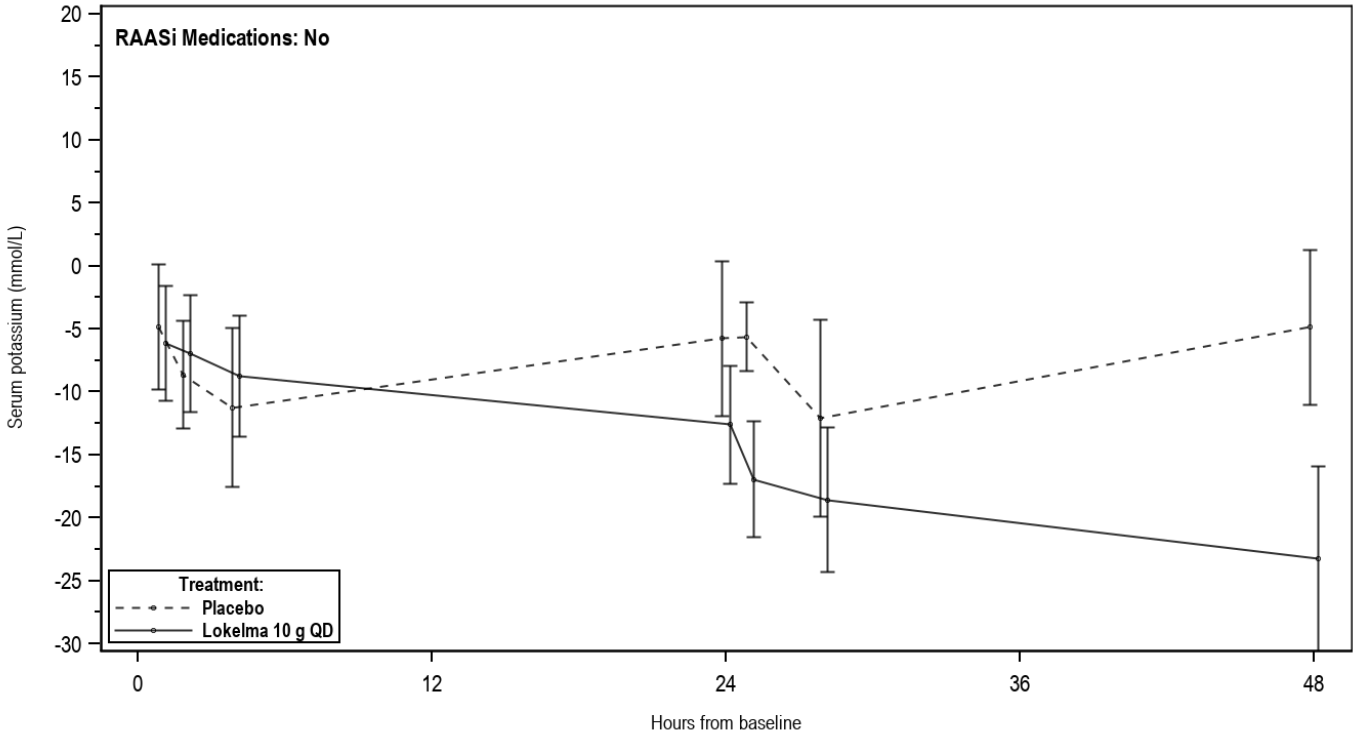
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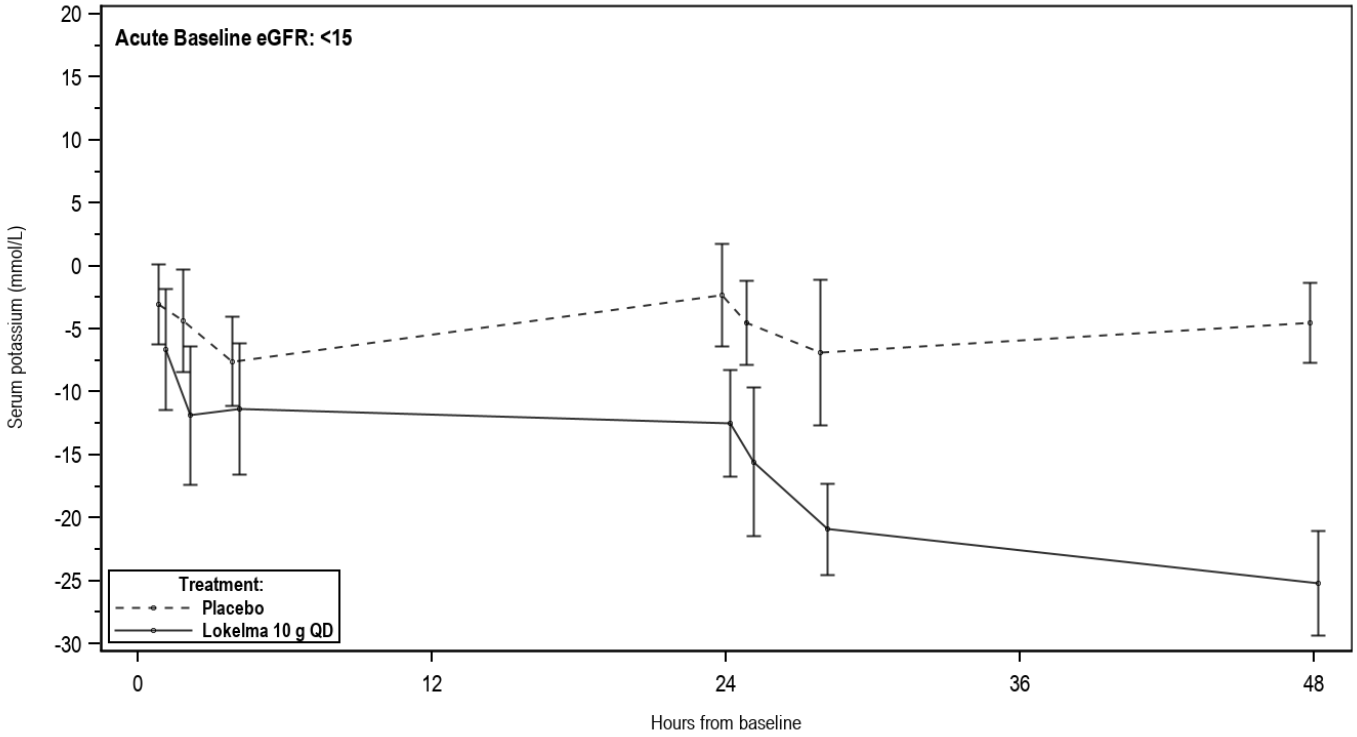
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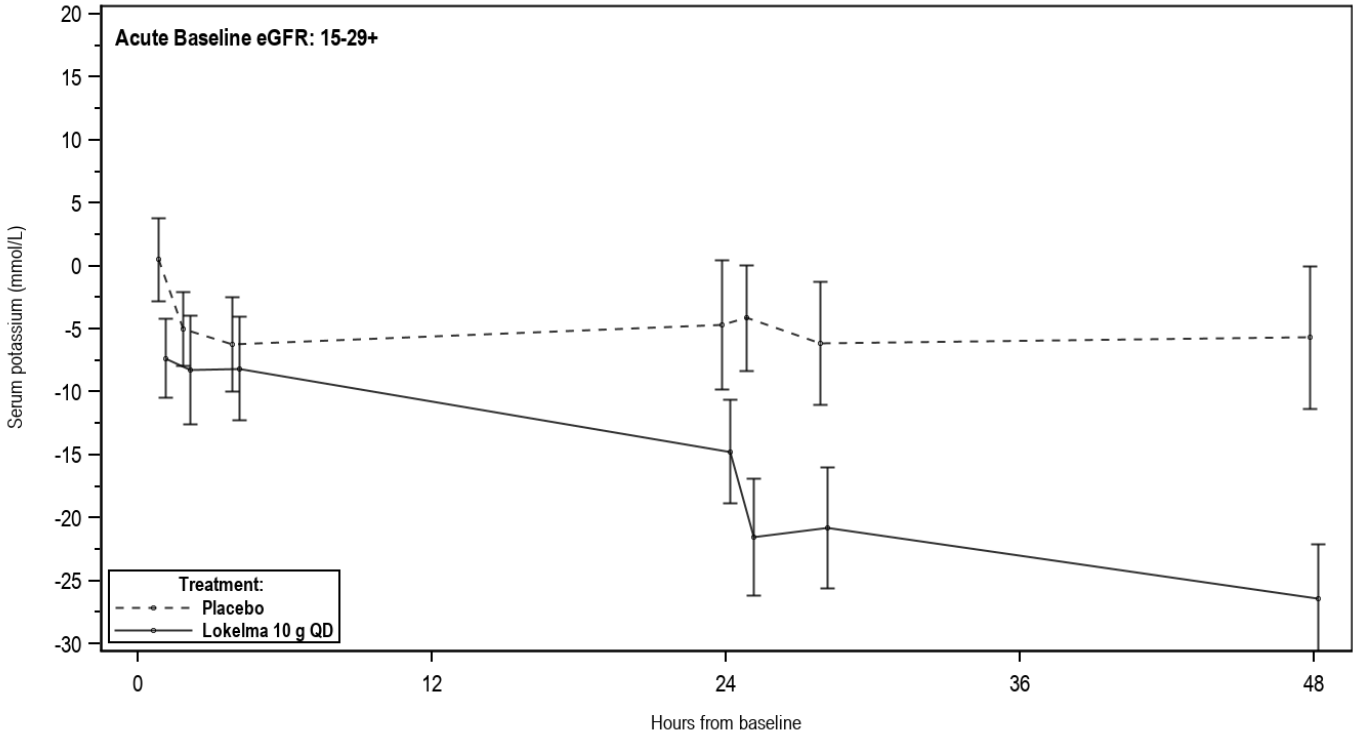
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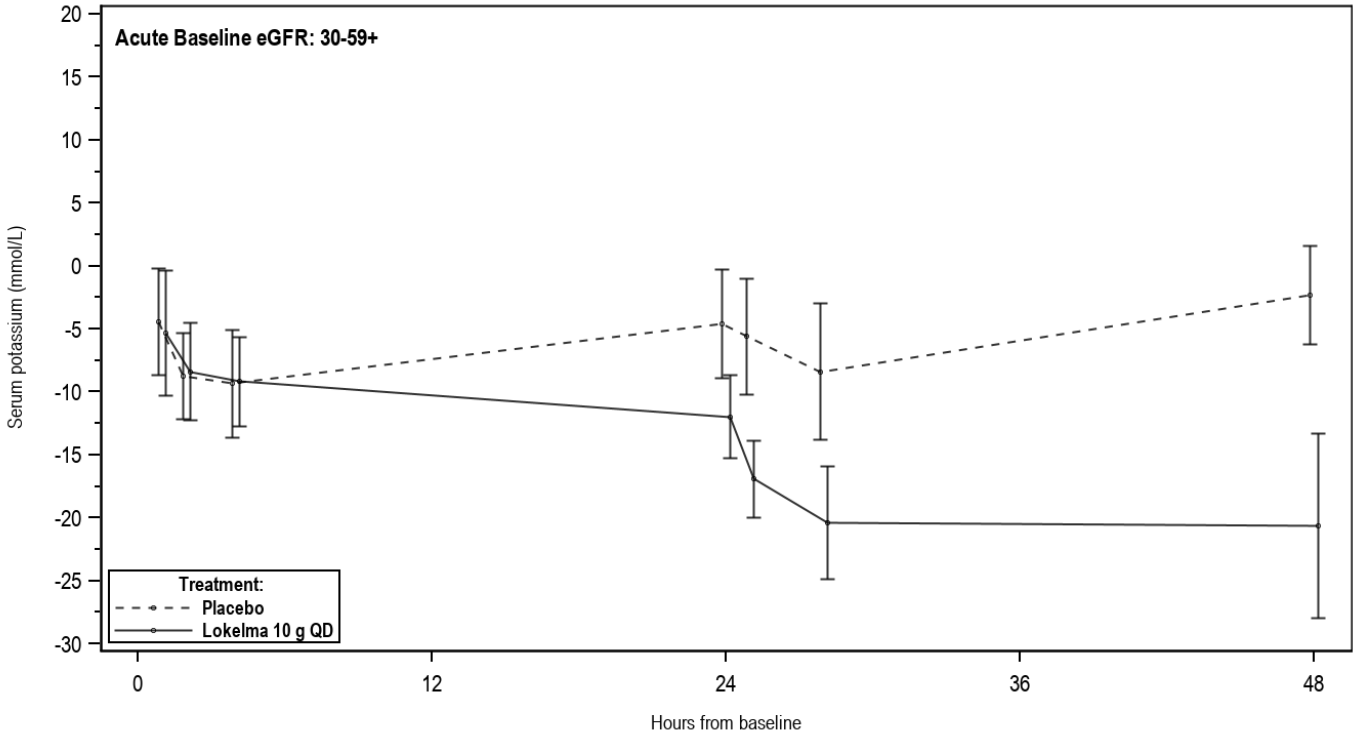
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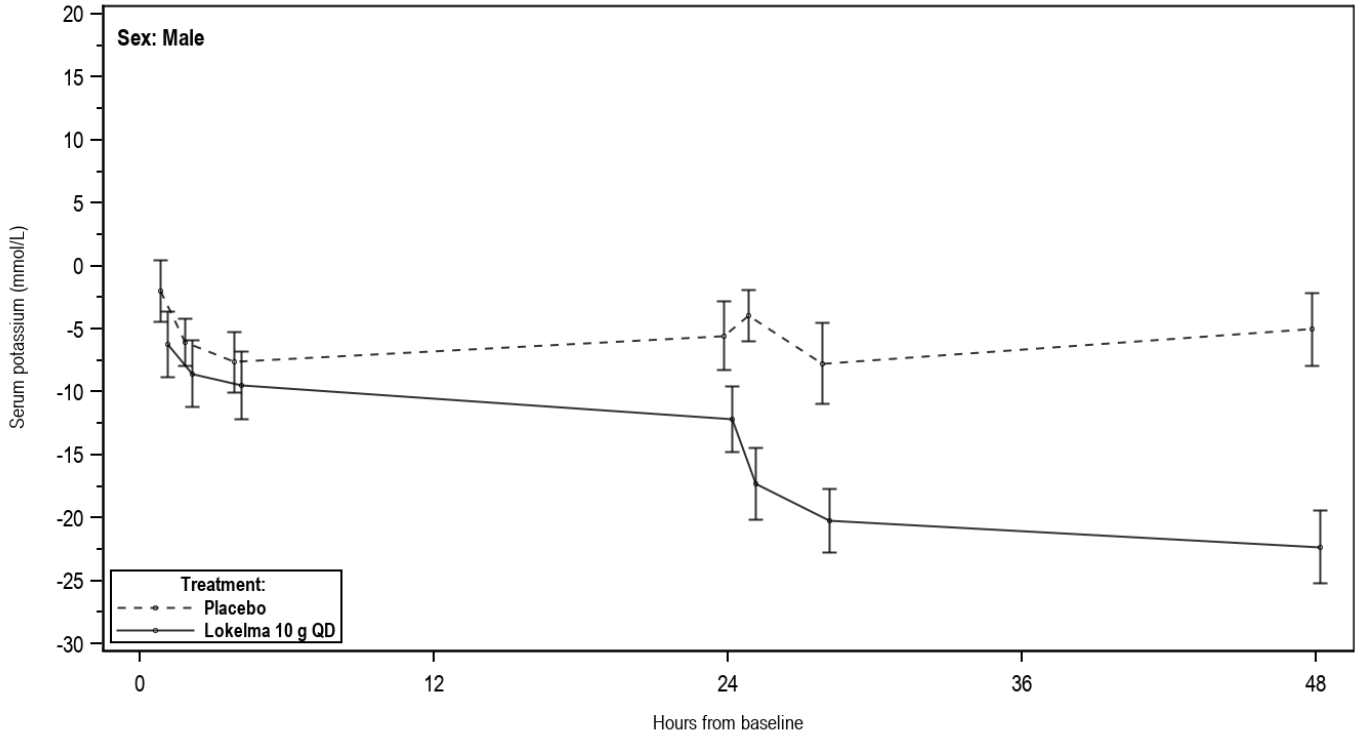
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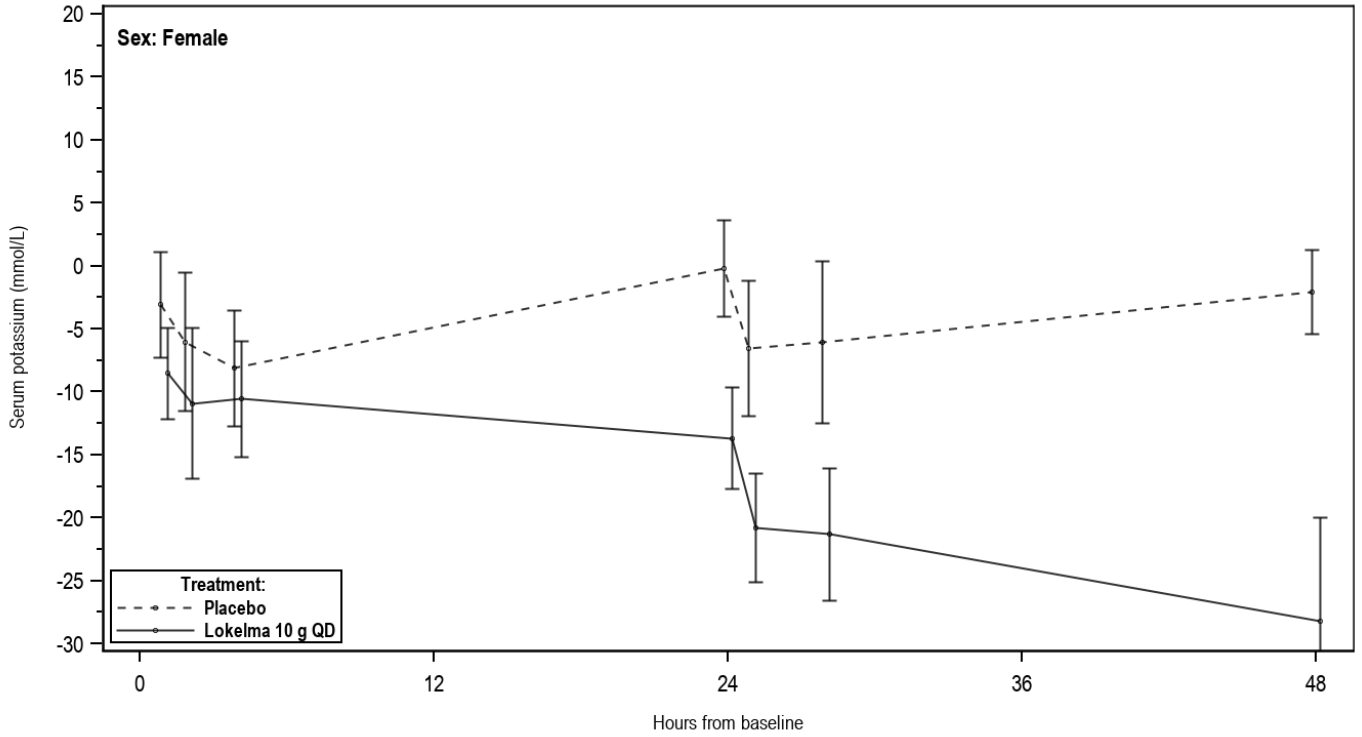
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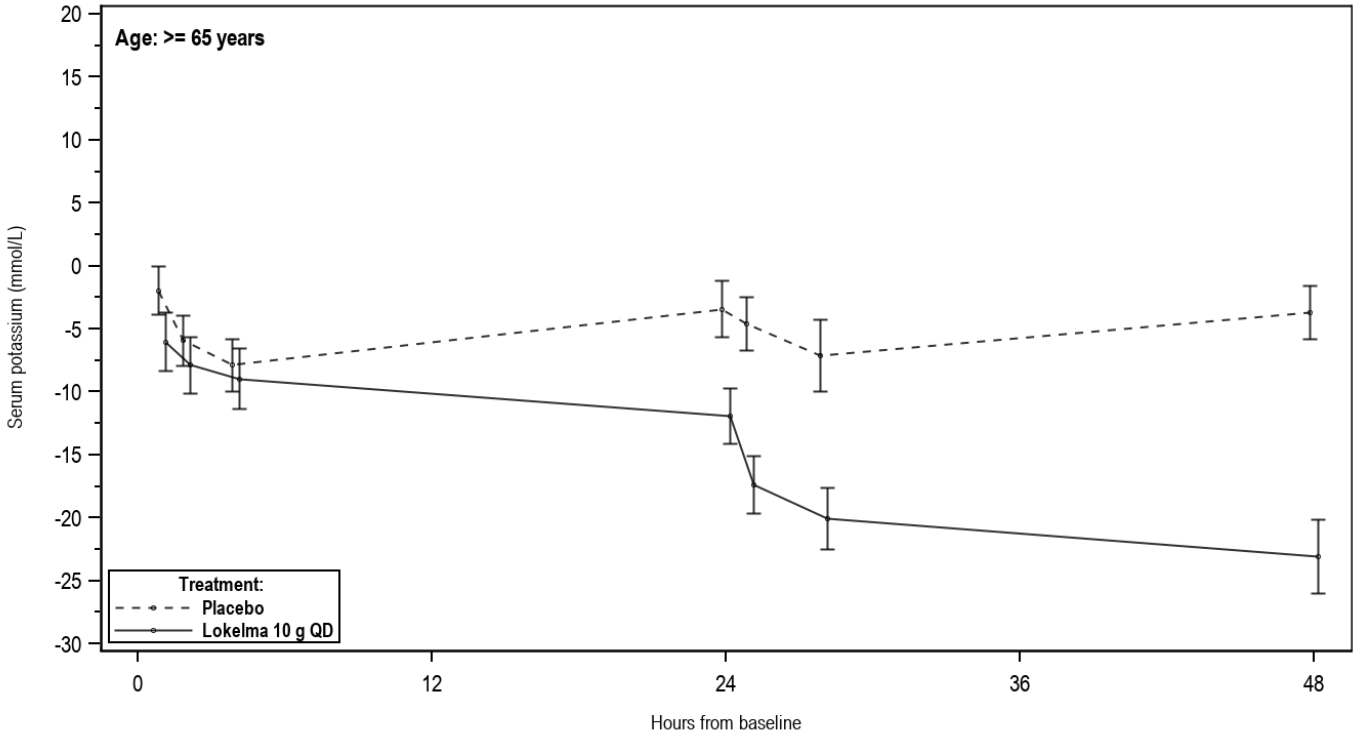
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Table 8.1.3.1 - Study ZS-002 Japan: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)					Lokelma 10g TID (N=36)							
Subgroup / Category	N	Patients with events [n(%)]	KM % at 24 hours	KM % at 48 hours	Median time (hours)	N	Patients with events [n(%)]	KM % at 24 hours	KM % at 48 hours	Median time (hours)	Hazard ratio (95% CI)	Hazard ratio p-value	p-value for interaction
Overall	33	22 (66.7%)	30.01	30.01	4.1	36	36 (100.0%)	13.89	0.00	2.9	2.30 (1.28, 4.12)	0.0051	
Baseline S-K													0.6119
<=5.3 mmol/L	6	5 (83.3%)	16.67	.	12.8	12	12 (100.0%)	25.00	0.00	3.8	4.64 (1.08, 19.95)	0.0391	
>5.3 - <=5.5 mmol/L	12	8 (66.7%)	33.33	33.33	3.9	12	12 (100.0%)	16.67	0.00	12.7	1.79 (0.72, 4.49)	0.2128	
>5.5 mmol/L	15	9 (60.0%)	32.82	.	5.7	12	12 (100.0%)	0.00	0.00	1.5	4.17 (1.41, 12.38)	0.0101	
Chronic kidney disease													0.9892
Yes	26	18 (69.2%)	28.09	28.09	4.0	26	26 (100.0%)	11.54	0.00	2.0	2.08 (1.07, 4.05)	0.0316	
No	7	4 (57.1%)	38.10	.	23.9	10	10 (100.0%)	20.00	0.00	3.8	2.30 (0.70, 7.60)	0.1722	
Congestive heart disease													-
Yes	4	2 (50.0%)	50.00	.	NR	3	3 (100.0%)	0.00	0.00	4.0	-	-	
No	29	20 (69.0%)	27.08	27.08	4.0	33	33 (100.0%)	15.15	0.00	2.0	-	-	
Diabetes mellitus													0.3140
Yes	16	9 (56.3%)	42.86	.	4.0	24	24 (100.0%)	12.50	0.00	1.5	2.90 (1.28, 6.59)	0.0110	
No	17	13 (76.5%)	18.82	18.82	5.7	12	12 (100.0%)	16.67	0.00	3.8	1.50 (0.64, 3.55)	0.3512	
RAASi medications													0.0320
Yes	27	16 (59.3%)	37.20	37.20	5.7	26	26 (100.0%)	15.38	0.00	1.8	3.13 (1.59, 6.17)	0.0010	
No	6	6 (100.0%)	0.00	0.00	1.9	10	10 (100.0%)	10.00	0.00	3.9	0.35 (0.10, 1.22)	0.0987	
Baseline eGFR													-
<15 ml/min/1.73m**2	11	7 (63.6%)	36.36	.	21.5	9	9 (100.0%)	0.00	0.00	1.2	-	-	
15- <30 ml/min/1.73m**2	11	7 (63.6%)	23.33	23.33	5.7	13	13 (100.0%)	15.38	0.00	3.8	-	-	
30- <60 ml/min/1.73m**2	11	8 (72.7%)	27.27	.	1.9	11	11 (100.0%)	18.18	0.00	1.9	-	-	
>=60 ml/min/1.73m**2	0	0 (.%)			NR	3	3 (100.0%)	33.33	0.00	3.8	-	-	
Sex													0.6313
Male	23	15 (65.2%)	29.96	29.96	4.0	28	28 (100.0%)	14.29	0.00	2.9	2.24 (1.13, 4.43)	0.0208	
Female	10	7 (70.0%)	30.00	.	3.1	8	8 (100.0%)	12.50	0.00	2.8	2.22 (0.72, 6.82)	0.1640	
Age (years)													-
<65 years	1	1 (100.0%)	0.00	0.00	1.0	5	5 (100.0%)	0.00	0.00	1.1	-	-	
>=65 years	32	21 (65.6%)	30.95	30.95	4.1	31	31 (100.0%)	16.13	0.00	3.8	-	-	

Hazard ratio derived from Cox proportional hazard model with the following effects:
Acute phase treatment group, acute phase baseline eGFR, acute phase baseline S-K, age group (<65, >=65 years) and binary indicators for RAASi use, chronic kidney disease, congestive heart disease and diabetes mellitus.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
NR: median not reached

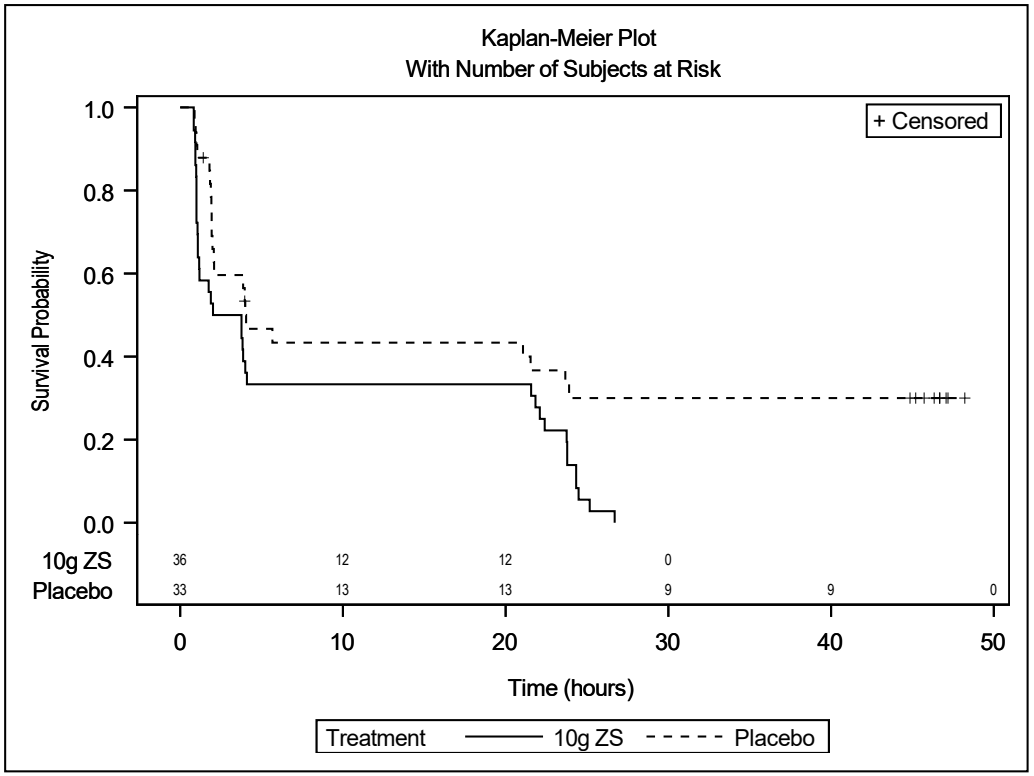
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Figure 8.1.3.2 - Study ZS-002 Japan: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Overall



Plots shown for subgroups where interaction p-value is <=0.05

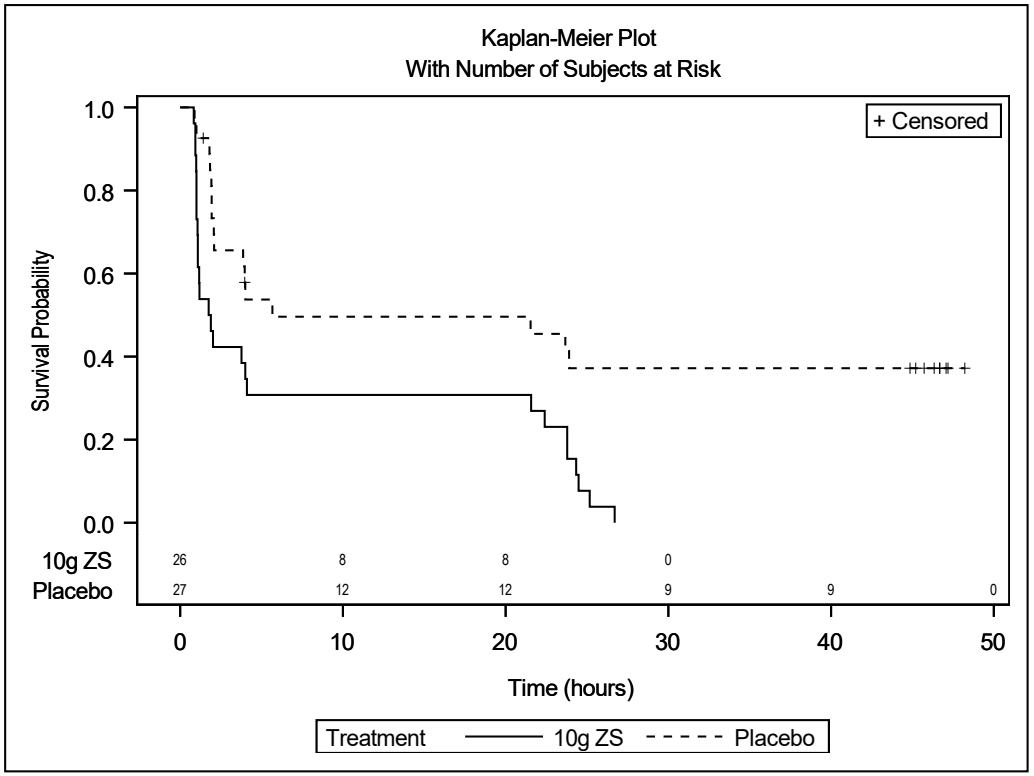
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Figure 8.1.3.2 - Study ZS-002 Japan: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

RAASi medications: Yes



Plots shown for subgroups where interaction p-value is <=0.05

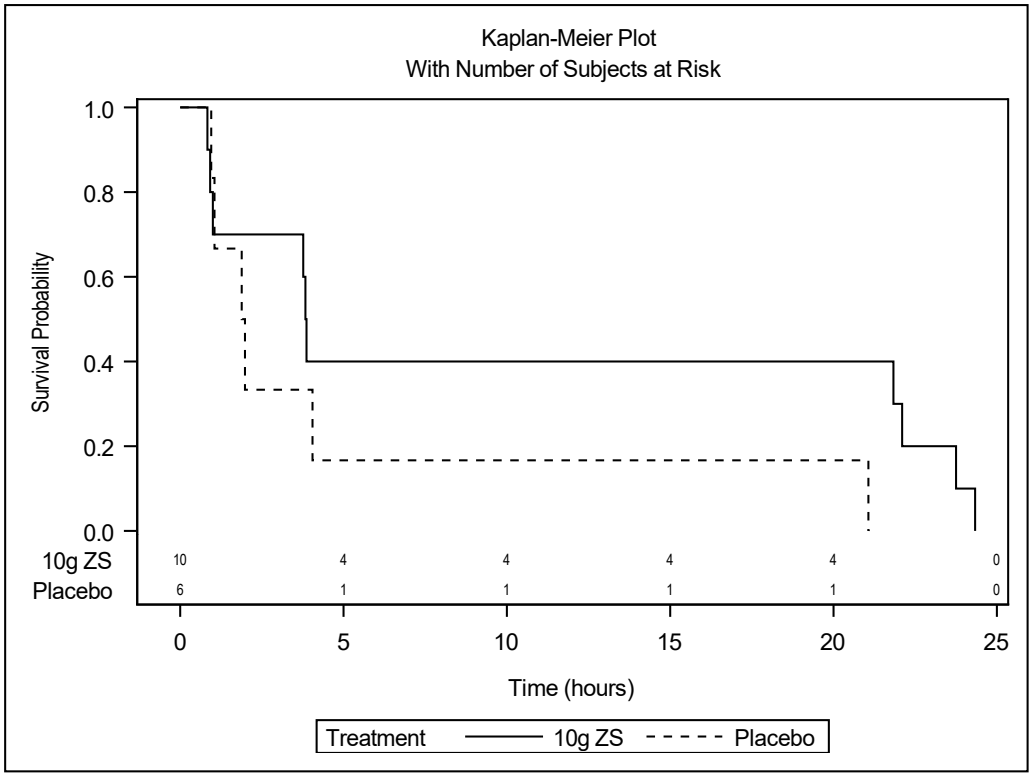
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RAASi medications: No



Plots shown for subgroups where interaction p-value is <=0.05

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Table 8.1.4.1 - Study ZS-002 Japan: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)					Lokelma 10g TID (N=36)							
Subgroup / Category	N	Patients with events [n(%)]	KM % at 24 hours	KM % at 48 hours	Median time (hours)	N	Patients with events [n(%)]	KM % at 24 hours	KM % at 48 hours	Median time (hours)	Hazard ratio (95% CI)	Hazard ratio p-value	p-value for interaction
Overall	33	19 (57.6%)	40.52	40.52	3.9	36	36 (100.0%)	5.56	0.00	1.8	2.06 (1.16, 3.66)	0.0134	
Baseline S-K													0.1675
<=5.3 mmol/L	6	6 (100.0%)	0.00	0.00	1.8	12	12 (100.0%)	0.00	0.00	1.0	1.66 (0.35, 7.80)	0.5221	
>5.3 - <=5.5 mmol/L	12	9 (75.0%)	25.00	25.00	2.0	12	12 (100.0%)	8.33	0.00	1.5	1.62 (0.67, 3.92)	0.2871	
>5.5 mmol/L	15	4 (26.7%)	71.08	.	NR	12	12 (100.0%)	8.33	0.00	4.1	5.01 (1.54, 16.31)	0.0075	
Chronic kidney disease													0.5128
Yes	26	14 (53.8%)	44.32	44.32	4.0	26	26 (100.0%)	3.85	0.00	1.9	2.14 (1.09, 4.20)	0.0268	
No	7	5 (71.4%)	28.57	.	1.9	10	10 (100.0%)	10.00	0.00	1.1	1.52 (0.51, 4.53)	0.4510	
Congestive heart disease													-
Yes	4	3 (75.0%)	25.00	.	1.5	3	3 (100.0%)	0.00	0.00	21.6	-	-	
No	29	16 (55.2%)	42.62	42.62	4.0	33	33 (100.0%)	6.06	0.00	1.1	-	-	
Diabetes mellitus													0.6449
Yes	16	10 (62.5%)	36.46	.	2.9	24	24 (100.0%)	8.33	0.00	2.0	1.99 (0.93, 4.26)	0.0753	
No	17	9 (52.9%)	44.34	44.34	4.1	12	12 (100.0%)	0.00	0.00	1.4	2.44 (1.00, 5.92)	0.0496	
RAASi medications													0.1107
Yes	27	14 (51.9%)	45.96	45.96	4.1	26	26 (100.0%)	7.69	0.00	2.1	2.53 (1.30, 4.93)	0.0064	
No	6	5 (83.3%)	16.67	.	1.9	10	10 (100.0%)	0.00	0.00	1.1	0.72 (0.21, 2.43)	0.5940	
Baseline eGFR													-
<15 ml/min/1.73m**2	11	6 (54.5%)	45.45	.	4.1	9	9 (100.0%)	0.00	0.00	1.8	-	-	
15- <30 ml/min/1.73m**2	11	4 (36.4%)	58.92	58.92	NR	13	13 (100.0%)	7.69	0.00	2.0	-	-	
30- <60 ml/min/1.73m**2	11	9 (81.8%)	18.18	.	1.9	11	11 (100.0%)	9.09	0.00	3.8	-	-	
>=60 ml/min/1.73m**2	0	0 (.%)			NR	3	3 (100.0%)	0.00	0.00	0.9	-	-	
Sex													0.1140
Male	23	13 (56.5%)	40.51	40.51	4.0	28	28 (100.0%)	7.14	0.00	2.1	1.89 (0.95, 3.76)	0.0680	
Female	10	6 (60.0%)	40.00	.	2.0	8	8 (100.0%)	0.00	0.00	1.0	6.39 (1.70, 24.07)	0.0061	
Age (years)													-
<65 years	1	1 (100.0%)	0.00	0.00	1.0	5	5 (100.0%)	0.00	0.00	21.2	-	-	
>=65 years	32	18 (56.3%)	41.79	41.79	3.9	31	31 (100.0%)	6.45	0.00	1.8	-	-	

Hazard ratio derived from Cox proportional hazard model with the following effects:
Acute phase treatment group, acute phase baseline eGFR, acute phase baseline S-K, age group (<65, >=65 years) and binary indicators for RAASi use, chronic kidney disease, congestive heart disease and diabetes mellitus.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
'.' in KM % columns denotes number at risk has reached zero before the timepoint
NR: median not reached

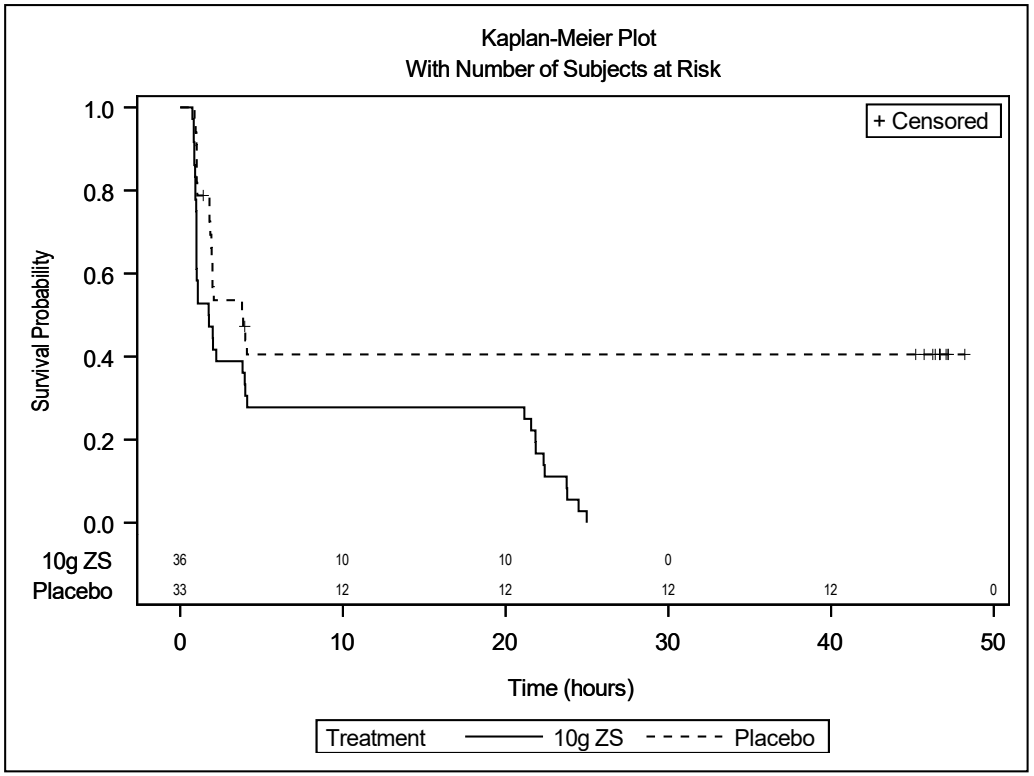
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Figure 8.1.4.2 - Study ZS-002 Japan: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Overall



Plots shown for subgroups where interaction p-value is <=0.05

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Table 8.1.5.1 - Study ZS-002 Japan: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)		Lokelma 10g QD (N=36)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Overall											
1 hour	33	7 (21.2%)	36	17 (47.2%)	2.43 (0.73, 8.09)	0.1490	1.48 (0.59, 3.72)	0.4036	11.7 (-36.7, 60.0)	0.6358	
2 hours	32	14 (43.8%)	36	21 (58.3%)	1.25 (0.39, 4.03)	0.7085	0.97 (0.48, 1.96)	0.9262	3.7 (-43.9, 51.2)	0.8798	
4 hours	32	14 (43.8%)	36	23 (63.9%)	1.74 (0.59, 5.16)	0.3175	1.18 (0.59, 2.34)	0.6399	10.3 (-33.0, 53.6)	0.6415	
24 hours	31	9 (29.0%)	36	30 (83.3%)	12.99 (3.59, 46.98)	<.0001	2.58 (1.21, 5.51)	0.0141	47.2 (3.4, 91.0)	0.0346	
25 hours	31	6 (19.4%)	36	35 (97.2%)	287.51 (15.34, >999.99)	0.0002	4.77 (1.99, 11.44)	0.0005	75.2 (35.9, 114.5)	0.0002	
28 hours	31	12 (38.7%)	36	35 (97.2%)	83.23 (6.65, >999.99)	0.0006	2.36 (1.21, 4.59)	0.0116	57.6 (16.2, 99.1)	0.0064	
48 hours	31	5 (16.1%)	36	33 (91.7%)	58.57 (11.98, 286.25)	<.0001	5.46 (2.11, 14.10)	0.0005	73.7 (34.9, 112.4)	0.0002	
Baseline S-K											
1 hour											0.8500
<=5.3 mmol/L	6	2 (33.3%)	12	10 (83.3%)	3.61 (0.22, 60.54)	0.3724	2.03 (0.34, 12.15)	0.4359	31.7 (-47.5, 110.8)	0.4332	
>5.3 - <=5.5 mmol/L	12	4 (33.3%)	12	6 (50.0%)	1.96 (0.37, 10.50)	0.4328	1.49 (0.42, 5.27)	0.5401	12.7 (-38.1, 63.5)	0.6234	
>5.5 mmol/L	15	1 (6.7%)	12	1 (8.3%)	1.08 (0.06, 20.04)	0.9594	1.08 (0.07, 17.49)	0.9595	NC	NC	
2 hours											0.6344
<=5.3 mmol/L	6	6 (100.0%)	12	11 (91.7%)	n/a	n/a	0.96 (0.27, 3.46)	0.9481	-4.5 (-125.9, 116.9)	0.9419	
>5.3 - <=5.5 mmol/L	12	6 (50.0%)	12	6 (50.0%)	0.91 (0.17, 4.87)	0.9088	0.99 (0.32, 3.09)	0.9918	-11.9 (-70.1, 46.3)	0.6890	
>5.5 mmol/L	14	2 (14.3%)	12	4 (33.3%)	2.96 (0.35, 24.89)	0.3172	2.10 (0.38, 11.57)	0.3924	13.7 (-77.7, 105.2)	0.7683	
4 hours											0.6305
<=5.3 mmol/L	6	4 (66.7%)	12	12 (100.0%)	n/a	n/a	1.42 (0.35, 5.71)	0.6241	26.2 (-83.3, 135.8)	0.6385	
>5.3 - <=5.5 mmol/L	12	7 (58.3%)	12	6 (50.0%)	0.71 (0.14, 3.58)	0.6804	0.86 (0.29, 2.55)	0.7804	-9.2 (-70.8, 52.4)	0.7700	
>5.5 mmol/L	14	3 (21.4%)	12	5 (41.7%)	2.34 (0.40, 13.66)	0.3465	1.76 (0.42, 7.41)	0.4409	18.2 (-44.5, 81.0)	0.5690	
24 hours											<.0001
<=5.3 mmol/L	6	3 (50.0%)	12	12 (100.0%)	n/a	n/a	1.77 (0.39, 8.06)	0.4605	33.6 (-58.7, 125.8)	0.4755	
>5.3 - <=5.5 mmol/L	12	6 (50.0%)	12	10 (83.3%)	5.97 (0.81, 44.23)	0.0805	1.74 (0.63, 4.83)	0.2887	42.1 (-32.1, 116.4)	0.2662	
>5.5 mmol/L	13	0 (0.0%)	12	8 (66.7%)	n/a	n/a	n/a	n/a	NC	NC	
25 hours											0.0857
<=5.3 mmol/L	6	4 (66.7%)	12	12 (100.0%)	n/a	n/a	1.42 (0.35, 5.71)	0.6241	26.2 (-83.3, 135.8)	0.6385	
>5.3 - <=5.5 mmol/L	12	1 (8.3%)	12	12 (100.0%)	n/a	n/a	12.14 (1.57, 93.72)	0.0166	92.2 (7.5, 176.8)	0.0328	
>5.5 mmol/L	13	1 (7.7%)	12	11 (91.7%)	131.36 (7.17, >999.99)	0.0010	11.80 (1.52, 91.81)	0.0184	83.5 (3.3, 163.7)	0.0412	
28 hours											0.1947
<=5.3 mmol/L	6	4 (66.7%)	12	12 (100.0%)	n/a	n/a	1.42 (0.35, 5.71)	0.6241	26.2 (-83.3, 135.8)	0.6385	
>5.3 - <=5.5 mmol/L	12	7 (58.3%)	12	12 (100.0%)	n/a	n/a	1.79 (0.70, 4.60)	0.2244	48.5 (-20.2, 117.1)	0.1663	
>5.5 mmol/L	13	1 (7.7%)	12	11 (91.7%)	137.34 (7.11, >999.99)	0.0011	11.97 (1.54, 93.09)	0.0177	82.9 (14.4, 151.4)	0.0176	
48 hours											<.0001
<=5.3 mmol/L	6	3 (50.0%)	12	10 (83.3%)	1.10 (0.06, 19.00)	0.9501	1.24 (0.25, 6.18)	0.7936	14.1 (-68.8, 97.0)	0.7392	
>5.3 - <=5.5 mmol/L	12	2 (16.7%)	12	12 (100.0%)	n/a	n/a	6.02 (1.34, 26.98)	0.0190	84.5 (23.3, 145.7)	0.0068	
>5.5 mmol/L	13	0 (0.0%)	12	11 (91.7%)	n/a	n/a	n/a	n/a	NC	NC	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline S-K.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 8.1.5.1 - Study ZS-002 Japan: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)		Lokelma 10g QD (N=36)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Chronic kidney disease											
1 hour											0.4702
Yes	26	4 (15.4%)	26	11 (42.3%)	2.88 (0.69, 12.11)	0.1486	1.84 (0.56, 6.00)	0.3127	13.7 (-42.0, 69.4)	0.6303	
No	7	3 (42.9%)	10	6 (60.0%)	1.81 (0.15, 21.58)	0.6370	1.04 (0.24, 4.54)	0.9562	7.2 (-119.5, 133.8)	0.9118	
2 hours											0.3760
Yes	25	9 (36.0%)	26	15 (57.7%)	1.76 (0.49, 6.31)	0.3835	1.20 (0.51, 2.81)	0.6777	9.1 (-45.7, 63.8)	0.7447	
No	7	5 (71.4%)	10	6 (60.0%)	0.09 (<0.01, 7.90)	0.2960	0.58 (0.16, 2.13)	0.4157	-9.9 (-130.5, 110.6)	0.8720	
4 hours											0.9698
Yes	25	11 (44.0%)	26	17 (65.4%)	1.74 (0.51, 5.89)	0.3749	1.22 (0.56, 2.66)	0.6214	13.9 (-35.0, 62.8)	0.5781	
No	7	3 (42.9%)	10	6 (60.0%)	1.81 (0.15, 21.58)	0.6370	1.04 (0.24, 4.54)	0.9562	7.2 (-119.5, 133.8)	0.9118	
24 hours											0.9053
Yes	25	7 (28.0%)	26	22 (84.6%)	16.70 (3.09, 90.24)	0.0011	2.51 (1.05, 5.99)	0.0383	38.7 (-15.8, 93.2)	0.1643	
No	6	2 (33.3%)	10	8 (80.0%)	9.55 (0.84, 108.00)	0.0683	2.43 (0.52, 11.43)	0.2622	51.0 (-24.7, 126.7)	0.1869	
25 hours											0.7955
Yes	25	5 (20.0%)	26	25 (96.2%)	241.78 (8.63, >999.99)	0.0012	4.25 (1.60, 11.33)	0.0038	57.6 (1.6, 113.5)	0.0438	
No	6	1 (16.7%)	10	10 (100.0%)	n/a	n/a	6.03 (0.77, 47.14)	0.0869	96.2 (10.3, 182.1)	0.0281	
28 hours											0.7164
Yes	25	10 (40.0%)	26	25 (96.2%)	42.29 (3.77, 473.95)	0.0024	2.09 (0.99, 4.45)	0.0547	48.4 (-0.3, 97.1)	0.0514	
No	6	2 (33.3%)	10	10 (100.0%)	n/a	n/a	3.01 (0.66, 13.77)	0.1549	70.3 (-11.2, 151.7)	0.0908	
48 hours											0.9990
Yes	25	4 (16.0%)	26	24 (92.3%)	55.91 (9.17, 340.95)	<.0001	5.45 (1.85, 16.09)	0.0021	73.4 (27.2, 119.7)	0.0019	
No	6	1 (16.7%)	10	9 (90.0%)	80.41 (2.16, >999.99)	0.0175	5.46 (0.69, 43.09)	0.1074	85.8 (4.2, 167.4)	0.0394	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline S-K.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 8.1.5.1 - Study ZS-002 Japan: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)		Lokelma 10g QD (N=36)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Congestive heart disease											
1 hour											-
Yes	4	2 (50.0%)	3	0 (0.0%)	-	-	-	-	-	-	
No	29	5 (17.2%)	33	17 (51.5%)	-	-	-	-	-	-	
2 hours											-
Yes	4	2 (50.0%)	3	0 (0.0%)	-	-	-	-	-	-	
No	28	12 (42.9%)	33	21 (63.6%)	-	-	-	-	-	-	
4 hours											-
Yes	4	1 (25.0%)	3	1 (33.3%)	-	-	-	-	-	-	
No	28	13 (46.4%)	33	22 (66.7%)	-	-	-	-	-	-	
24 hours											-
Yes	4	1 (25.0%)	3	2 (66.7%)	-	-	-	-	-	-	
No	27	8 (29.6%)	33	28 (84.8%)	-	-	-	-	-	-	
25 hours											-
Yes	4	1 (25.0%)	3	3 (100.0%)	-	-	-	-	-	-	
No	27	5 (18.5%)	33	32 (97.0%)	-	-	-	-	-	-	
28 hours											-
Yes	4	2 (50.0%)	3	3 (100.0%)	-	-	-	-	-	-	
No	27	10 (37.0%)	33	32 (97.0%)	-	-	-	-	-	-	
48 hours											-
Yes	4	1 (25.0%)	3	2 (66.7%)	-	-	-	-	-	-	
No	27	4 (14.8%)	33	31 (93.9%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline S-K.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 8.1.5.1 - Study ZS-002 Japan: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)		Lokelma 10g QD (N=36)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Diabetes mellitus											
1 hour											0.6417
Yes	16	4 (25.0%)	24	11 (45.8%)	1.98 (0.42, 9.26)	0.3868	1.32 (0.39, 4.45)	0.6504	11.1 (-51.0, 73.3)	0.7254	
No	17	3 (17.6%)	12	6 (50.0%)	3.95 (0.47, 33.12)	0.2056	1.71 (0.42, 7.02)	0.4545	14.1 (-62.9, 91.1)	0.7195	
2 hours											0.7677
Yes	16	7 (43.8%)	24	13 (54.2%)	1.21 (0.29, 5.12)	0.7957	0.97 (0.37, 2.56)	0.9546	4.9 (-54.6, 64.5)	0.8707	
No	16	7 (43.8%)	12	8 (66.7%)	1.59 (0.16, 15.50)	0.6908	1.02 (0.36, 2.86)	0.9707	0.6 (-77.4, 78.7)	0.9874	
4 hours											0.4869
Yes	16	6 (37.5%)	24	16 (66.7%)	3.19 (0.79, 12.94)	0.1039	1.60 (0.61, 4.17)	0.3364	26.7 (-18.6, 72.0)	0.2485	
No	16	8 (50.0%)	12	7 (58.3%)	0.53 (0.07, 3.79)	0.5271	0.81 (0.29, 2.26)	0.6833	-13.0 (-95.2, 69.2)	0.7562	
24 hours											0.6720
Yes	15	5 (33.3%)	24	19 (79.2%)	8.34 (1.81, 38.50)	0.0066	2.30 (0.86, 6.20)	0.0984	48.7 (1.4, 96.0)	0.0434	
No	16	4 (25.0%)	12	11 (91.7%)	44.48 (2.12, 931.36)	0.0145	2.76 (0.86, 8.86)	0.0884	44.4 (-40.1, 128.9)	0.3030	
25 hours											0.1717
Yes	15	1 (6.7%)	24	23 (95.8%)	338.22 (18.29, >999.99)	<.0001	14.34 (1.94, 106.27)	0.0091	89.2 (47.0, 131.5)	<.0001	
No	16	5 (31.3%)	12	12 (100.0%)	n/a	n/a	2.42 (0.83, 7.03)	0.1037	44.4 (-35.6, 124.4)	0.2771	
28 hours											0.8790
Yes	15	6 (40.0%)	24	24 (100.0%)	n/a	n/a	2.49 (1.02, 6.09)	0.0462	62.6 (10.0, 115.2)	0.0197	
No	16	6 (37.5%)	12	11 (91.7%)	15.67 (1.13, 217.69)	0.0404	1.84 (0.66, 5.07)	0.2414	31.5 (-43.1, 106.1)	0.4079	
48 hours											0.6848
Yes	15	2 (13.3%)	24	22 (91.7%)	73.12 (8.94, 598.39)	<.0001	6.85 (1.61, 29.16)	0.0092	79.7 (35.0, 124.4)	0.0005	
No	16	3 (18.8%)	12	11 (91.7%)	44.45 (3.07, 644.49)	0.0054	3.84 (1.04, 14.22)	0.0436	52.6 (-51.7, 156.9)	0.3227	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline S-K.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 8.1.5.1 - Study ZS-002 Japan: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)		Lokelma 10g QD (N=36)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
RAASi medications											
1 hour											0.6527
Yes	27	5 (18.5%)	26	11 (42.3%)	2.98 (0.72, 12.35)	0.1318	1.67 (0.56, 4.98)	0.3549	13.0 (-41.3, 67.3)	0.6389	
No	6	2 (33.3%)	10	6 (60.0%)	1.20 (0.10, 14.20)	0.8855	1.04 (0.18, 5.90)	0.9682	2.1 (-148.5, 152.6)	0.9784	
2 hours											0.6783
Yes	26	10 (38.5%)	26	13 (50.0%)	1.39 (0.39, 4.95)	0.6116	1.06 (0.45, 2.46)	0.8986	5.9 (-47.2, 59.0)	0.8271	
No	6	4 (66.7%)	10	8 (80.0%)	<0.01 (<0.01, >999.99)	0.9448	0.69 (0.18, 2.57)	0.5758	-15.8 (-135.6, 104.0)	0.7960	
4 hours											0.4082
Yes	26	10 (38.5%)	26	16 (61.5%)	2.45 (0.71, 8.42)	0.1539	1.40 (0.63, 3.13)	0.4107	17.5 (-31.2, 66.3)	0.4802	
No	6	4 (66.7%)	10	7 (70.0%)	0.20 (<0.01, 4.96)	0.3228	0.66 (0.17, 2.54)	0.5508	-25.0 (-169.5, 119.4)	0.7340	
24 hours											0.3404
Yes	25	6 (24.0%)	26	21 (80.8%)	15.98 (3.65, 69.86)	0.0002	3.20 (1.29, 7.97)	0.0124	52.6 (1.8, 103.3)	0.0422	
No	6	3 (50.0%)	10	9 (90.0%)	3.64 (0.19, 68.28)	0.3876	1.29 (0.31, 5.31)	0.7263	15.8 (-87.6, 119.3)	0.7643	
25 hours											0.9092
Yes	25	5 (20.0%)	26	25 (96.2%)	183.19 (10.65, >999.99)	0.0003	4.69 (1.79, 12.29)	0.0017	75.4 (28.7, 122.2)	0.0016	
No	6	1 (16.7%)	10	10 (100.0%)	n/a	n/a	4.67 (0.53, 40.94)	0.1637	58.4 (-51.8, 168.5)	0.2989	
28 hours											0.1928
Yes	25	8 (32.0%)	26	26 (100.0%)	n/a	n/a	3.04 (1.37, 6.73)	0.0063	68.6 (18.1, 119.1)	0.0077	
No	6	4 (66.7%)	10	9 (90.0%)	1.43 (0.06, 36.22)	0.8301	1.01 (0.28, 3.66)	0.9824	-1.7 (-116.1, 112.6)	0.9761	
48 hours											0.9048
Yes	25	4 (16.0%)	26	24 (92.3%)	75.95 (10.63, 542.44)	<.0001	5.65 (1.96, 16.34)	0.0014	75.6 (29.2, 122.1)	0.0014	
No	6	1 (16.7%)	10	9 (90.0%)	28.55 (1.32, 616.53)	0.0325	4.38 (0.49, 39.52)	0.1880	52.5 (-55.1, 160.1)	0.3386	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline S-K.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 8.1.5.1 - Study ZS-002 Japan: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)		Lokelma 10g QD (N=36)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Baseline eGFR											
1 hour											-
<15 ml/min/1.73m**2	11	2 (18.2%)	9	4 (44.4%)	-	-	-	-	-	-	
15- <30 ml/min/1.73m**2	11	1 (9.1%)	13	5 (38.5%)	-	-	-	-	-	-	
30- <60 ml/min/1.73m**2	11	4 (36.4%)	11	5 (45.5%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	0	0 (0.0%)	3	3 (100.0%)	-	-	-	-	-	-	
2 hours											-
<15 ml/min/1.73m**2	11	3 (27.3%)	9	6 (66.7%)	-	-	-	-	-	-	
15- <30 ml/min/1.73m**2	10	3 (30.0%)	13	7 (53.8%)	-	-	-	-	-	-	
30- <60 ml/min/1.73m**2	11	8 (72.7%)	11	5 (45.5%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	0	0 (0.0%)	3	3 (100.0%)	-	-	-	-	-	-	
4 hours											-
<15 ml/min/1.73m**2	11	5 (45.5%)	9	7 (77.8%)	-	-	-	-	-	-	
15- <30 ml/min/1.73m**2	10	3 (30.0%)	13	6 (46.2%)	-	-	-	-	-	-	
30- <60 ml/min/1.73m**2	11	6 (54.5%)	11	7 (63.6%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	0	0 (0.0%)	3	3 (100.0%)	-	-	-	-	-	-	
24 hours											-
<15 ml/min/1.73m**2	11	3 (27.3%)	9	8 (88.9%)	-	-	-	-	-	-	
15- <30 ml/min/1.73m**2	9	2 (22.2%)	13	11 (84.6%)	-	-	-	-	-	-	
30- <60 ml/min/1.73m**2	11	4 (36.4%)	11	8 (72.7%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	0	0 (0.0%)	3	3 (100.0%)	-	-	-	-	-	-	
25 hours											-
<15 ml/min/1.73m**2	11	2 (18.2%)	9	8 (88.9%)	-	-	-	-	-	-	
15- <30 ml/min/1.73m**2	9	2 (22.2%)	13	13 (100.0%)	-	-	-	-	-	-	
30- <60 ml/min/1.73m**2	11	2 (18.2%)	11	11 (100.0%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	0	0 (0.0%)	3	3 (100.0%)	-	-	-	-	-	-	
28 hours											-
<15 ml/min/1.73m**2	11	4 (36.4%)	9	9 (100.0%)	-	-	-	-	-	-	
15- <30 ml/min/1.73m**2	9	2 (22.2%)	13	12 (92.3%)	-	-	-	-	-	-	
30- <60 ml/min/1.73m**2	11	6 (54.5%)	11	11 (100.0%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	0	0 (0.0%)	3	3 (100.0%)	-	-	-	-	-	-	
48 hours											-
<15 ml/min/1.73m**2	11	3 (27.3%)	9	9 (100.0%)	-	-	-	-	-	-	
15- <30 ml/min/1.73m**2	9	1 (11.1%)	13	12 (92.3%)	-	-	-	-	-	-	
30- <60 ml/min/1.73m**2	11	1 (9.1%)	11	9 (81.8%)	-	-	-	-	-	-	
>=60 ml/min/1.73m**2	0	0 (0.0%)	3	3 (100.0%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline S-K.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 8.1.5.1 - Study ZS-002 Japan: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)		Lokelma 10g QD (N=36)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Sex											
1 hour											0.3888
Male	23	5 (21.7%)	28	11 (39.3%)	1.09 (0.22, 5.34)	0.9183	0.92 (0.29, 2.93)	0.8814	4.7 (-60.6, 70.0)	0.8881	
Female	10	2 (20.0%)	8	6 (75.0%)	12.12 (1.04, 141.37)	0.0465	3.22 (0.63, 16.35)	0.1591	39.1 (-43.0, 121.2)	0.3506	
2 hours											0.8003
Male	22	9 (40.9%)	28	15 (53.6%)	0.92 (0.21, 4.05)	0.9135	0.84 (0.35, 2.05)	0.7024	1.5 (-60.8, 63.8)	0.9633	
Female	10	5 (50.0%)	8	6 (75.0%)	2.35 (0.24, 22.89)	0.4614	1.26 (0.37, 4.21)	0.7126	18.7 (-59.9, 97.4)	0.6402	
4 hours											0.3582
Male	22	11 (50.0%)	28	17 (60.7%)	1.09 (0.31, 3.86)	0.8940	0.98 (0.44, 2.15)	0.9549	3.5 (-47.2, 54.2)	0.8933	
Female	10	3 (30.0%)	8	6 (75.0%)	8.97 (0.59, 136.34)	0.1139	2.03 (0.49, 8.31)	0.3268	29.3 (-54.9, 113.6)	0.4948	
24 hours											0.1712
Male	21	8 (38.1%)	28	22 (78.6%)	5.92 (1.51, 23.16)	0.0106	1.85 (0.81, 4.22)	0.1437	38.2 (-7.6, 84.1)	0.1024	
Female	10	1 (10.0%)	8	8 (100.0%)	n/a	n/a	9.22 (1.13, 75.47)	0.0384	73.3 (-49.0, 195.6)	0.2399	
25 hours											0.4281
Male	21	3 (14.3%)	28	27 (96.4%)	252.43 (13.83, >999.99)	0.0002	6.53 (1.97, 21.68)	0.0022	70.8 (16.9, 124.7)	0.0101	
Female	10	3 (30.0%)	8	8 (100.0%)	n/a	n/a	2.96 (0.77, 11.43)	0.1157	64.4 (-21.4, 150.2)	0.1414	
28 hours											0.6297
Male	21	9 (42.9%)	28	27 (96.4%)	42.32 (3.90, 459.63)	0.0021	2.16 (1.01, 4.65)	0.0476	56.5 (9.3, 103.7)	0.0189	
Female	10	3 (30.0%)	8	8 (100.0%)	n/a	n/a	2.89 (0.75, 11.14)	0.1237	54.6 (-57.9, 167.2)	0.3414	
48 hours											0.7526
Male	21	4 (19.0%)	28	27 (96.4%)	290.75 (9.59, >999.99)	0.0011	4.82 (1.67, 13.90)	0.0036	66.0 (12.8, 119.2)	0.0150	
Female	10	1 (10.0%)	8	6 (75.0%)	31.19 (1.85, 525.50)	0.0170	7.86 (0.90, 68.64)	0.0621	63.8 (-42.5, 170.0)	0.2394	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline S-K.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 8.1.5.1 - Study ZS-002 Japan: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=33)		Lokelma 10g QD (N=36)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Age (years)											
1 hour											-
<65 years	1	1 (100.0%)	5	2 (40.0%)	-	-	-	-	-	-	
>=65 years	32	6 (18.8%)	31	15 (48.4%)	-	-	-	-	-	-	
2 hours											-
<65 years	1	1 (100.0%)	5	2 (40.0%)	-	-	-	-	-	-	
>=65 years	31	13 (41.9%)	31	19 (61.3%)	-	-	-	-	-	-	
4 hours											-
<65 years	1	0 (0.0%)	5	2 (40.0%)	-	-	-	-	-	-	
>=65 years	31	14 (45.2%)	31	21 (67.7%)	-	-	-	-	-	-	
24 hours											-
<65 years	1	1 (100.0%)	5	4 (80.0%)	-	-	-	-	-	-	
>=65 years	30	8 (26.7%)	31	26 (83.9%)	-	-	-	-	-	-	
25 hours											-
<65 years	1	1 (100.0%)	5	5 (100.0%)	-	-	-	-	-	-	
>=65 years	30	5 (16.7%)	31	30 (96.8%)	-	-	-	-	-	-	
28 hours											-
<65 years	1	1 (100.0%)	5	5 (100.0%)	-	-	-	-	-	-	
>=65 years	30	11 (36.7%)	31	30 (96.8%)	-	-	-	-	-	-	
48 hours											-
<65 years	1	1 (100.0%)	5	4 (80.0%)	-	-	-	-	-	-	
>=65 years	30	4 (13.3%)	31	29 (93.5%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline S-K.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 8.2.1.1 - Study ZS-002 Japan: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	1 (3.0%)	36	5 (13.9%)	5.16 (0.57 , 46.73)	0.1443	4.58 (0.56 , 37.22)	0.1542	10.86 (-1.86 , 23.58)	0.0943	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 8.2.1.2 - Study ZS-002 Japan: Subjects experiencing any serious adverse event (SAE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	36	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 8.2.1.3 - Study ZS-002 Japan: Subjects experiencing any AE leading to discontinuation of study medication (DAE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	36	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 8.2.1.4 - Study ZS-002 Japan: Subjects experiencing any AE graded as severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	36	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 8.2.1.5 - Study ZS-002 Japan: Subjects experiencing any AE graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	1 (3.0%)	36	5 (13.9%)	5.16 (0.57 , 46.73)	0.1443	4.58 (0.56 , 37.22)	0.1542	10.86 (-1.86 , 23.58)	0.0943	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 8.2.1.6 - Study ZS-002 Japan: Subjects experiencing any AE resulting in death, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	36	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 8.2.1.7 - Study ZS-002 Japan: Adverse events leading to discontinuation (DAE) by SOC and PT, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)	
Subgroup / Category / SOC / PT	**N**	**n (%)**	**N**	**n (%)**
No data for listing				

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Table 8.2.1.8 - Study ZS-002 Japan: Adverse events (AE) by SOC and PT occurring in at least 10% of subjects in any treatment group, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	33	1 (3.0%)	36	5 (13.9%)	5.16 (0.57 , 46.73)	0.1443	4.58 (0.56 , 37.22)	0.1542	10.86 (-1.86 , 23.58)	0.0943	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 8.2.1.9 - Study ZS-002 Japan: Serious adverse events (SAE) by SOC and PT occurring in at least 5% of subjects in any treatment group, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	33	0 (0.0%)	36	0 (0.0%)							

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 8.2.1.10 - Study ZS-002 Japan: AEs graded as severe by SOC and PT occurring in at least 5% of subjects in any treatment group, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	33	0 (0.0%)	36	0 (0.0%)							

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 8.2.1.11 - Study ZS-002 Japan: AEs graded as non-severe by SOC and PT occurring in at least 10% of subjects in any treatment group, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	33	1 (3.0%)	36	5 (13.9%)	5.16 (0.57 , 46.73)	0.1443	4.58 (0.56 , 37.22)	0.1542	10.86 (-1.86 , 23.58)	0.0943	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 8.2.2.1 - Study ZS-002 Japan: AEs of special interest: urinary tract infection—subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	36	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_zs002j_aesi_uti_ae.pdf generated by zs002j_ae_soc_pt.sas at 16:15:12 on 25 February 2021

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Table 8.2.2.2 - Study ZS-002 Japan: AEs of special interest: urinary tract infection—subjects experiencing any serious adverse event (SAE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	36	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 8.2.2.3 - Study ZS-002 Japan: AEs of special interest: urinary tract infection—subjects experiencing any AE graded as severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	36	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 8.2.2.4 - Study ZS-002 Japan: AEs of special interest: urinary tract infection—subjects experiencing any AE graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=36)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	36	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Anhang 4-G4: Studie ZS003

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Table 2.1.1.1 - Study ZS-003 acute: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value
Overall	158	143					
Through 24 hours							
Time			-0.00122	0.000241	-5.04	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00251	0.000340	-7.38	<.0001	
Through 48 hours							
Time			-0.00093	0.000149	-6.27	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00218	0.000211	-10.33	<.0001	
Acute Baseline S-K value							<.0001
<=5.3 mmol/L	95	94					
Through 24 hours							
Time			-0.00073	0.000302	-2.43	0.0161	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00256	0.000418	-6.13	<.0001	
Through 48 hours							
Time			-0.00057	0.000185	-3.10	0.0022	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00201	0.000258	-7.80	<.0001	
5.4-5.5 mmol/L	22	27					
Through 24 hours							
Time			-0.00226	0.000651	-3.47	0.0011	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00192	0.000813	-2.36	0.0196	
Through 48 hours							
Time			-0.00106	0.000373	-2.84	0.0067	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00295	0.000481	-6.12	<.0001	
>5.5 mmol/L	41	22					
Through 24 hours							
Time			-0.00180	0.000505	-3.56	0.0007	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00319	0.000842	-3.79	0.0002	
Through 48 hours							
Time			-0.00176	0.000272	-6.45	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00248	0.000448	-5.53	<.0001	
Chronic kidney disease							0.0114
Yes	96	83					
Through 24 hours							
Time			-0.00094	0.000303	-3.10	0.0023	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00323	0.000427	-7.57	<.0001	
Through 48 hours							
Time			-0.00092	0.000186	-4.95	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00261	0.000267	-9.79	<.0001	

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix. Covariates for CHD, CKD, diabetes mellitus and RAASi use are also included.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.

Interaction p-values are based on analysis through 48 hours.

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Table 2.1.1.1 - Study ZS-003 acute: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value
Chronic kidney disease *(contd.)*							
No	62	60					
Through 24 hours							
Time			-0.00157	0.000401	-3.91	0.0002	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00164	0.000559	-2.94	0.0035	
Through 48 hours							
Time			-0.00094	0.000242	-3.87	0.0002	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00165	0.000336	-4.91	<.0001	
Congestive Heart Disease							0.3460
Yes	66	59					
Through 24 hours							
Time			-0.00110	0.000384	-2.85	0.0051	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00259	0.000537	-4.82	<.0001	
Through 48 hours							
Time			-0.00094	0.000227	-4.15	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00243	0.000323	-7.52	<.0001	
No	92	84					
Through 24 hours							
Time			-0.00132	0.000311	-4.25	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00242	0.000441	-5.49	<.0001	
Through 48 hours							
Time			-0.00093	0.000196	-4.74	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00200	0.000277	-7.21	<.0001	
Diabetes mellitus							0.4419
Yes	96	81					
Through 24 hours							
Time			-0.00136	0.000291	-4.66	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00244	0.000414	-5.91	<.0001	
Through 48 hours							
Time			-0.00096	0.000180	-5.33	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00236	0.000253	-9.33	<.0001	
No	62	62					
Through 24 hours							
Time			-0.00101	0.000419	-2.41	0.0177	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00262	0.000585	-4.48	<.0001	
Through 48 hours							
Time			-0.00089	0.000255	-3.48	0.0007	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00197	0.000360	-5.48	<.0001	

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix. Covariates for CHD, CKD, diabetes mellitus and RAASi use are also included.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.

Interaction p-values are based on analysis through 48 hours.

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Table 2.1.1.1 - Study ZS-003 acute: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value
RAASi Medications							0.9803
Yes	101	96					
Through 24 hours							
Time			-0.00109	0.000296	-3.67	0.0003	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00252	0.000411	-6.12	<.0001	
Through 48 hours							
Time			-0.00095	0.000185	-5.16	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00214	0.000260	-8.24	<.0001	
No	57	47					
Through 24 hours							
Time			-0.00149	0.000417	-3.56	0.0006	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00244	0.000602	-4.06	<.0001	
Through 48 hours							
Time			-0.00092	0.000255	-3.62	0.0005	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00222	0.000368	-6.02	<.0001	
Acute Baseline eGFR							0.0002
<15	15	10					
Through 24 hours							
Time			-0.00223	0.000668	-3.34	0.0029	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00154	0.001081	-1.42	0.1588	
Through 48 hours							
Time			-0.00075	0.000424	-1.77	0.0902	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00331	0.000669	-4.95	<.0001	
15-29+	44	42					
Through 24 hours							
Time			-0.00141	0.000416	-3.38	0.0011	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00268	0.000576	-4.65	<.0001	
Through 48 hours							
Time			-0.00117	0.000256	-4.56	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00265	0.000355	-7.46	<.0001	
30-59+	61	50					
Through 24 hours							
Time			-0.00074	0.000404	-1.83	0.0695	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00334	0.000589	-5.67	<.0001	
Through 48 hours							
Time			-0.00078	0.000233	-3.34	0.0011	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00252	0.000344	-7.33	<.0001	

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix. Covariates for CHD, CKD, diabetes mellitus and RAASi use are also included.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.

Interaction p-values are based on analysis through 48 hours.

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Table 2.1.1.1 - Study ZS-003 acute: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value
Acute Baseline eGFR *(contd.)*							
>=60	38	41					
Through 24 hours							
Time			-0.00136	0.000540	-2.53	0.0135	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00157	0.000723	-2.17	0.0310	
Through 48 hours							
Time			-0.00096	0.000321	-2.99	0.0037	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00104	0.000429	-2.42	0.0159	
Sex							0.2423
Male	98	80					
Through 24 hours							
Time			-0.00162	0.000300	-5.40	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00233	0.000440	-5.29	<.0001	
Through 48 hours							
Time			-0.00113	0.000185	-6.11	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00192	0.000270	-7.09	<.0001	
Female	60	63					
Through 24 hours							
Time			-0.00060	0.000406	-1.48	0.1412	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00279	0.000547	-5.11	<.0001	
Through 48 hours							
Time			-0.00063	0.000249	-2.52	0.0129	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00256	0.000341	-7.49	<.0001	
Age							0.1961
<65 years	66	54					
Through 24 hours							
Time			-0.00108	0.000375	-2.88	0.0048	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00266	0.000548	-4.85	<.0001	
Through 48 hours							
Time			-0.00102	0.000231	-4.42	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00169	0.000342	-4.94	<.0001	
>=65 years	92	89					
Through 24 hours							
Time			-0.00133	0.000322	-4.12	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00238	0.000444	-5.36	<.0001	
Through 48 hours							
Time			-0.00089	0.000193	-4.62	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00244	0.000268	-9.11	<.0001	

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix. Covariates for CHD, CKD, diabetes mellitus and RAASi use are also included.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.

Interaction p-values are based on analysis through 48 hours.

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Table 2.1.1.1 - Study ZS-003 acute: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value
Region							0.7877
USA	148	133					
Through 24 hours							
Time			-0.00112	0.000251	-4.45	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00267	0.000352	-7.59	<.0001	
Through 48 hours							
Time			-0.00091	0.000155	-5.86	<.0001	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00221	0.000220	-10.05	<.0001	
Rest of world	10	10					
Through 24 hours							
Time			-0.00258	0.001115	-2.32	0.0325	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00010	0.001615	-0.06	0.9516	
Through 48 hours							
Time			-0.00145	0.000537	-2.69	0.0149	
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00152	0.000746	-2.04	0.0437	

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix. Covariates for CHD, CKD, diabetes mellitus and RAASi use are also included.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.

Interaction p-values are based on analysis through 48 hours.

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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Overall																
Baseline																
Absolute value	158	5.30 (0.365)	5.3 (5.1, 5.6)	4.5, 6.4			143	5.26 (0.337)	5.2 (5.0, 5.4)	4.5, 6.5						
Day 1 / 1-hr Post-dose 1																
Absolute value	158	5.31 (0.583)	5.2 (4.9, 5.8)	3.8, 6.7			143	5.15 (0.499)	5.1 (4.8, 5.4)	3.9, 6.7						
Change from baseline	158	0.01 (0.404)	0.0 (-0.2, 0.2)	-1.7, 1.2	0.01 (0.032)	(-0.05, 0.08)	143	-0.11 (0.361)	-0.1 (-0.3, 0.1)	-1.3, 0.9	-0.11 (0.033)	(-0.18, -0.05)	-0.13 (-0.22, -0.04)	0.0065	-0.30 (-0.53, -0.08)	
Percent change from baseline	158	0.09 (7.606)	0.0 (-4.0, 4.3)	-30.9, 21.8			143	-2.08 (6.873)	-1.9 (-6.1, 1.9)	-24.1, 16.7						
Day 1 / 2-hr Post-dose 1																
Absolute value	158	5.30 (0.549)	5.3 (4.9, 5.7)	3.8, 6.7			143	5.08 (0.469)	5.1 (4.7, 5.4)	4.0, 6.7						
Change from baseline	158	0.00 (0.423)	0.0 (-0.3, 0.3)	-1.6, 1.0	0.00 (0.032)	(-0.06, 0.07)	143	-0.18 (0.360)	-0.2 (-0.4, 0.1)	-1.1, 0.9	-0.19 (0.033)	(-0.25, -0.12)	-0.19 (-0.28, -0.10)	<.0001	-0.46 (-0.69, -0.23)	
Percent change from baseline	158	0.03 (7.911)	0.0 (-5.4, 5.4)	-27.3, 22.2			143	-3.43 (6.779)	-3.6 (-6.9, 1.7)	-20.4, 17.3						
Day 1 / 4-hr Post-dose 1																
Absolute value	158	5.08 (0.509)	5.0 (4.7, 5.4)	3.9, 6.3			143	4.89 (0.479)	4.9 (4.5, 5.2)	3.8, 6.5						
Change from baseline	158	-0.22 (0.429)	-0.2 (-0.5, 0.0)	-1.4, 0.9	-0.21 (0.034)	(-0.28, -0.15)	143	-0.37 (0.445)	-0.3 (-0.6, 0.0)	-2.2, 0.7	-0.37 (0.036)	(-0.44, -0.30)	-0.16 (-0.26, -0.06)	0.0014	-0.34 (-0.57, -0.12)	
Percent change from baseline	158	-4.05 (8.021)	-3.9 (-9.3, 0.0)	-25.5, 20.0			143	-6.91 (8.249)	-6.2 (-12.0, 0.0)	-36.7, 13.7						
Day 2 / 0-hr Pre-dose																
Absolute value	158	5.12 (0.461)	5.1 (4.8, 5.4)	4.0, 6.3			140	4.73 (0.411)	4.7 (4.5, 5.0)	3.9, 6.2						
Change from baseline	158	-0.18 (0.363)	-0.2 (-0.4, 0.0)	-1.4, 0.8	-0.18 (0.028)	(-0.24, -0.12)	140	-0.52 (0.364)	-0.5 (-0.8, -0.3)	-1.7, 0.4	-0.53 (0.030)	(-0.59, -0.47)	-0.35 (-0.43, -0.27)	<.0001	-0.93 (-1.17, -0.69)	
Percent change from baseline	158	-3.40 (6.819)	-3.8 (-7.7, 0.0)	-25.5, 17.0			140	-9.85 (6.693)	-10.2 (-13.5, -5.7)	-30.4, 7.1						
Day 2 / 1-hr Post-dose 1																
Absolute value	157	5.06 (0.535)	5.0 (4.6, 5.5)	4.0, 6.3			140	4.58 (0.438)	4.6 (4.3, 4.9)	3.5, 5.6						
Change from baseline	157	-0.24 (0.484)	-0.2 (-0.5, 0.1)	-2.2, 1.1	-0.23 (0.036)	(-0.30, -0.16)	140	-0.68 (0.437)	-0.7 (-0.9, -0.4)	-2.1, 0.5	-0.68 (0.038)	(-0.76, -0.61)	-0.45 (-0.55, -0.35)	<.0001	-0.94 (-1.18, -0.70)	
Percent change from baseline	157	-4.42 (8.904)	-3.9 (-10.0, 1.9)	-35.5, 21.6			140	-12.70 (8.091)	-13.5 (-17.8, -7.7)	-37.5, 11.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	157	5.08 (0.505)	5.1 (4.7, 5.4)	4.0, 6.4			140	4.64 (0.430)	4.6 (4.3, 5.0)	3.7, 6.7						
Change from baseline	157	-0.22 (0.440)	-0.2 (-0.5, 0.1)	-1.4, 1.0	-0.22 (0.033)	(-0.28, -0.15)	140	-0.62 (0.420)	-0.6 (-0.9, -0.3)	-1.8, 0.5	-0.62 (0.035)	(-0.69, -0.55)	-0.41 (-0.50, -0.31)	<.0001	-0.92 (-1.16, -0.68)	
Percent change from baseline	157	-4.08 (8.253)	-3.8 (-9.8, 1.8)	-22.6, 21.3			140	-11.58 (7.645)	-11.9 (-17.1, -6.2)	-32.7, 8.1						
Day 3 / 0-hr Pre-dose																
Absolute value	157	5.05 (0.474)	5.1 (4.7, 5.3)	3.9, 6.4			140	4.52 (0.463)	4.4 (4.2, 4.8)	3.4, 6.2						
Change from baseline	157	-0.25 (0.413)	-0.3 (-0.6, 0.1)	-1.4, 0.8	-0.24 (0.035)	(-0.31, -0.18)	140	-0.73 (0.496)	-0.8 (-1.1, -0.5)	-1.9, 1.0	-0.74 (0.037)	(-0.81, -0.67)	-0.49 (-0.59, -0.39)	<.0001	-1.06 (-1.31, -0.82)	
Percent change from baseline	157	-4.62 (7.751)	-5.2 (-10.6, 1.8)	-24.1, 15.6			140	-13.76 (9.044)	-14.8 (-20.2, -8.5)	-33.9, 19.2						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Lokelma

Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value																0.1366
<=5.3 mmol/L																
Baseline																
Absolute value	95	5.05 (0.196)	5.1 (4.9, 5.2)	4.5, 5.3			94	5.07 (0.186)	5.1 (4.9, 5.2)	4.5, 5.3						
Day 1 / 1-hr Post-dose 1																
Absolute value	95	5.03 (0.445)	5.0 (4.7, 5.3)	3.8, 6.3			94	4.99 (0.389)	5.0 (4.7, 5.3)	3.9, 5.9						
Change from baseline	95	-0.03 (0.375)	0.0 (-0.2, 0.2)	-1.3, 1.0	-0.03 (0.036)	(-0.10, 0.05)	94	-0.08 (0.330)	-0.1 (-0.3, 0.1)	-1.0, 0.7	-0.08 (0.037)	(-0.15, -0.01)	-0.05 (-0.16, 0.05)	0.3025	-0.15 (-0.44, 0.13)	
Percent change from baseline	95	-0.56 (7.357)	0.0 (-4.1, 3.8)	-25.5, 19.2			94	-1.61 (6.532)	-1.9 (-6.0, 2.0)	-20.0, 14.3						
Day 1 / 2-hr Post-dose 1																
Absolute value	95	5.08 (0.440)	5.1 (4.8, 5.4)	3.8, 6.3			94	4.92 (0.385)	4.9 (4.7, 5.2)	4.0, 6.1						
Change from baseline	95	0.02 (0.380)	0.0 (-0.3, 0.3)	-0.9, 1.0	0.02 (0.037)	(-0.05, 0.09)	94	-0.15 (0.347)	-0.1 (-0.3, 0.1)	-1.0, 0.9	-0.15 (0.038)	(-0.23, -0.08)	-0.17 (-0.28, -0.07)	0.0012	-0.48 (-0.77, -0.19)	
Percent change from baseline	95	0.40 (7.552)	0.0 (-5.7, 5.7)	-19.1, 22.2			94	-3.03 (6.776)	-2.2 (-6.0, 1.9)	-19.2, 17.3						
Day 1 / 4-hr Post-dose 1																
Absolute value	95	4.88 (0.416)	4.9 (4.6, 5.1)	3.9, 6.1			94	4.81 (0.425)	4.8 (4.5, 5.2)	3.8, 5.9						
Change from baseline	95	-0.18 (0.390)	-0.2 (-0.4, 0.0)	-0.9, 0.9	-0.18 (0.040)	(-0.26, -0.10)	94	-0.26 (0.393)	-0.2 (-0.5, 0.0)	-1.2, 0.7	-0.26 (0.040)	(-0.34, -0.18)	-0.08 (-0.20, 0.03)	0.1424	-0.22 (-0.50, 0.07)	
Percent change from baseline	95	-3.49 (7.769)	-3.8 (-8.0, 0.0)	-17.6, 20.0			94	-5.17 (7.726)	-4.0 (-10.0, 0.0)	-24.0, 13.7						
Day 2 / 0-hr Pre-dose																
Absolute value	95	4.94 (0.377)	4.9 (4.7, 5.1)	4.0, 6.0			92	4.63 (0.348)	4.6 (4.4, 4.9)	3.9, 5.3						
Change from baseline	95	-0.11 (0.337)	-0.1 (-0.3, 0.0)	-0.9, 0.8	-0.12 (0.034)	(-0.18, -0.05)	92	-0.44 (0.326)	-0.4 (-0.6, -0.3)	-1.3, 0.2	-0.44 (0.035)	(-0.51, -0.37)	-0.33 (-0.42, -0.23)	<.0001	-0.98 (-1.28, -0.68)	
Percent change from baseline	95	-2.25 (6.696)	-2.1 (-6.1, 0.0)	-18.4, 17.0			92	-8.66 (6.350)	-8.2 (-12.4, -4.9)	-25.0, 3.9						
Day 2 / 1-hr Post-dose 1																
Absolute value	95	4.89 (0.469)	4.9 (4.5, 5.2)	4.0, 6.2			92	4.52 (0.406)	4.5 (4.2, 4.8)	3.5, 5.4						
Change from baseline	95	-0.16 (0.418)	-0.2 (-0.5, 0.1)	-0.9, 1.1	-0.16 (0.042)	(-0.24, -0.08)	92	-0.55 (0.391)	-0.6 (-0.9, -0.3)	-1.5, 0.5	-0.55 (0.042)	(-0.63, -0.46)	-0.39 (-0.50, -0.27)	<.0001	-0.95 (-1.25, -0.65)	
Percent change from baseline	95	-3.20 (8.289)	-3.8 (-9.8, 2.0)	-18.0, 21.6			92	-10.73 (7.742)	-11.8 (-16.8, -5.1)	-30.0, 11.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	95	4.92 (0.476)	4.9 (4.6, 5.2)	4.0, 6.1			92	4.57 (0.341)	4.5 (4.3, 4.8)	3.9, 5.3						
Change from baseline	95	-0.14 (0.427)	-0.1 (-0.5, 0.1)	-1.1, 1.0	-0.14 (0.040)	(-0.22, -0.06)	92	-0.49 (0.342)	-0.5 (-0.7, -0.3)	-1.2, 0.3	-0.49 (0.040)	(-0.57, -0.41)	-0.36 (-0.47, -0.24)	<.0001	-0.92 (-1.22, -0.62)	
Percent change from baseline	95	-2.74 (8.440)	-2.0 (-9.4, 2.0)	-21.6, 21.3			92	-9.68 (6.645)	-9.7 (-14.4, -5.1)	-23.1, 6.1						
Day 3 / 0-hr Pre-dose																
Absolute value	95	4.90 (0.446)	4.9 (4.6, 5.2)	3.9, 6.1			92	4.49 (0.480)	4.4 (4.2, 4.8)	3.4, 6.2						
Change from baseline	95	-0.15 (0.407)	-0.1 (-0.5, 0.1)	-1.0, 0.8	-0.15 (0.044)	(-0.24, -0.07)	92	-0.57 (0.455)	-0.6 (-0.9, -0.3)	-1.6, 1.0	-0.57 (0.045)	(-0.66, -0.49)	-0.42 (-0.54, -0.30)	<.0001	-0.97 (-1.28, -0.67)	
Percent change from baseline	95	-3.03 (8.037)	-2.1 (-9.8, 2.0)	-19.2, 15.6			92	-11.30 (8.900)	-11.8 (-17.1, -5.8)	-30.2, 19.2						
5.4-5.5 mmol/L																
Baseline																
Absolute value	22	5.47 (0.048)	5.5 (5.4, 5.5)	5.4, 5.5			27	5.43 (0.048)	5.4 (5.4, 5.5)	5.4, 5.5						
Day 1 / 1-hr Post-dose 1																
Absolute value	22	5.41 (0.597)	5.4 (5.1, 5.7)	3.8, 6.7			27	5.17 (0.449)	5.1 (4.8, 5.5)	4.1, 6.3						
Change from baseline	22	-0.06 (0.600)	-0.1 (-0.4, 0.3)	-1.7, 1.2	-0.05 (0.112)	(-0.27, 0.18)	27	-0.26 (0.440)	-0.3 (-0.6, 0.0)	-1.3, 0.9	-0.28 (0.101)	(-0.48, -0.07)	-0.23 (-0.54, 0.08)	0.1392	-0.39 (-0.96, 0.17)	
Percent change from baseline	22	-1.07 (10.923)	-1.8 (-7.3, 5.6)	-30.9, 21.8			27	-4.85 (8.114)	-5.6 (-11.1, 0.0)	-24.1, 16.7						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value *(contd.)*																
5.4-5.5 mmol/L *(contd.)*																
Day 1 / 2-hr Post-dose 1																
Absolute value	22	5.38 (0.481)	5.4 (5.2, 5.6)	4.0, 6.3			27	5.19 (0.398)	5.2 (4.9, 5.4)	4.3, 6.0						
Change from baseline	22	-0.09 (0.496)	-0.0 (-0.3, 0.2)	-1.5, 0.8	-0.08 (0.095)	(-0.27, 0.11)	27	-0.24 (0.392)	-0.2 (-0.5, 0.0)	-1.1, 0.6	-0.26 (0.086)	(-0.43, -0.08)	-0.18 (-0.44, 0.08)	0.1742	-0.35 (-0.92, 0.22)	
Percent change from baseline	22	-1.64 (9.034)	-0.9 (-5.5, 3.6)	-27.3, 14.5			27	-4.50 (7.211)	-3.7 (-9.3, 0.0)	-20.4, 11.1						
Day 1 / 4-hr Post-dose 1																
Absolute value	22	5.20 (0.477)	5.2 (4.9, 5.4)	4.1, 6.2			27	4.81 (0.417)	4.8 (4.5, 5.2)	4.0, 5.6						
Change from baseline	22	-0.26 (0.485)	-0.3 (-0.5, 0.0)	-1.4, 0.7	-0.25 (0.097)	(-0.44, -0.06)	27	-0.62 (0.408)	-0.6 (-0.9, -0.3)	-1.5, 0.2	-0.63 (0.087)	(-0.81, -0.46)	-0.38 (-0.65, -0.12)	0.0053	-0.81 (-1.39, -0.22)	
Percent change from baseline	22	-4.81 (8.837)	-5.5 (-9.3, 0.0)	-25.5, 12.7			27	-11.46 (7.514)	-11.1 (-16.7, -5.5)	-27.3, 3.7						
Day 2 / 0-hr Pre-dose																
Absolute value	22	5.07 (0.319)	5.1 (4.9, 5.3)	4.1, 5.6			26	4.79 (0.343)	4.7 (4.6, 5.1)	4.2, 5.5						
Change from baseline	22	-0.40 (0.333)	-0.4 (-0.6, -0.2)	-1.4, 0.2	-0.38 (0.073)	(-0.53, -0.23)	26	-0.65 (0.336)	-0.7 (-0.8, -0.4)	-1.3, 0.1	-0.66 (0.067)	(-0.80, -0.53)	-0.28 (-0.48, -0.08)	0.0083	-0.75 (-1.34, -0.16)	
Percent change from baseline	22	-7.21 (6.062)	-6.4 (-10.9, -3.6)	-25.5, 3.7			26	-11.89 (6.182)	-13.0 (-14.8, -7.3)	-23.6, 1.9						
Day 2 / 1-hr Post-dose 1																
Absolute value	22	5.15 (0.492)	5.1 (4.9, 5.5)	4.2, 6.2			26	4.50 (0.433)	4.6 (4.2, 4.8)	3.6, 5.3						
Change from baseline	22	-0.32 (0.503)	-0.4 (-0.6, 0.1)	-1.3, 0.7	-0.31 (0.100)	(-0.51, -0.11)	26	-0.93 (0.434)	-0.9 (-1.2, -0.6)	-1.9, -0.2	-0.95 (0.092)	(-1.13, -0.76)	-0.64 (-0.91, -0.36)	<.0001	-1.31 (-1.94, -0.69)	
Percent change from baseline	22	-5.88 (9.162)	-6.5 (-10.9, 1.8)	-23.6, 12.7			26	-17.19 (7.947)	-16.5 (-22.2, -11.1)	-34.5, -3.6						
Day 2 / 4-hr Post-dose 1																
Absolute value	22	5.22 (0.396)	5.4 (4.9, 5.6)	4.4, 5.7			26	4.51 (0.401)	4.4 (4.2, 4.9)	3.7, 5.3						
Change from baseline	22	-0.25 (0.413)	-0.1 (-0.6, 0.1)	-1.1, 0.3	-0.23 (0.087)	(-0.41, -0.06)	26	-0.92 (0.407)	-1.1 (-1.2, -0.5)	-1.8, -0.2	-0.94 (0.080)	(-1.10, -0.77)	-0.70 (-0.95, -0.46)	<.0001	-1.65 (-2.31, -1.00)	
Percent change from baseline	22	-4.46 (7.523)	-1.8 (-10.9, 1.8)	-20.0, 5.6			26	-16.97 (7.447)	-19.4 (-22.2, -9.3)	-32.7, -3.6						
Day 3 / 0-hr Pre-dose																
Absolute value	22	5.10 (0.316)	5.2 (4.9, 5.3)	4.5, 5.7			26	4.45 (0.383)	4.3 (4.2, 4.8)	3.7, 5.1						
Change from baseline	22	-0.37 (0.317)	-0.4 (-0.6, -0.2)	-1.0, 0.3	-0.35 (0.078)	(-0.51, -0.20)	26	-0.99 (0.385)	-1.1 (-1.2, -0.6)	-1.8, -0.3	-1.00 (0.071)	(-1.14, -0.86)	-0.65 (-0.86, -0.43)	<.0001	-1.74 (-2.41, -1.08)	
Percent change from baseline	22	-6.73 (5.789)	-6.4 (-10.9, -3.6)	-18.2, 5.6			26	-18.18 (7.053)	-20.4 (-22.2, -11.1)	-32.7, -5.6						
>5.5 mmol/L																
Baseline																
Absolute value	41	5.79 (0.178)	5.8 (5.6, 5.9)	5.6, 6.4			22	5.84 (0.238)	5.8 (5.6, 6.0)	5.6, 6.5						
Day 1 / 1-hr Post-dose 1																
Absolute value	41	5.91 (0.344)	5.9 (5.8, 6.2)	5.2, 6.5			22	5.80 (0.449)	5.8 (5.6, 6.0)	5.0, 6.7						
Change from baseline	41	0.13 (0.319)	0.1 (-0.1, 0.3)	-0.4, 0.8	0.12 (0.052)	(0.02, 0.23)	22	-0.04 (0.347)	-0.1 (-0.2, 0.2)	-0.6, 0.9	-0.03 (0.071)	(-0.17, 0.11)	-0.15 (-0.33, 0.02)	0.0841	-0.50 (-1.02, 0.03)	
Percent change from baseline	41	2.21 (5.557)	1.8 (-1.7, 5.2)	-7.1, 14.3			22	-0.66 (6.000)	-1.7 (-3.4, 3.4)	-10.7, 15.5						
Day 1 / 2-hr Post-dose 1																
Absolute value	41	5.79 (0.491)	5.9 (5.5, 6.1)	4.3, 6.7			22	5.62 (0.438)	5.6 (5.3, 5.8)	5.0, 6.7						
Change from baseline	41	0.00 (0.476)	0.1 (-0.2, 0.3)	-1.6, 0.8	-0.00 (0.069)	(-0.14, 0.14)	22	-0.22 (0.378)	-0.2 (-0.5, 0.1)	-1.1, 0.6	-0.22 (0.095)	(-0.41, -0.03)	-0.22 (-0.45, 0.02)	0.0706	-0.51 (-1.03, 0.02)	
Percent change from baseline	41	0.07 (8.182)	1.7 (-3.5, 5.4)	-27.1, 14.3			22	-3.81 (6.382)	-3.5 (-8.6, 1.7)	-18.0, 9.8						
Day 1 / 4-hr Post-dose 1																
Absolute value	41	5.50 (0.458)	5.4 (5.2, 5.9)	4.6, 6.3			22	5.33 (0.545)	5.4 (5.0, 5.6)	3.8, 6.5						
Change from baseline	41	-0.29 (0.481)	-0.3 (-0.6, 0.1)	-1.3, 0.7	-0.29 (0.078)	(-0.45, -0.14)	22	-0.51 (0.544)	-0.4 (-0.8, -0.1)	-2.2, 0.2	-0.51 (0.106)	(-0.72, -0.30)	-0.22 (-0.48, 0.05)	0.1081	-0.44 (-0.97, 0.08)	

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value *(contd.)*																
>5.5 mmol/L *(contd.)*																
Day 1 / 4-hr Post-dose 1 *(contd.)*																
Percent change from baseline	41	-4.95 (8.232)	-5.4 (-10.2, 1.7)	-22.0, 12.5			22	-8.73 (9.070)	-7.0 (-13.8, -1.8)	-36.7, 3.6						
Day 2 / 0-hr Pre-dose																
Absolute value	41	5.55 (0.420)	5.6 (5.2, 5.9)	4.8, 6.3			22	5.12 (0.492)	5.1 (4.9, 5.3)	3.9, 6.2						
Change from baseline	41	-0.23 (0.393)	-0.2 (-0.5, 0.1)	-1.1, 0.5	-0.23 (0.064)	(-0.36, -0.11)	22	-0.72 (0.436)	-0.8 (-1.0, -0.5)	-1.7, 0.4	-0.72 (0.088)	(-0.89, -0.54)	-0.48 (-0.70, -0.27)	<.0001	-1.20 (-1.76, -0.64)	
Percent change from baseline	41	-4.00 (6.808)	-3.5 (-8.6, 1.7)	-18.6, 8.8			22	-12.39 (7.627)	-12.2 (-16.9, -8.9)	-30.4, 7.1						
Day 2 / 1-hr Post-dose 1																
Absolute value	40	5.40 (0.541)	5.6 (5.0, 5.8)	4.0, 6.3			22	4.93 (0.427)	5.0 (4.8, 5.1)	3.5, 5.6						
Change from baseline	40	-0.38 (0.584)	-0.3 (-0.8, 0.0)	-2.2, 0.6	-0.38 (0.082)	(-0.54, -0.21)	22	-0.91 (0.399)	-0.9 (-1.1, -0.7)	-2.1, -0.2	-0.91 (0.111)	(-1.13, -0.69)	-0.53 (-0.81, -0.25)	0.0003	-1.01 (-1.56, -0.46)	
Percent change from baseline	40	-6.51 (9.849)	-4.3 (-13.0, 0.9)	-35.5, 10.5			22	-15.62 (6.895)	-15.0 (-17.9, -12.1)	-37.5, -3.4						
Day 2 / 4-hr Post-dose 1																
Absolute value	40	5.38 (0.473)	5.4 (5.0, 5.7)	4.6, 6.4			22	5.07 (0.541)	5.0 (4.8, 5.3)	4.0, 6.7						
Change from baseline	40	-0.41 (0.439)	-0.4 (-0.7, -0.1)	-1.4, 0.5	-0.40 (0.073)	(-0.55, -0.26)	22	-0.77 (0.508)	-0.8 (-1.1, -0.6)	-1.6, 0.5	-0.76 (0.099)	(-0.96, -0.56)	-0.36 (-0.61, -0.11)	0.0052	-0.78 (-1.31, -0.24)	
Percent change from baseline	40	-7.06 (7.536)	-7.1 (-12.2, -1.8)	-22.6, 8.5			22	-13.14 (8.665)	-13.8 (-18.6, -10.7)	-28.6, 8.1						
Day 3 / 0-hr Pre-dose																
Absolute value	40	5.37 (0.459)	5.3 (5.1, 5.7)	4.4, 6.4			22	4.74 (0.429)	4.8 (4.5, 4.9)	3.7, 5.5						
Change from baseline	40	-0.42 (0.411)	-0.5 (-0.7, -0.1)	-1.4, 0.6	-0.41 (0.068)	(-0.55, -0.28)	22	-1.10 (0.470)	-1.1 (-1.4, -0.8)	-1.9, -0.3	-1.10 (0.092)	(-1.28, -0.91)	-0.69 (-0.92, -0.46)	<.0001	-1.59 (-2.18, -1.00)	
Percent change from baseline	40	-7.24 (7.135)	-8.8 (-11.6, -2.6)	-24.1, 10.3			22	-18.81 (7.830)	-19.0 (-24.1, -14.3)	-33.9, -5.4						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Chronic kidney disease																0.0003
Yes																
Baseline																
Absolute value	96	5.33 (0.371)	5.3 (5.1, 5.6)	4.5, 6.4			83	5.31 (0.342)	5.3 (5.1, 5.5)	4.8, 6.5						
Day 1 / 1-hr Post-dose 1																
Absolute value	96	5.39 (0.554)	5.3 (5.0, 5.9)	3.8, 6.5			83	5.19 (0.489)	5.2 (4.9, 5.5)	4.1, 6.7						
Change from baseline	96	0.06 (0.358)	0.0 (-0.2, 0.3)	-1.3, 0.9	0.06 (0.038)	(-0.01, 0.14)	83	-0.11 (0.375)	-0.1 (-0.3, 0.1)	-1.3, 0.9	-0.12 (0.041)	(-0.20, -0.03)	-0.18 (-0.29, -0.07)	0.0017	-0.48 (-0.78, -0.18)	
Percent change from baseline	96	1.09 (6.759)	0.0 (-3.7, 5.4)	-25.5, 17.3			83	-2.13 (7.035)	-1.9 (-5.6, 1.9)	-24.1, 16.7						
Day 1 / 2-hr Post-dose 1																
Absolute value	96	5.43 (0.526)	5.4 (5.1, 5.8)	3.8, 6.7			83	5.13 (0.436)	5.2 (4.8, 5.4)	4.2, 6.4						
Change from baseline	96	0.11 (0.347)	0.1 (-0.1, 0.3)	-0.9, 1.0	0.11 (0.037)	(0.03, 0.18)	83	-0.18 (0.373)	-0.2 (-0.4, 0.0)	-1.1, 0.9	-0.18 (0.040)	(-0.26, -0.11)	-0.29 (-0.40, -0.18)	<.0001	-0.80 (-1.10, -0.49)	
Percent change from baseline	96	1.96 (6.600)	1.9 (-1.9, 5.9)	-19.1, 22.2			83	-3.33 (6.965)	-3.6 (-6.9, 0.0)	-20.4, 17.3						
Day 1 / 4-hr Post-dose 1																
Absolute value	96	5.18 (0.544)	5.1 (4.8, 5.5)	3.9, 6.3			83	4.88 (0.471)	4.9 (4.6, 5.2)	3.8, 6.5						
Change from baseline	96	-0.15 (0.439)	-0.2 (-0.5, 0.1)	-1.2, 0.9	-0.15 (0.045)	(-0.24, -0.06)	83	-0.42 (0.461)	-0.4 (-0.7, -0.1)	-2.2, 0.3	-0.43 (0.048)	(-0.52, -0.33)	-0.28 (-0.41, -0.15)	<.0001	-0.61 (-0.91, -0.31)	
Percent change from baseline	96	-2.79 (8.295)	-3.8 (-8.9, 2.8)	-20.7, 20.0			83	-7.84 (8.319)	-7.4 (-12.7, -1.8)	-36.7, 5.9						
Day 2 / 0-hr Pre-dose																
Absolute value	96	5.21 (0.468)	5.1 (4.9, 5.5)	4.1, 6.3			80	4.74 (0.370)	4.7 (4.5, 5.0)	3.9, 5.7						
Change from baseline	96	-0.12 (0.340)	-0.1 (-0.4, 0.1)	-0.9, 0.8	-0.12 (0.034)	(-0.18, -0.05)	80	-0.57 (0.339)	-0.5 (-0.8, -0.4)	-1.7, 0.1	-0.57 (0.037)	(-0.64, -0.50)	-0.45 (-0.55, -0.36)	<.0001	-1.33 (-1.65, -1.00)	
Percent change from baseline	96	-2.16 (6.412)	-2.1 (-6.9, 1.7)	-15.3, 17.0			80	-10.57 (6.102)	-9.9 (-13.5, -6.7)	-30.4, 2.0						
Day 2 / 1-hr Post-dose 1																
Absolute value	95	5.18 (0.503)	5.1 (4.8, 5.6)	4.1, 6.2			80	4.55 (0.417)	4.6 (4.3, 4.9)	3.5, 5.4						
Change from baseline	95	-0.14 (0.413)	-0.1 (-0.5, 0.1)	-1.1, 1.1	-0.14 (0.042)	(-0.22, -0.05)	80	-0.75 (0.441)	-0.8 (-1.0, -0.5)	-2.1, 0.3	-0.76 (0.046)	(-0.85, -0.67)	-0.62 (-0.74, -0.50)	<.0001	-1.43 (-1.77, -1.10)	
Percent change from baseline	95	-2.62 (7.796)	-2.0 (-8.7, 2.1)	-19.3, 21.6			80	-14.01 (7.981)	-14.5 (-18.6, -9.2)	-37.5, 6.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	95	5.11 (0.496)	5.2 (4.7, 5.5)	4.0, 6.3			80	4.66 (0.456)	4.7 (4.3, 5.0)	3.7, 6.7						
Change from baseline	95	-0.21 (0.413)	-0.1 (-0.5, 0.1)	-1.2, 0.9	-0.21 (0.043)	(-0.29, -0.12)	80	-0.65 (0.449)	-0.7 (-1.0, -0.3)	-1.8, 0.5	-0.65 (0.047)	(-0.74, -0.56)	-0.44 (-0.57, -0.32)	<.0001	-1.02 (-1.33, -0.70)	
Percent change from baseline	95	-3.86 (7.668)	-2.1 (-9.8, 1.8)	-21.6, 17.6			80	-12.02 (8.102)	-12.6 (-17.8, -6.2)	-32.7, 8.1						
Day 3 / 0-hr Pre-dose																
Absolute value	95	5.10 (0.466)	5.1 (4.7, 5.3)	4.1, 6.4			80	4.48 (0.460)	4.4 (4.2, 4.8)	3.4, 6.2						
Change from baseline	95	-0.22 (0.381)	-0.2 (-0.5, 0.1)	-1.0, 0.7	-0.21 (0.043)	(-0.30, -0.13)	80	-0.83 (0.499)	-0.8 (-1.2, -0.5)	-1.9, 1.0	-0.83 (0.047)	(-0.92, -0.73)	-0.62 (-0.74, -0.49)	<.0001	-1.39 (-1.72, -1.05)	
Percent change from baseline	95	-3.98 (7.191)	-3.9 (-9.6, 1.8)	-18.2, 15.6			80	-15.34 (8.965)	-16.3 (-21.8, -9.8)	-33.9, 19.2						
No																
Baseline																
Absolute value	62	5.26 (0.355)	5.2 (5.0, 5.5)	4.7, 6.2			60	5.19 (0.319)	5.2 (5.0, 5.3)	4.5, 6.1						
Day 1 / 1-hr Post-dose 1																
Absolute value	62	5.19 (0.612)	5.1 (4.7, 5.6)	3.8, 6.7			60	5.09 (0.511)	5.0 (4.8, 5.4)	3.9, 6.6						
Change from baseline	62	-0.07 (0.458)	-0.1 (-0.3, 0.1)	-1.7, 1.2	-0.06 (0.054)	(-0.17, 0.04)	60	-0.10 (0.345)	-0.1 (-0.3, 0.1)	-1.0, 0.7	-0.11 (0.055)	(-0.22, 0.00)	-0.05 (-0.20, 0.11)	0.5555	-0.07 (-0.42, 0.29)	
Percent change from baseline	62	-1.46 (8.586)	-1.9 (-6.0, 2.0)	-30.9, 21.8			60	-2.00 (6.700)	-2.0 (-6.2, 2.1)	-20.0, 14.3						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Chronic kidney disease *(contd.)*																
No *(contd.)*																
Day 1 / 2-hr Post-dose 1																
Absolute value	62	5.10 (0.528)	5.0 (4.7, 5.5)	4.0, 6.3			60	5.01 (0.506)	5.0 (4.7, 5.4)	4.0, 6.7						
Change from baseline	62	-0.16 (0.477)	-0.1 (-0.4, 0.1)	-1.6, 1.0	-0.15 (0.053)	(-0.26, -0.05)	60	-0.18 (0.344)	-0.1 (-0.3, 0.1)	-0.9, 0.6	-0.19 (0.054)	(-0.30, -0.08)	-0.04 (-0.19, 0.11)	0.6119	-0.05 (-0.40, 0.31)	
Percent change from baseline	62	-2.95 (8.853)	-2.1 (-7.8, 2.0)	-27.3, 18.9			60	-3.57 (6.569)	-2.9 (-6.9, 1.8)	-16.7, 9.8						
Day 1 / 4-hr Post-dose 1																
Absolute value	62	4.94 (0.417)	4.9 (4.7, 5.2)	4.0, 5.9			60	4.90 (0.493)	4.9 (4.5, 5.3)	3.8, 6.1						
Change from baseline	62	-0.32 (0.395)	-0.3 (-0.6, 0.0)	-1.4, 0.5	-0.32 (0.050)	(-0.41, -0.22)	60	-0.29 (0.415)	-0.3 (-0.6, 0.0)	-1.2, 0.7	-0.30 (0.051)	(-0.40, -0.20)	0.01 (-0.13, 0.15)	0.8620	0.08 (-0.28, 0.43)	
Percent change from baseline	62	-6.01 (7.212)	-5.2 (-11.5, 0.0)	-25.5, 9.4			60	-5.61 (8.042)	-6.0 (-11.4, 0.0)	-24.0, 13.7						
Day 2 / 0-hr Pre-dose																
Absolute value	62	4.98 (0.417)	5.0 (4.8, 5.2)	4.0, 6.0			60	4.72 (0.463)	4.7 (4.4, 5.0)	3.9, 6.2						
Change from baseline	62	-0.29 (0.377)	-0.3 (-0.5, -0.1)	-1.4, 0.5	-0.28 (0.047)	(-0.37, -0.18)	60	-0.46 (0.390)	-0.5 (-0.7, -0.2)	-1.3, 0.4	-0.47 (0.048)	(-0.57, -0.38)	-0.19 (-0.33, -0.06)	0.0047	-0.46 (-0.82, -0.10)	
Percent change from baseline	62	-5.31 (7.035)	-5.6 (-10.0, -1.9)	-25.5, 9.6			60	-8.89 (7.351)	-10.4 (-13.5, -2.8)	-25.0, 7.1						
Day 2 / 1-hr Post-dose 1																
Absolute value	62	4.88 (0.534)	4.8 (4.5, 5.1)	4.0, 6.3			60	4.62 (0.465)	4.6 (4.2, 5.0)	3.5, 5.6						
Change from baseline	62	-0.39 (0.548)	-0.3 (-0.7, -0.1)	-2.2, 0.7	-0.38 (0.060)	(-0.50, -0.26)	60	-0.57 (0.412)	-0.6 (-0.9, -0.2)	-1.5, 0.5	-0.58 (0.061)	(-0.70, -0.46)	-0.20 (-0.37, -0.03)	0.0195	-0.38 (-0.73, -0.02)	
Percent change from baseline	62	-7.19 (9.809)	-6.3 (-12.7, -1.8)	-35.5, 14.9			60	-10.95 (7.968)	-11.4 (-16.8, -4.0)	-30.0, 11.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	62	5.02 (0.517)	4.9 (4.7, 5.4)	4.0, 6.4			60	4.61 (0.395)	4.6 (4.3, 4.9)	3.9, 6.0						
Change from baseline	62	-0.24 (0.482)	-0.3 (-0.5, 0.0)	-1.4, 1.0	-0.23 (0.053)	(-0.34, -0.13)	60	-0.58 (0.378)	-0.6 (-0.8, -0.3)	-1.3, 0.4	-0.59 (0.054)	(-0.69, -0.48)	-0.35 (-0.50, -0.20)	<.0001	-0.77 (-1.14, -0.41)	
Percent change from baseline	62	-4.43 (9.132)	-6.1 (-10.4, 0.0)	-22.6, 21.3			60	-10.99 (7.012)	-11.3 (-15.2, -6.3)	-23.6, 7.1						
Day 3 / 0-hr Pre-dose																
Absolute value	62	4.96 (0.479)	5.0 (4.6, 5.3)	3.9, 6.2			60	4.58 (0.465)	4.5 (4.2, 4.9)	3.7, 5.9						
Change from baseline	62	-0.30 (0.455)	-0.3 (-0.7, 0.1)	-1.4, 0.8	-0.29 (0.056)	(-0.41, -0.18)	60	-0.61 (0.470)	-0.7 (-0.9, -0.3)	-1.6, 0.6	-0.62 (0.057)	(-0.73, -0.51)	-0.33 (-0.49, -0.17)	<.0001	-0.67 (-1.03, -0.30)	
Percent change from baseline	62	-5.61 (8.506)	-6.0 (-12.0, 2.0)	-24.1, 15.1			60	-11.65 (8.782)	-12.7 (-18.0, -5.7)	-30.2, 11.3						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Congestive Heart Disease																0.8586
Yes																
Baseline																
Absolute value	66	5.34 (0.396)	5.3 (5.1, 5.6)	4.6, 6.4			59	5.28 (0.349)	5.3 (5.0, 5.4)	4.8, 6.5						
Day 1 / 1-hr Post-dose 1																
Absolute value	66	5.38 (0.596)	5.3 (5.0, 5.8)	4.1, 6.7			59	5.20 (0.531)	5.2 (4.8, 5.5)	4.1, 6.7						
Change from baseline	66	0.04 (0.397)	0.0 (-0.2, 0.3)	-0.7, 1.2	0.05 (0.048)	(-0.05, 0.14)	59	-0.08 (0.364)	-0.1 (-0.3, 0.1)	-1.3, 0.9	-0.09 (0.051)	(-0.19, 0.01)	-0.13 (-0.27, 0.01)	0.0608	-0.33 (-0.68, 0.02)	
Percent change from baseline	66	0.72 (7.509)	0.0 (-3.9, 5.2)	-13.7, 21.8			59	-1.62 (6.853)	-1.9 (-5.5, 2.0)	-24.1, 15.5						
Day 1 / 2-hr Post-dose 1																
Absolute value	66	5.31 (0.590)	5.3 (4.9, 5.7)	3.8, 6.7			59	5.15 (0.457)	5.2 (4.8, 5.4)	4.2, 6.4						
Change from baseline	66	-0.03 (0.394)	0.0 (-0.2, 0.2)	-1.6, 0.8	-0.02 (0.048)	(-0.12, 0.07)	59	-0.13 (0.379)	-0.1 (-0.3, 0.1)	-1.1, 0.9	-0.14 (0.051)	(-0.24, -0.04)	-0.12 (-0.25, 0.02)	0.0998	-0.28 (-0.63, 0.07)	
Percent change from baseline	66	-0.55 (7.292)	0.0 (-3.6, 4.0)	-27.1, 14.5			59	-2.45 (7.110)	-1.9 (-6.0, 1.9)	-20.4, 17.3						
Day 1 / 4-hr Post-dose 1																
Absolute value	66	5.13 (0.546)	5.1 (4.8, 5.4)	3.9, 6.3			59	4.92 (0.505)	4.9 (4.5, 5.2)	3.8, 6.5						
Change from baseline	66	-0.21 (0.427)	-0.2 (-0.5, 0.1)	-1.3, 0.7	-0.21 (0.055)	(-0.32, -0.10)	59	-0.36 (0.482)	-0.4 (-0.6, 0.0)	-2.2, 0.6	-0.37 (0.058)	(-0.48, -0.25)	-0.16 (-0.32, -0.00)	0.0457	-0.34 (-0.69, 0.01)	
Percent change from baseline	66	-3.91 (7.936)	-3.8 (-9.3, 1.7)	-22.0, 12.7			59	-6.76 (8.696)	-7.4 (-12.0, 0.0)	-36.7, 11.3						
Day 2 / 0-hr Pre-dose																
Absolute value	66	5.18 (0.452)	5.1 (4.8, 5.5)	4.2, 6.2			59	4.77 (0.447)	4.7 (4.5, 5.1)	3.9, 6.0						
Change from baseline	66	-0.16 (0.355)	-0.2 (-0.4, 0.0)	-1.1, 0.8	-0.16 (0.044)	(-0.25, -0.07)	59	-0.51 (0.379)	-0.5 (-0.8, -0.3)	-1.7, 0.4	-0.51 (0.047)	(-0.61, -0.42)	-0.35 (-0.48, -0.23)	<.0001	-0.94 (-1.31, -0.57)	
Percent change from baseline	66	-2.95 (6.642)	-3.6 (-7.3, 0.0)	-18.6, 17.0			59	-9.58 (6.992)	-8.6 (-14.8, -5.7)	-30.4, 7.1						
Day 2 / 1-hr Post-dose 1																
Absolute value	66	5.07 (0.549)	5.0 (4.6, 5.6)	4.0, 6.2			59	4.52 (0.424)	4.6 (4.2, 4.8)	3.5, 5.4						
Change from baseline	66	-0.27 (0.476)	-0.2 (-0.5, 0.0)	-2.2, 0.8	-0.27 (0.054)	(-0.37, -0.16)	59	-0.77 (0.411)	-0.8 (-1.1, -0.6)	-2.1, 0.3	-0.77 (0.057)	(-0.88, -0.66)	-0.51 (-0.66, -0.35)	<.0001	-1.11 (-1.49, -0.74)	
Percent change from baseline	66	-4.95 (8.537)	-4.1 (-9.8, 0.0)	-35.5, 16.0			59	-14.40 (7.522)	-15.1 (-18.9, -10.7)	-37.5, 5.9						
Day 2 / 4-hr Post-dose 1																
Absolute value	66	5.13 (0.523)	5.2 (4.7, 5.5)	4.0, 6.4			59	4.68 (0.510)	4.7 (4.3, 5.0)	4.0, 6.7						
Change from baseline	66	-0.21 (0.355)	-0.1 (-0.5, 0.0)	-1.1, 0.6	-0.20 (0.050)	(-0.30, -0.10)	59	-0.60 (0.465)	-0.7 (-1.0, -0.2)	-1.6, 0.5	-0.60 (0.053)	(-0.71, -0.50)	-0.40 (-0.54, -0.26)	<.0001	-0.96 (-1.33, -0.59)	
Percent change from baseline	66	-3.90 (6.605)	-2.8 (-8.5, 0.0)	-21.6, 11.3			59	-11.26 (8.507)	-13.0 (-18.0, -4.1)	-28.6, 8.1						
Day 3 / 0-hr Pre-dose																
Absolute value	66	5.10 (0.482)	5.1 (4.8, 5.3)	3.9, 6.3			59	4.50 (0.471)	4.4 (4.2, 4.9)	3.4, 5.5						
Change from baseline	66	-0.24 (0.375)	-0.2 (-0.5, 0.0)	-1.0, 0.7	-0.24 (0.050)	(-0.34, -0.14)	59	-0.78 (0.466)	-0.8 (-1.1, -0.4)	-1.9, 0.2	-0.79 (0.053)	(-0.89, -0.68)	-0.55 (-0.70, -0.41)	<.0001	-1.29 (-1.68, -0.91)	
Percent change from baseline	66	-4.43 (7.057)	-4.1 (-9.8, 0.0)	-18.2, 14.0			59	-14.72 (8.458)	-15.7 (-21.0, -7.7)	-33.9, 3.9						
No																
Baseline																
Absolute value	92	5.28 (0.341)	5.2 (5.1, 5.6)	4.5, 6.2			84	5.24 (0.329)	5.2 (5.0, 5.4)	4.5, 6.1						
Day 1 / 1-hr Post-dose 1																
Absolute value	92	5.26 (0.572)	5.2 (4.9, 5.8)	3.8, 6.5			84	5.11 (0.475)	5.1 (4.8, 5.4)	3.9, 6.6						
Change from baseline	92	-0.02 (0.410)	0.0 (-0.2, 0.2)	-1.7, 1.0	-0.01 (0.042)	(-0.09, 0.07)	84	-0.13 (0.360)	-0.1 (-0.4, 0.1)	-1.0, 0.9	-0.13 (0.044)	(-0.22, -0.04)	-0.12 (-0.24, -0.00)	0.0496	-0.29 (-0.58, 0.01)	
Percent change from baseline	92	-0.36 (7.683)	0.0 (-4.0, 3.8)	-30.9, 19.2			84	-2.40 (6.909)	-2.0 (-7.5, 1.9)	-20.0, 16.7						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

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	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Congestive Heart Disease *(contd.)*																
No *(contd.)*																
Day 1 / 2-hr Post-dose 1																
Absolute value	92	5.29 (0.521)	5.3 (4.9, 5.7)	4.0, 6.6			84	5.02 (0.472)	5.0 (4.7, 5.3)	4.0, 6.7						
Change from baseline	92	0.02 (0.443)	0.0 (-0.3, 0.3)	-1.5, 1.0	0.02 (0.042)	(-0.06, 0.11)	84	-0.22 (0.344)	-0.2 (-0.5, 0.0)	-1.0, 0.6	-0.22 (0.044)	(-0.31, -0.13)	-0.24 (-0.36, -0.12)	<.0001	-0.59 (-0.89, -0.29)	
Percent change from baseline	92	0.45 (8.341)	0.0 (-5.8, 5.9)	-27.3, 22.2			84	-4.12 (6.491)	-3.7 (-8.2, 0.0)	-19.2, 11.1						
Day 1 / 4-hr Post-dose 1																
Absolute value	92	5.05 (0.482)	5.0 (4.7, 5.3)	4.1, 6.3			84	4.87 (0.461)	4.8 (4.5, 5.2)	3.8, 6.1						
Change from baseline	92	-0.22 (0.433)	-0.2 (-0.5, 0.0)	-1.4, 0.9	-0.22 (0.043)	(-0.31, -0.14)	84	-0.37 (0.420)	-0.3 (-0.6, -0.0)	-1.5, 0.7	-0.38 (0.045)	(-0.47, -0.29)	-0.16 (-0.28, -0.03)	0.0135	-0.35 (-0.64, -0.05)	
Percent change from baseline	92	-4.15 (8.123)	-4.0 (-9.3, 0.0)	-25.5, 20.0			84	-7.01 (7.972)	-6.2 (-12.1, -0.9)	-27.3, 13.7						
Day 2 / 0-hr Pre-dose																
Absolute value	92	5.08 (0.466)	5.0 (4.8, 5.3)	4.0, 6.3			81	4.70 (0.382)	4.7 (4.5, 5.0)	3.9, 6.2						
Change from baseline	92	-0.20 (0.370)	-0.2 (-0.4, 0.0)	-1.4, 0.7	-0.19 (0.037)	(-0.27, -0.12)	81	-0.53 (0.355)	-0.6 (-0.7, -0.3)	-1.3, 0.1	-0.54 (0.039)	(-0.61, -0.46)	-0.34 (-0.45, -0.24)	<.0001	-0.92 (-1.23, -0.60)	
Percent change from baseline	92	-3.72 (6.961)	-4.0 (-8.1, 0.9)	-25.5, 13.7			81	-10.04 (6.503)	-10.6 (-13.2, -5.9)	-25.0, 2.2						
Day 2 / 1-hr Post-dose 1																
Absolute value	91	5.05 (0.527)	5.0 (4.6, 5.4)	4.1, 6.3			81	4.63 (0.444)	4.6 (4.3, 5.0)	3.5, 5.6						
Change from baseline	91	-0.22 (0.492)	-0.2 (-0.5, 0.1)	-1.6, 1.1	-0.21 (0.048)	(-0.30, -0.12)	81	-0.61 (0.445)	-0.6 (-0.9, -0.3)	-1.9, 0.5	-0.62 (0.050)	(-0.71, -0.52)	-0.41 (-0.54, -0.27)	<.0001	-0.83 (-1.14, -0.52)	
Percent change from baseline	91	-4.04 (9.188)	-3.8 (-10.0, 2.0)	-25.8, 21.6			81	-11.46 (8.309)	-12.5 (-16.4, -5.6)	-34.5, 11.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	91	5.04 (0.490)	5.0 (4.7, 5.4)	4.0, 6.2			81	4.61 (0.361)	4.6 (4.3, 4.9)	3.7, 5.3						
Change from baseline	91	-0.23 (0.495)	-0.3 (-0.6, 0.1)	-1.4, 1.0	-0.22 (0.044)	(-0.31, -0.14)	81	-0.63 (0.388)	-0.6 (-0.8, -0.4)	-1.8, 0.2	-0.63 (0.047)	(-0.73, -0.54)	-0.41 (-0.54, -0.28)	<.0001	-0.89 (-1.20, -0.57)	
Percent change from baseline	91	-4.22 (9.301)	-5.4 (-11.5, 2.0)	-22.6, 21.3			81	-11.81 (6.996)	-10.7 (-15.7, -7.0)	-32.7, 3.9						
Day 3 / 0-hr Pre-dose																
Absolute value	91	5.01 (0.468)	5.0 (4.6, 5.3)	4.1, 6.4			81	4.54 (0.459)	4.5 (4.2, 4.8)	3.7, 6.2						
Change from baseline	91	-0.26 (0.440)	-0.3 (-0.6, 0.1)	-1.4, 0.8	-0.25 (0.048)	(-0.34, -0.16)	81	-0.70 (0.517)	-0.7 (-1.0, -0.5)	-1.8, 1.0	-0.70 (0.050)	(-0.80, -0.60)	-0.45 (-0.59, -0.32)	<.0001	-0.92 (-1.23, -0.60)	
Percent change from baseline	91	-4.76 (8.254)	-5.7 (-11.3, 2.0)	-24.1, 15.6			81	-13.05 (9.437)	-14.3 (-19.6, -8.8)	-32.7, 19.2						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Diabetes mellitus																0.6524
Yes																
Baseline																
Absolute value	96	5.34 (0.328)	5.3 (5.1, 5.6)	4.7, 6.2			81	5.28 (0.310)	5.2 (5.1, 5.4)	4.8, 6.1						
Day 1 / 1-hr Post-dose 1																
Absolute value	96	5.37 (0.513)	5.3 (5.0, 5.8)	4.4, 6.6			81	5.22 (0.481)	5.2 (4.9, 5.5)	4.1, 6.7						
Change from baseline	96	0.03 (0.343)	0.0 (-0.2, 0.2)	-0.7, 1.1	0.03 (0.037)	(-0.04, 0.10)	81	-0.06 (0.364)	-0.1 (-0.3, 0.1)	-1.3, 0.9	-0.06 (0.040)	(-0.14, 0.02)	-0.09 (-0.20, 0.02)	0.0911	-0.23 (-0.53, 0.06)	
Percent change from baseline	96	0.42 (6.432)	0.0 (-3.8, 4.1)	-13.2, 20.0			81	-1.08 (6.823)	-1.7 (-5.4, 2.0)	-24.1, 16.7						
Day 1 / 2-hr Post-dose 1																
Absolute value	96	5.36 (0.504)	5.3 (4.9, 5.7)	4.3, 6.6			81	5.19 (0.451)	5.2 (4.9, 5.4)	4.3, 6.7						
Change from baseline	96	0.02 (0.380)	0.0 (-0.2, 0.2)	-1.6, 1.0	0.03 (0.038)	(-0.05, 0.10)	81	-0.10 (0.367)	-0.1 (-0.3, 0.1)	-1.1, 0.9	-0.10 (0.042)	(-0.18, -0.02)	-0.13 (-0.24, -0.01)	0.0275	-0.31 (-0.61, -0.01)	
Percent change from baseline	96	0.38 (6.939)	0.0 (-2.9, 4.1)	-27.1, 18.9			81	-1.76 (6.813)	-1.7 (-5.9, 2.0)	-20.4, 17.3						
Day 1 / 4-hr Post-dose 1																
Absolute value	96	5.19 (0.478)	5.1 (4.9, 5.5)	4.2, 6.3			81	4.95 (0.484)	5.0 (4.6, 5.3)	3.8, 6.1						
Change from baseline	96	-0.15 (0.418)	-0.1 (-0.5, 0.1)	-1.3, 0.9	-0.14 (0.045)	(-0.23, -0.05)	81	-0.33 (0.477)	-0.2 (-0.6, 0.0)	-2.2, 0.7	-0.34 (0.048)	(-0.43, -0.24)	-0.20 (-0.33, -0.07)	0.0034	-0.41 (-0.71, -0.12)	
Percent change from baseline	96	-2.65 (7.680)	-2.1 (-8.7, 2.7)	-22.0, 17.3			81	-6.13 (8.756)	-4.2 (-11.1, 0.0)	-36.7, 13.7						
Day 2 / 0-hr Pre-dose																
Absolute value	96	5.16 (0.440)	5.1 (4.8, 5.4)	4.2, 6.3			80	4.78 (0.391)	4.8 (4.5, 5.0)	4.0, 6.2						
Change from baseline	96	-0.18 (0.336)	-0.2 (-0.4, 0.0)	-1.1, 0.8	-0.18 (0.034)	(-0.24, -0.11)	80	-0.50 (0.337)	-0.5 (-0.7, -0.3)	-1.3, 0.4	-0.50 (0.037)	(-0.58, -0.43)	-0.33 (-0.42, -0.23)	<.0001	-0.94 (-1.25, -0.63)	
Percent change from baseline	96	-3.36 (6.216)	-3.8 (-7.5, 0.0)	-18.6, 15.4			80	-9.35 (6.160)	-9.2 (-13.3, -5.7)	-23.6, 7.1						
Day 2 / 1-hr Post-dose 1																
Absolute value	95	5.18 (0.517)	5.2 (4.8, 5.6)	4.0, 6.3			80	4.62 (0.404)	4.6 (4.3, 4.9)	3.6, 5.6						
Change from baseline	95	-0.15 (0.484)	-0.1 (-0.5, 0.2)	-2.2, 1.1	-0.14 (0.045)	(-0.23, -0.05)	80	-0.66 (0.406)	-0.7 (-0.9, -0.4)	-1.9, 0.3	-0.66 (0.049)	(-0.76, -0.56)	-0.52 (-0.65, -0.39)	<.0001	-1.12 (-1.44, -0.80)	
Percent change from baseline	95	-2.72 (8.859)	-2.0 (-9.1, 3.4)	-35.5, 21.6			80	-12.30 (7.499)	-13.3 (-16.5, -7.9)	-34.5, 6.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	95	5.11 (0.484)	5.2 (4.8, 5.5)	4.0, 6.4			80	4.68 (0.382)	4.7 (4.4, 5.0)	3.7, 6.0						
Change from baseline	95	-0.22 (0.436)	-0.2 (-0.5, 0.1)	-1.2, 1.0	-0.21 (0.042)	(-0.29, -0.13)	80	-0.60 (0.404)	-0.7 (-0.9, -0.3)	-1.8, 0.4	-0.61 (0.046)	(-0.70, -0.52)	-0.40 (-0.52, -0.27)	<.0001	-0.91 (-1.22, -0.60)	
Percent change from baseline	95	-4.01 (8.205)	-3.4 (-9.4, 1.8)	-20.7, 21.3			80	-11.28 (7.339)	-12.2 (-16.5, -6.1)	-32.7, 7.1						
Day 3 / 0-hr Pre-dose																
Absolute value	95	5.08 (0.432)	5.1 (4.8, 5.3)	4.2, 6.1			80	4.54 (0.455)	4.4 (4.2, 4.8)	3.7, 6.2						
Change from baseline	95	-0.25 (0.410)	-0.3 (-0.6, 0.1)	-1.0, 0.8	-0.24 (0.045)	(-0.33, -0.15)	80	-0.74 (0.501)	-0.8 (-1.0, -0.5)	-1.8, 1.0	-0.75 (0.049)	(-0.84, -0.65)	-0.50 (-0.64, -0.37)	<.0001	-1.08 (-1.40, -0.77)	
Percent change from baseline	95	-4.55 (7.667)	-5.2 (-10.6, 1.8)	-18.2, 15.1			80	-13.84 (9.111)	-15.3 (-20.0, -9.0)	-32.7, 19.2						
No																
Baseline																
Absolute value	62	5.24 (0.413)	5.1 (5.0, 5.5)	4.5, 6.4			62	5.23 (0.369)	5.2 (5.0, 5.4)	4.5, 6.5						
Day 1 / 1-hr Post-dose 1																
Absolute value	62	5.23 (0.673)	5.2 (4.8, 5.8)	3.8, 6.7			62	5.05 (0.509)	5.0 (4.8, 5.4)	3.9, 6.5						
Change from baseline	62	-0.02 (0.486)	0.0 (-0.3, 0.3)	-1.7, 1.2	-0.02 (0.055)	(-0.13, 0.09)	62	-0.18 (0.350)	-0.2 (-0.4, 0.1)	-1.0, 0.7	-0.18 (0.055)	(-0.29, -0.07)	-0.16 (-0.32, -0.01)	0.0419	-0.37 (-0.73, -0.02)	
Percent change from baseline	62	-0.42 (9.166)	0.0 (-5.9, 5.1)	-30.9, 21.8			62	-3.38 (6.772)	-3.4 (-8.0, 1.8)	-20.0, 13.5						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Diabetes mellitus *(contd.)*																
No *(contd.)*																
Day 1 / 2-hr Post-dose 1																
Absolute value	62	5.21 (0.606)	5.2 (4.8, 5.6)	3.8, 6.7			62	4.93 (0.455)	4.9 (4.6, 5.2)	4.0, 6.4						
Change from baseline	62	-0.03 (0.483)	0.0 (-0.3, 0.3)	-1.5, 1.0	-0.03 (0.052)	(-0.13, 0.07)	62	-0.30 (0.319)	-0.3 (-0.5, -0.1)	-1.0, 0.4	-0.30 (0.052)	(-0.40, -0.19)	-0.27 (-0.41, -0.12)	0.0004	-0.65 (-1.01, -0.29)	
Percent change from baseline	62	-0.52 (9.251)	0.8 (-6.1, 6.0)	-27.3, 22.2			62	-5.61 (6.128)	-4.8 (-9.4, -1.9)	-19.2, 8.0						
Day 1 / 4-hr Post-dose 1																
Absolute value	62	4.91 (0.513)	4.9 (4.6, 5.2)	3.9, 6.1			62	4.81 (0.464)	4.8 (4.5, 5.1)	3.8, 6.5						
Change from baseline	62	-0.33 (0.425)	-0.3 (-0.6, 0.0)	-1.4, 0.9	-0.33 (0.051)	(-0.43, -0.23)	62	-0.42 (0.399)	-0.4 (-0.6, -0.1)	-1.3, 0.3	-0.42 (0.051)	(-0.52, -0.32)	-0.09 (-0.23, 0.05)	0.2111	-0.21 (-0.56, 0.14)	
Percent change from baseline	62	-6.21 (8.117)	-5.9 (-12.2, 0.0)	-25.5, 20.0			62	-7.91 (7.487)	-8.2 (-12.5, -1.9)	-24.0, 6.7						
Day 2 / 0-hr Pre-dose																
Absolute value	62	5.05 (0.489)	5.0 (4.7, 5.4)	4.0, 6.2			60	4.67 (0.431)	4.6 (4.4, 5.0)	3.9, 5.7						
Change from baseline	62	-0.19 (0.405)	-0.2 (-0.4, 0.0)	-1.4, 0.8	-0.19 (0.049)	(-0.28, -0.09)	60	-0.56 (0.398)	-0.6 (-0.8, -0.3)	-1.7, 0.1	-0.56 (0.049)	(-0.66, -0.46)	-0.37 (-0.51, -0.24)	<.0001	-0.92 (-1.29, -0.54)	
Percent change from baseline	62	-3.45 (7.713)	-3.8 (-7.8, 0.0)	-25.5, 17.0			60	-10.50 (7.345)	-10.7 (-14.8, -5.8)	-30.4, 2.2						
Day 2 / 1-hr Post-dose 1																
Absolute value	62	4.87 (0.507)	4.8 (4.5, 5.1)	4.0, 6.1			60	4.53 (0.476)	4.5 (4.2, 4.9)	3.5, 5.4						
Change from baseline	62	-0.38 (0.455)	-0.3 (-0.7, -0.1)	-1.6, 0.9	-0.38 (0.057)	(-0.49, -0.26)	60	-0.70 (0.477)	-0.8 (-1.0, -0.3)	-2.1, 0.5	-0.71 (0.057)	(-0.82, -0.60)	-0.33 (-0.49, -0.17)	<.0001	-0.70 (-1.06, -0.33)	
Percent change from baseline	62	-7.03 (8.387)	-6.1 (-12.7, -2.0)	-25.8, 17.6			60	-13.24 (8.856)	-14.1 (-18.6, -5.8)	-37.5, 11.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	62	5.02 (0.535)	5.0 (4.6, 5.4)	4.0, 6.3			60	4.59 (0.486)	4.5 (4.3, 5.0)	3.9, 6.7						
Change from baseline	62	-0.23 (0.450)	-0.2 (-0.5, 0.1)	-1.4, 0.9	-0.22 (0.055)	(-0.33, -0.12)	60	-0.63 (0.444)	-0.6 (-1.1, -0.3)	-1.6, 0.5	-0.64 (0.056)	(-0.75, -0.53)	-0.42 (-0.57, -0.26)	<.0001	-0.91 (-1.28, -0.54)	
Percent change from baseline	62	-4.19 (8.392)	-3.9 (-10.0, 1.9)	-22.6, 17.6			60	-11.98 (8.079)	-11.3 (-20.2, -6.8)	-28.6, 8.1						
Day 3 / 0-hr Pre-dose																
Absolute value	62	4.99 (0.532)	5.1 (4.6, 5.2)	3.9, 6.4			60	4.50 (0.477)	4.4 (4.2, 4.9)	3.4, 5.9						
Change from baseline	62	-0.25 (0.420)	-0.3 (-0.6, 0.1)	-1.4, 0.7	-0.25 (0.056)	(-0.36, -0.14)	60	-0.72 (0.495)	-0.7 (-1.2, -0.4)	-1.9, 0.6	-0.73 (0.057)	(-0.84, -0.62)	-0.48 (-0.64, -0.32)	<.0001	-1.03 (-1.40, -0.65)	
Percent change from baseline	62	-4.74 (7.940)	-5.1 (-10.9, 2.0)	-24.1, 15.6			60	-13.64 (9.028)	-14.0 (-20.9, -7.5)	-33.9, 11.3						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Lokelma

Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
RAASi Medications																0.5814
Yes																
Baseline																
Absolute value	101	5.28 (0.365)	5.2 (5.0, 5.6)	4.5, 6.2			96	5.26 (0.314)	5.3 (5.1, 5.4)	4.5, 6.5						
Day 1 / 1-hr Post-dose 1																
Absolute value	101	5.24 (0.553)	5.2 (4.8, 5.6)	4.1, 6.5			96	5.16 (0.503)	5.2 (4.8, 5.4)	4.0, 6.7						
Change from baseline	101	-0.04 (0.338)	0.0 (-0.3, 0.1)	-0.7, 0.9	-0.04 (0.037)	(-0.12, 0.03)	96	-0.10 (0.387)	-0.1 (-0.3, 0.1)	-1.3, 0.9	-0.10 (0.038)	(-0.18, -0.03)	-0.06 (-0.16, 0.04)	0.2600	-0.16 (-0.44, 0.12)	
Percent change from baseline	101	-0.93 (6.408)	0.0 (-5.7, 2.2)	-13.7, 17.3			96	-1.93 (7.315)	-1.9 (-6.0, 2.0)	-24.1, 16.7						
Day 1 / 2-hr Post-dose 1																
Absolute value	101	5.29 (0.560)	5.3 (4.8, 5.7)	3.8, 6.6			96	5.10 (0.471)	5.1 (4.8, 5.4)	4.2, 6.7						
Change from baseline	101	0.01 (0.400)	0.0 (-0.3, 0.3)	-0.9, 1.0	0.01 (0.040)	(-0.07, 0.09)	96	-0.17 (0.393)	-0.1 (-0.3, 0.1)	-1.1, 0.9	-0.17 (0.041)	(-0.25, -0.09)	-0.18 (-0.29, -0.06)	0.0023	-0.44 (-0.72, -0.16)	
Percent change from baseline	101	0.12 (7.625)	0.0 (-5.7, 5.7)	-19.1, 22.2			96	-3.10 (7.347)	-2.0 (-6.1, 1.9)	-20.4, 17.3						
Day 1 / 4-hr Post-dose 1																
Absolute value	101	5.09 (0.539)	5.0 (4.7, 5.4)	3.9, 6.3			96	4.89 (0.500)	4.9 (4.5, 5.3)	3.8, 6.5						
Change from baseline	101	-0.19 (0.414)	-0.2 (-0.5, 0.0)	-1.2, 0.9	-0.19 (0.043)	(-0.28, -0.11)	96	-0.38 (0.465)	-0.3 (-0.6, -0.1)	-2.2, 0.7	-0.38 (0.045)	(-0.47, -0.29)	-0.19 (-0.31, -0.06)	0.0029	-0.42 (-0.70, -0.14)	
Percent change from baseline	101	-3.66 (7.854)	-3.8 (-8.9, 0.0)	-20.7, 20.0			96	-7.11 (8.598)	-6.2 (-11.9, -1.8)	-36.7, 13.7						
Day 2 / 0-hr Pre-dose																
Absolute value	101	5.12 (0.453)	5.1 (4.8, 5.4)	4.1, 6.2			93	4.75 (0.430)	4.7 (4.5, 5.0)	3.9, 6.2						
Change from baseline	101	-0.17 (0.341)	-0.2 (-0.4, 0.0)	-1.4, 0.8	-0.17 (0.035)	(-0.24, -0.10)	93	-0.52 (0.372)	-0.5 (-0.8, -0.3)	-1.3, 0.4	-0.52 (0.036)	(-0.59, -0.45)	-0.35 (-0.45, -0.25)	<.0001	-0.98 (-1.27, -0.68)	
Percent change from baseline	101	-3.10 (6.432)	-3.6 (-7.1, 0.0)	-25.5, 17.0			93	-9.72 (6.923)	-10.0 (-13.7, -5.7)	-25.0, 7.1						
Day 2 / 1-hr Post-dose 1																
Absolute value	101	5.06 (0.551)	5.0 (4.6, 5.5)	4.0, 6.3			93	4.59 (0.442)	4.6 (4.3, 4.9)	3.5, 5.6						
Change from baseline	101	-0.23 (0.443)	-0.2 (-0.5, 0.1)	-2.2, 0.8	-0.22 (0.043)	(-0.31, -0.14)	93	-0.67 (0.432)	-0.7 (-0.9, -0.4)	-1.7, 0.5	-0.67 (0.045)	(-0.76, -0.59)	-0.45 (-0.57, -0.33)	<.0001	-1.01 (-1.31, -0.72)	
Percent change from baseline	101	-4.26 (8.160)	-3.8 (-9.3, 1.8)	-35.5, 16.0			93	-12.60 (8.109)	-13.5 (-18.0, -7.5)	-30.9, 11.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	101	5.05 (0.505)	5.0 (4.7, 5.4)	4.0, 6.4			93	4.62 (0.429)	4.6 (4.3, 5.0)	3.7, 6.0						
Change from baseline	101	-0.23 (0.387)	-0.2 (-0.5, 0.0)	-1.2, 0.8	-0.23 (0.039)	(-0.31, -0.16)	93	-0.65 (0.408)	-0.7 (-0.9, -0.4)	-1.8, 0.4	-0.65 (0.040)	(-0.73, -0.57)	-0.42 (-0.53, -0.31)	<.0001	-1.04 (-1.34, -0.74)	
Percent change from baseline	101	-4.40 (7.246)	-3.9 (-9.4, 0.0)	-20.7, 16.3			93	-12.17 (7.533)	-12.2 (-17.6, -7.0)	-32.7, 7.1						
Day 3 / 0-hr Pre-dose																
Absolute value	101	5.03 (0.477)	5.1 (4.7, 5.3)	3.9, 6.4			93	4.54 (0.483)	4.4 (4.2, 4.9)	3.4, 6.2						
Change from baseline	101	-0.25 (0.420)	-0.3 (-0.6, 0.1)	-1.4, 0.7	-0.25 (0.044)	(-0.34, -0.16)	93	-0.73 (0.491)	-0.7 (-1.1, -0.5)	-1.8, 1.0	-0.73 (0.046)	(-0.82, -0.64)	-0.48 (-0.61, -0.35)	<.0001	-1.05 (-1.35, -0.75)	
Percent change from baseline	101	-4.64 (7.881)	-5.2 (-10.6, 1.8)	-24.1, 15.6			93	-13.69 (9.009)	-14.3 (-20.0, -8.3)	-30.2, 19.2						
No																
Baseline																
Absolute value	57	5.34 (0.367)	5.3 (5.1, 5.5)	4.7, 6.4			47	5.24 (0.382)	5.2 (5.0, 5.5)	4.5, 6.2						
Day 1 / 1-hr Post-dose 1																
Absolute value	57	5.44 (0.619)	5.3 (5.1, 5.9)	3.8, 6.7			47	5.12 (0.495)	5.1 (4.8, 5.5)	3.9, 6.5						
Change from baseline	57	0.10 (0.490)	0.1 (-0.2, 0.3)	-1.7, 1.2	0.11 (0.057)	(-0.00, 0.23)	47	-0.12 (0.305)	-0.1 (-0.4, 0.1)	-0.7, 0.6	-0.14 (0.063)	(-0.26, -0.01)	-0.25 (-0.42, -0.08)	0.0043	-0.54 (-0.93, -0.15)	
Percent change from baseline	57	1.90 (9.148)	2.0 (-3.7, 6.2)	-30.9, 21.8			47	-2.37 (5.929)	-2.0 (-7.4, 1.9)	-15.2, 12.0						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
RAASi Medications *(contd.)*																
No *(contd.)*																
Day 1 / 2-hr Post-dose 1																
Absolute value	57	5.32 (0.534)	5.3 (5.0, 5.7)	4.0, 6.7			47	5.03 (0.465)	5.1 (4.7, 5.4)	4.0, 6.1						
Change from baseline	57	-0.01 (0.464)	0.0 (-0.2, 0.2)	-1.6, 1.0	-0.00 (0.052)	(-0.10, 0.10)	47	-0.21 (0.281)	-0.2 (-0.4, 0.0)	-0.8, 0.4	-0.23 (0.057)	(-0.34, -0.11)	-0.23 (-0.38, -0.07)	0.0042	-0.52 (-0.91, -0.12)	
Percent change from baseline	57	-0.13 (8.462)	0.0 (-3.5, 4.2)	-27.3, 18.9			47	-4.11 (5.448)	-4.1 (-7.8, 0.0)	-15.4, 8.0						
Day 1 / 4-hr Post-dose 1																
Absolute value	57	5.07 (0.457)	5.1 (4.8, 5.4)	4.1, 6.0			47	4.89 (0.438)	4.8 (4.6, 5.2)	3.9, 5.9						
Change from baseline	57	-0.26 (0.455)	-0.3 (-0.6, 0.0)	-1.4, 0.8	-0.25 (0.054)	(-0.36, -0.14)	47	-0.35 (0.407)	-0.4 (-0.6, 0.0)	-1.3, 0.3	-0.36 (0.059)	(-0.48, -0.24)	-0.11 (-0.27, 0.05)	0.1720	-0.20 (-0.58, 0.19)	
Percent change from baseline	57	-4.74 (8.334)	-5.4 (-10.3, 0.0)	-25.5, 15.7			47	-6.48 (7.558)	-6.8 (-12.2, 0.0)	-23.5, 6.0						
Day 2 / 0-hr Pre-dose																
Absolute value	57	5.12 (0.479)	5.0 (4.8, 5.4)	4.0, 6.3			47	4.70 (0.372)	4.7 (4.4, 5.1)	3.9, 5.4						
Change from baseline	57	-0.21 (0.401)	-0.2 (-0.5, 0.0)	-1.1, 0.7	-0.20 (0.048)	(-0.30, -0.11)	47	-0.54 (0.350)	-0.5 (-0.7, -0.3)	-1.7, 0.1	-0.55 (0.052)	(-0.66, -0.45)	-0.35 (-0.49, -0.21)	<.0001	-0.86 (-1.26, -0.45)	
Percent change from baseline	57	-3.92 (7.485)	-3.9 (-9.1, 0.0)	-18.6, 13.7			47	-10.10 (6.276)	-10.6 (-13.0, -6.0)	-30.4, 2.0						
Day 2 / 1-hr Post-dose 1																
Absolute value	56	5.06 (0.508)	5.0 (4.6, 5.5)	4.2, 6.2			47	4.56 (0.432)	4.6 (4.2, 4.9)	3.5, 5.2						
Change from baseline	56	-0.27 (0.555)	-0.3 (-0.6, 0.1)	-1.6, 1.1	-0.25 (0.064)	(-0.37, -0.12)	47	-0.69 (0.450)	-0.7 (-0.9, -0.4)	-2.1, 0.3	-0.70 (0.070)	(-0.84, -0.56)	-0.45 (-0.64, -0.27)	<.0001	-0.83 (-1.23, -0.42)	
Percent change from baseline	56	-4.72 (10.182)	-5.9 (-11.5, 1.9)	-25.8, 21.6			47	-12.89 (8.140)	-13.0 (-17.2, -7.8)	-37.5, 6.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	56	5.13 (0.506)	5.1 (4.8, 5.5)	4.0, 6.1			47	4.69 (0.433)	4.7 (4.4, 5.0)	4.0, 6.7						
Change from baseline	56	-0.20 (0.527)	-0.2 (-0.6, 0.2)	-1.4, 1.0	-0.18 (0.061)	(-0.30, -0.06)	47	-0.56 (0.442)	-0.5 (-0.8, -0.3)	-1.6, 0.5	-0.57 (0.067)	(-0.70, -0.44)	-0.39 (-0.57, -0.21)	<.0001	-0.73 (-1.13, -0.33)	
Percent change from baseline	56	-3.52 (9.860)	-2.7 (-11.4, 3.5)	-22.6, 21.3			47	-10.41 (7.810)	-9.6 (-14.8, -6.0)	-28.6, 8.1						
Day 3 / 0-hr Pre-dose																
Absolute value	56	5.07 (0.473)	5.1 (4.7, 5.3)	4.2, 6.3			47	4.50 (0.425)	4.5 (4.2, 4.8)	3.7, 5.3						
Change from baseline	56	-0.25 (0.404)	-0.3 (-0.6, 0.1)	-1.0, 0.8	-0.23 (0.057)	(-0.34, -0.12)	47	-0.74 (0.512)	-0.8 (-1.1, -0.4)	-1.9, 0.2	-0.76 (0.063)	(-0.88, -0.63)	-0.53 (-0.69, -0.36)	<.0001	-1.08 (-1.50, -0.67)	
Percent change from baseline	56	-4.59 (7.583)	-4.9 (-10.9, 1.9)	-17.5, 15.1			47	-13.88 (9.207)	-15.7 (-20.4, -8.6)	-33.9, 4.1						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline eGFR																0.0004
<15																
Baseline																
Absolute value	15	5.41 (0.287)	5.5 (5.2, 5.6)	4.7, 5.8			10	5.50 (0.258)	5.5 (5.3, 5.6)	5.1, 5.9						
Day 1 / 1-hr Post-dose 1																
Absolute value	15	5.51 (0.508)	5.4 (5.1, 5.8)	4.9, 6.6			10	5.30 (0.302)	5.3 (5.1, 5.4)	4.8, 5.8						
Change from baseline	15	0.10 (0.372)	0.0 (-0.1, 0.2)	-0.2, 1.1	0.09 (0.089)	(-0.09, 0.28)	10	-0.20 (0.262)	-0.2 (-0.5, 0.0)	-0.6, 0.1	-0.19 (0.109)	(-0.41, 0.04)	-0.28 (-0.57, 0.01)	0.0595	-0.90 (-1.74, -0.06)	
Percent change from baseline	15	1.80 (6.775)	0.0 (-2.0, 3.6)	-3.8, 20.0			10	-3.58 (4.748)	-2.7 (-8.5, 0.0)	-11.1, 2.0						
Day 1 / 2-hr Post-dose 1																
Absolute value	15	5.51 (0.456)	5.4 (5.2, 5.9)	4.8, 6.4			10	5.33 (0.327)	5.2 (5.1, 5.7)	4.8, 5.8						
Change from baseline	15	0.10 (0.336)	0.0 (0.0, 0.4)	-0.6, 0.8	0.09 (0.084)	(-0.08, 0.26)	10	-0.17 (0.287)	-0.2 (-0.3, 0.1)	-0.7, 0.2	-0.16 (0.103)	(-0.37, 0.05)	-0.25 (-0.53, 0.03)	0.0728	-0.85 (-1.68, -0.02)	
Percent change from baseline	15	1.83 (6.098)	0.0 (0.0, 7.3)	-10.7, 14.3			10	-3.04 (5.114)	-2.7 (-5.6, 1.8)	-11.9, 3.8						
Day 1 / 4-hr Post-dose 1																
Absolute value	15	5.25 (0.444)	5.2 (5.0, 5.4)	4.6, 6.2			10	4.97 (0.383)	4.9 (4.7, 5.3)	4.3, 5.5						
Change from baseline	15	-0.16 (0.381)	-0.1 (-0.5, 0.0)	-0.7, 0.7	-0.17 (0.095)	(-0.37, 0.03)	10	-0.53 (0.356)	-0.5 (-0.8, -0.4)	-1.1, 0.0	-0.52 (0.117)	(-0.76, -0.28)	-0.35 (-0.66, -0.04)	0.0299	-1.00 (-1.84, -0.15)	
Percent change from baseline	15	-2.92 (6.874)	-2.1 (-8.9, 0.0)	-12.7, 12.7			10	-9.59 (6.374)	-8.4 (-14.5, -6.8)	-20.4, 0.0						
Day 2 / 0-hr Pre-dose																
Absolute value	15	5.15 (0.354)	5.1 (4.9, 5.3)	4.7, 5.8			9	4.91 (0.190)	5.0 (4.9, 5.0)	4.6, 5.1						
Change from baseline	15	-0.25 (0.300)	-0.3 (-0.5, 0.0)	-0.8, 0.3	-0.26 (0.071)	(-0.41, -0.11)	9	-0.61 (0.271)	-0.6 (-0.8, -0.4)	-1.0, -0.3	-0.58 (0.093)	(-0.77, -0.39)	-0.32 (-0.56, -0.07)	0.0138	-1.24 (-2.13, -0.34)	
Percent change from baseline	15	-4.61 (5.579)	-5.6 (-9.1, 0.0)	-14.3, 6.4			9	-10.94 (4.457)	-10.7 (-14.8, -7.3)	-16.9, -5.6						
Day 2 / 1-hr Post-dose 1																
Absolute value	15	5.44 (0.346)	5.5 (5.2, 5.6)	4.6, 5.9			9	4.64 (0.309)	4.6 (4.4, 4.8)	4.2, 5.1						
Change from baseline	15	0.03 (0.329)	0.0 (-0.3, 0.3)	-0.5, 0.7	0.02 (0.081)	(-0.15, 0.19)	9	-0.88 (0.331)	-0.9 (-1.0, -0.8)	-1.5, -0.3	-0.84 (0.105)	(-1.06, -0.62)	-0.87 (-1.15, -0.59)	<.0001	-2.76 (-3.90, -1.63)	
Percent change from baseline	15	0.74 (6.378)	0.0 (-5.2, 5.5)	-9.8, 14.9			9	-15.81 (5.630)	-16.4 (-17.9, -13.6)	-25.4, -5.7						
Day 2 / 4-hr Post-dose 1																
Absolute value	15	5.20 (0.457)	5.4 (4.8, 5.5)	4.4, 5.8			9	4.72 (0.415)	4.8 (4.4, 5.0)	4.0, 5.3						
Change from baseline	15	-0.21 (0.538)	0.0 (-0.7, 0.1)	-1.1, 1.0	-0.22 (0.130)	(-0.49, 0.06)	9	-0.80 (0.517)	-1.0 (-1.2, -0.6)	-1.4, 0.2	-0.77 (0.169)	(-1.12, -0.42)	-0.56 (-1.00, -0.11)	0.0169	-1.12 (-2.00, -0.23)	
Percent change from baseline	15	-3.55 (10.305)	0.0 (-13.7, 1.9)	-20.0, 21.3			9	-14.27 (9.335)	-18.5 (-20.3, -10.7)	-25.9, 3.9						
Day 3 / 0-hr Pre-dose																
Absolute value	15	5.24 (0.394)	5.4 (5.0, 5.6)	4.4, 5.8			9	4.49 (0.285)	4.4 (4.3, 4.7)	4.2, 5.0						
Change from baseline	15	-0.17 (0.370)	-0.1 (-0.6, 0.1)	-0.7, 0.4	-0.18 (0.093)	(-0.37, 0.02)	9	-1.03 (0.394)	-1.1 (-1.2, -0.8)	-1.7, -0.3	-1.01 (0.122)	(-1.26, -0.75)	-0.83 (-1.15, -0.51)	<.0001	-2.29 (-3.34, -1.24)	
Percent change from baseline	15	-2.98 (7.023)	-1.9 (-10.7, 1.8)	-13.7, 8.5			9	-18.54 (6.565)	-20.3 (-21.8, -14.3)	-28.8, -5.7						
15-29+																
Baseline																
Absolute value	44	5.40 (0.394)	5.4 (5.1, 5.7)	4.6, 6.4			42	5.40 (0.414)	5.3 (5.1, 5.7)	4.8, 6.5						
Day 1 / 1-hr Post-dose 1																
Absolute value	44	5.52 (0.493)	5.4 (5.1, 6.0)	4.6, 6.5			42	5.39 (0.558)	5.3 (5.0, 5.6)	4.5, 6.7						
Change from baseline	44	0.12 (0.342)	0.1 (-0.1, 0.3)	-0.5, 1.0	0.12 (0.051)	(0.01, 0.22)	42	-0.01 (0.311)	-0.1 (-0.2, 0.1)	-0.6, 0.9	-0.01 (0.053)	(-0.12, 0.09)	-0.13 (-0.28, 0.02)	0.0787	-0.40 (-0.82, 0.03)	
Percent change from baseline	44	2.21 (6.393)	2.0 (-1.8, 5.8)	-9.1, 19.2			42	-0.34 (5.706)	-1.6 (-3.9, 2.0)	-11.1, 16.7						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

Lokelma

Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline eGFR *(contd.)*																
15-29+ *(contd.)*																
Day 1 / 2-hr Post-dose 1																
Absolute value	44	5.54 (0.480)	5.5 (5.2, 6.0)	4.6, 6.7			42	5.34 (0.457)	5.3 (5.0, 5.6)	4.6, 6.7						
Change from baseline	44	0.14 (0.316)	0.2 (-0.1, 0.3)	-0.5, 0.8	0.14 (0.048)	(0.04, 0.23)	42	-0.06 (0.318)	-0.1 (-0.2, 0.1)	-1.1, 0.6	-0.06 (0.049)	(-0.16, 0.03)	-0.20 (-0.34, -0.07)	0.0040	-0.63 (-1.07, -0.20)	
Percent change from baseline	44	2.62 (5.900)	3.4 (-1.7, 5.9)	-9.1, 15.4			42	-1.05 (5.636)	-1.8 (-3.9, 1.9)	-18.0, 11.1						
Day 1 / 4-hr Post-dose 1																
Absolute value	44	5.21 (0.457)	5.2 (4.9, 5.5)	4.3, 6.3			42	5.07 (0.482)	5.1 (4.8, 5.3)	3.8, 6.5						
Change from baseline	44	-0.20 (0.408)	-0.2 (-0.5, 0.0)	-1.0, 0.7	-0.19 (0.063)	(-0.32, -0.07)	42	-0.33 (0.476)	-0.2 (-0.6, 0.0)	-2.2, 0.6	-0.33 (0.064)	(-0.46, -0.21)	-0.14 (-0.32, 0.04)	0.1267	-0.31 (-0.74, 0.11)	
Percent change from baseline	44	-3.45 (7.425)	-4.6 (-9.0, 0.0)	-18.2, 12.5			42	-5.94 (8.197)	-4.1 (-10.0, 0.0)	-36.7, 11.3						
Day 2 / 0-hr Pre-dose																
Absolute value	44	5.26 (0.478)	5.3 (4.9, 5.5)	4.3, 6.2			42	4.88 (0.436)	4.9 (4.5, 5.1)	4.1, 6.2						
Change from baseline	44	-0.15 (0.337)	-0.2 (-0.4, 0.0)	-0.8, 0.8	-0.14 (0.048)	(-0.24, -0.05)	42	-0.52 (0.314)	-0.5 (-0.8, -0.3)	-1.1, 0.1	-0.52 (0.049)	(-0.61, -0.42)	-0.37 (-0.51, -0.24)	<.0001	-1.14 (-1.60, -0.68)	
Percent change from baseline	44	-2.64 (6.186)	-2.6 (-6.9, 0.0)	-13.6, 15.4			42	-9.49 (5.594)	-9.9 (-13.2, -5.9)	-20.4, 2.0						
Day 2 / 1-hr Post-dose 1																
Absolute value	44	5.19 (0.546)	5.1 (4.9, 5.7)	4.0, 6.2			42	4.69 (0.453)	4.7 (4.3, 5.1)	3.6, 5.6						
Change from baseline	44	-0.22 (0.493)	-0.3 (-0.5, 0.1)	-2.2, 0.8	-0.22 (0.065)	(-0.34, -0.09)	42	-0.71 (0.397)	-0.7 (-1.0, -0.4)	-1.9, 0.2	-0.71 (0.066)	(-0.85, -0.58)	-0.50 (-0.68, -0.31)	<.0001	-1.11 (-1.56, -0.66)	
Percent change from baseline	44	-3.86 (8.752)	-4.5 (-9.0, 1.8)	-35.5, 16.0			42	-13.10 (7.097)	-13.6 (-18.0, -8.0)	-34.5, 4.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	44	5.20 (0.464)	5.2 (4.8, 5.7)	4.5, 6.4			42	4.79 (0.490)	4.8 (4.4, 5.1)	4.0, 6.7						
Change from baseline	44	-0.20 (0.379)	-0.2 (-0.5, 0.0)	-0.9, 0.6	-0.20 (0.057)	(-0.31, -0.09)	42	-0.61 (0.413)	-0.7 (-0.9, -0.3)	-1.4, 0.5	-0.61 (0.059)	(-0.73, -0.50)	-0.41 (-0.58, -0.25)	<.0001	-1.04 (-1.49, -0.59)	
Percent change from baseline	44	-3.58 (6.860)	-2.7 (-8.9, 0.0)	-15.8, 11.5			42	-11.23 (7.256)	-12.6 (-16.4, -6.0)	-24.1, 8.1						
Day 3 / 0-hr Pre-dose																
Absolute value	44	5.15 (0.421)	5.2 (4.9, 5.3)	4.4, 6.3			42	4.53 (0.407)	4.6 (4.2, 4.8)	3.7, 5.5						
Change from baseline	44	-0.25 (0.405)	-0.3 (-0.6, 0.0)	-1.0, 0.7	-0.25 (0.057)	(-0.36, -0.14)	42	-0.87 (0.423)	-0.9 (-1.1, -0.5)	-1.8, 0.0	-0.87 (0.059)	(-0.99, -0.76)	-0.62 (-0.79, -0.46)	<.0001	-1.50 (-1.98, -1.02)	
Percent change from baseline	44	-4.41 (7.476)	-5.3 (-10.2, 0.9)	-17.5, 14.0			42	-15.93 (7.213)	-17.1 (-20.4, -10.2)	-32.7, 0.0						
30-59+																
Baseline																
Absolute value	61	5.29 (0.368)	5.2 (5.1, 5.6)	4.5, 5.9			50	5.23 (0.255)	5.2 (5.0, 5.4)	4.8, 5.9						
Day 1 / 1-hr Post-dose 1																
Absolute value	61	5.35 (0.601)	5.3 (4.9, 5.8)	4.1, 6.7			50	5.08 (0.405)	5.0 (4.9, 5.3)	4.1, 6.0						
Change from baseline	61	0.07 (0.380)	0.0 (-0.2, 0.3)	-0.6, 1.2	0.07 (0.050)	(-0.03, 0.17)	50	-0.15 (0.381)	-0.1 (-0.3, 0.1)	-1.3, 0.7	-0.15 (0.055)	(-0.26, -0.04)	-0.22 (-0.37, -0.07)	0.0036	-0.56 (-0.94, -0.18)	
Percent change from baseline	61	1.10 (7.178)	0.0 (-3.8, 5.2)	-12.8, 21.8			50	-2.75 (7.202)	-2.0 (-6.2, 1.9)	-24.1, 13.5						
Day 1 / 2-hr Post-dose 1																
Absolute value	61	5.29 (0.574)	5.3 (4.9, 5.6)	3.8, 6.6			50	4.96 (0.376)	5.0 (4.7, 5.3)	4.2, 5.5						
Change from baseline	61	0.00 (0.435)	0.0 (-0.2, 0.2)	-1.6, 1.0	0.01 (0.052)	(-0.09, 0.11)	50	-0.28 (0.372)	-0.3 (-0.5, 0.0)	-1.1, 0.4	-0.28 (0.058)	(-0.39, -0.17)	-0.29 (-0.44, -0.13)	0.0003	-0.69 (-1.07, -0.30)	
Percent change from baseline	61	0.08 (8.158)	0.0 (-3.8, 3.8)	-27.1, 22.2			50	-5.17 (7.054)	-4.9 (-9.6, 0.0)	-20.4, 7.8						
Day 1 / 4-hr Post-dose 1																
Absolute value	61	5.03 (0.542)	4.9 (4.6, 5.4)	3.9, 6.2			50	4.80 (0.482)	4.8 (4.5, 5.2)	3.9, 5.9						
Change from baseline	61	-0.25 (0.414)	-0.2 (-0.5, 0.0)	-1.3, 0.9	-0.25 (0.054)	(-0.36, -0.14)	50	-0.44 (0.429)	-0.5 (-0.7, -0.1)	-1.5, 0.3	-0.44 (0.060)	(-0.56, -0.32)	-0.19 (-0.35, -0.03)	0.0196	-0.44 (-0.81, -0.06)	

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

Lokelma

Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline eGFR *(contd.)*																
30-59+ *(contd.)*																
Day 1 / 4-hr Post-dose 1 *(contd.)*																
Percent change from baseline	61	-4.77 (7.850)	-4.2 (-9.3, 0.0)	-22.0, 20.0			50	-8.32 (8.110)	-8.7 (-13.2, -1.8)	-27.3, 5.9						
Day 2 / 0-hr Pre-dose																
Absolute value	61	5.16 (0.451)	5.1 (4.8, 5.5)	4.1, 6.3			48	4.65 (0.414)	4.6 (4.4, 5.0)	3.9, 6.0						
Change from baseline	61	-0.12 (0.358)	-0.1 (-0.3, 0.1)	-1.1, 0.8	-0.12 (0.048)	(-0.21, -0.02)	48	-0.58 (0.409)	-0.6 (-0.8, -0.3)	-1.7, 0.4	-0.59 (0.054)	(-0.69, -0.48)	-0.47 (-0.61, -0.33)	<.0001	-1.20 (-1.61, -0.79)	
Percent change from baseline	61	-2.23 (6.732)	-2.1 (-6.0, 1.7)	-18.6, 17.0			48	-10.99 (7.539)	-12.2 (-15.1, -5.8)	-30.4, 7.1						
Day 2 / 1-hr Post-dose 1																
Absolute value	60	5.08 (0.527)	5.0 (4.7, 5.5)	4.0, 6.3			48	4.51 (0.436)	4.6 (4.2, 4.8)	3.5, 5.4						
Change from baseline	60	-0.19 (0.454)	-0.2 (-0.5, 0.2)	-1.5, 1.1	-0.18 (0.058)	(-0.30, -0.07)	48	-0.73 (0.459)	-0.8 (-1.0, -0.5)	-2.1, 0.3	-0.74 (0.065)	(-0.86, -0.61)	-0.55 (-0.72, -0.38)	<.0001	-1.17 (-1.58, -0.76)	
Percent change from baseline	60	-3.58 (8.426)	-3.4 (-9.8, 3.4)	-25.4, 21.6			48	-13.74 (8.521)	-14.4 (-18.6, -8.7)	-37.5, 6.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	60	5.06 (0.564)	5.1 (4.6, 5.5)	4.0, 6.3			48	4.54 (0.417)	4.5 (4.3, 4.8)	3.7, 6.0						
Change from baseline	60	-0.21 (0.433)	-0.2 (-0.5, 0.1)	-1.2, 0.8	-0.20 (0.056)	(-0.31, -0.09)	48	-0.69 (0.441)	-0.7 (-0.9, -0.4)	-1.8, 0.4	-0.70 (0.062)	(-0.82, -0.58)	-0.50 (-0.66, -0.33)	<.0001	-1.09 (-1.50, -0.68)	
Percent change from baseline	60	-4.04 (8.145)	-3.9 (-10.1, 1.9)	-21.6, 15.1			48	-13.01 (8.076)	-13.6 (-18.0, -7.9)	-32.7, 7.1						
Day 3 / 0-hr Pre-dose																
Absolute value	60	5.06 (0.496)	5.1 (4.7, 5.3)	3.9, 6.4			48	4.45 (0.508)	4.3 (4.2, 4.7)	3.4, 6.2						
Change from baseline	60	-0.22 (0.384)	-0.2 (-0.5, 0.1)	-1.0, 0.7	-0.21 (0.058)	(-0.32, -0.09)	48	-0.79 (0.529)	-0.8 (-1.2, -0.5)	-1.9, 1.0	-0.80 (0.065)	(-0.92, -0.67)	-0.59 (-0.76, -0.42)	<.0001	-1.25 (-1.67, -0.84)	
Percent change from baseline	60	-4.06 (7.350)	-3.9 (-9.6, 2.0)	-18.2, 15.6			48	-14.90 (9.864)	-15.7 (-22.2, -9.4)	-33.9, 19.2						
>=60																
Baseline																
Absolute value	38	5.17 (0.315)	5.1 (5.0, 5.3)	4.7, 6.2			41	5.08 (0.253)	5.1 (4.9, 5.3)	4.5, 5.6						
Day 1 / 1-hr Post-dose 1																
Absolute value	38	4.93 (0.506)	4.9 (4.6, 5.2)	3.8, 5.9			41	4.95 (0.483)	4.9 (4.7, 5.3)	3.9, 5.9						
Change from baseline	38	-0.24 (0.428)	-0.2 (-0.4, 0.0)	-1.7, 0.6	-0.23 (0.069)	(-0.36, -0.09)	41	-0.13 (0.397)	-0.1 (-0.5, 0.1)	-1.0, 0.7	-0.15 (0.066)	(-0.28, -0.02)	0.08 (-0.12, 0.27)	0.4335	0.26 (-0.18, 0.71)	
Percent change from baseline	38	-4.65 (8.109)	-4.1 (-7.8, 0.0)	-30.9, 11.3			41	-2.67 (7.812)	-2.0 (-9.4, 2.2)	-20.0, 14.3						
Day 1 / 2-hr Post-dose 1																
Absolute value	38	4.96 (0.441)	4.8 (4.6, 5.3)	4.0, 5.8			41	4.89 (0.476)	4.8 (4.5, 5.2)	4.0, 6.1						
Change from baseline	38	-0.21 (0.471)	-0.3 (-0.5, 0.1)	-1.5, 0.7	-0.19 (0.068)	(-0.32, -0.05)	41	-0.19 (0.376)	-0.2 (-0.5, 0.1)	-0.8, 0.9	-0.21 (0.065)	(-0.34, -0.08)	-0.02 (-0.21, 0.17)	0.8341	0.03 (-0.41, 0.47)	
Percent change from baseline	38	-3.77 (8.888)	-5.7 (-9.8, 1.9)	-27.3, 13.7			41	-3.84 (7.335)	-4.0 (-9.3, 1.9)	-16.0, 17.3						
Day 1 / 4-hr Post-dose 1																
Absolute value	38	4.95 (0.507)	5.0 (4.5, 5.3)	4.1, 6.1			41	4.80 (0.452)	4.8 (4.5, 5.2)	3.8, 5.8						
Change from baseline	38	-0.22 (0.501)	-0.2 (-0.6, 0.1)	-1.4, 0.9	-0.20 (0.074)	(-0.35, -0.05)	41	-0.29 (0.444)	-0.3 (-0.6, 0.0)	-1.2, 0.7	-0.30 (0.071)	(-0.44, -0.16)	-0.10 (-0.31, 0.10)	0.3249	-0.15 (-0.59, 0.29)	
Percent change from baseline	38	-4.04 (9.450)	-3.9 (-11.8, 2.0)	-25.5, 17.3			41	-5.52 (8.704)	-5.9 (-12.0, 0.0)	-24.0, 13.7						
Day 2 / 0-hr Pre-dose																
Absolute value	38	4.87 (0.410)	4.8 (4.7, 5.1)	4.0, 5.8			41	4.64 (0.369)	4.7 (4.4, 4.8)	3.9, 5.3						
Change from baseline	38	-0.30 (0.403)	-0.3 (-0.6, -0.1)	-1.4, 0.7	-0.28 (0.059)	(-0.40, -0.17)	41	-0.44 (0.368)	-0.4 (-0.6, -0.2)	-1.3, 0.2	-0.46 (0.057)	(-0.57, -0.35)	-0.18 (-0.34, -0.01)	0.0349	-0.37 (-0.82, 0.07)	
Percent change from baseline	38	-5.66 (7.667)	-5.9 (-10.7, -2.0)	-25.5, 13.7			41	-8.64 (7.026)	-8.2 (-11.8, -4.1)	-25.0, 3.9						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline eGFR *(contd.)*																
>=60 *(contd.)*																
Day 2 / 1-hr Post-dose 1																
Absolute value	38	4.72 (0.415)	4.7 (4.4, 5.0)	4.1, 6.0			41	4.55 (0.438)	4.6 (4.2, 4.9)	3.5, 5.3						
Change from baseline	38	-0.45 (0.508)	-0.5 (-0.8, -0.2)	-1.6, 0.9	-0.43 (0.071)	(-0.58, -0.29)	41	-0.53 (0.444)	-0.6 (-0.9, -0.2)	-1.5, 0.5	-0.55 (0.069)	(-0.69, -0.41)	-0.12 (-0.31, 0.08)	0.2429	-0.18 (-0.62, 0.27)	
Percent change from baseline	38	-8.43 (9.374)	-9.3 (-15.4, -3.8)	-25.8, 17.6			41	-10.40 (8.669)	-11.5 (-16.7, -3.9)	-30.0, 11.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	38	4.90 (0.427)	4.9 (4.7, 5.1)	4.0, 6.0			41	4.59 (0.345)	4.6 (4.3, 4.9)	3.9, 5.2						
Change from baseline	38	-0.27 (0.490)	-0.3 (-0.6, 0.0)	-1.4, 0.9	-0.25 (0.063)	(-0.38, -0.13)	41	-0.50 (0.360)	-0.5 (-0.7, -0.2)	-1.2, 0.1	-0.51 (0.061)	(-0.63, -0.39)	-0.26 (-0.44, -0.09)	0.0041	-0.54 (-0.99, -0.09)	
Percent change from baseline	38	-4.94 (9.239)	-5.9 (-10.9, 0.0)	-22.6, 17.6			41	-9.67 (6.860)	-9.3 (-13.5, -4.4)	-23.1, 2.0						
Day 3 / 0-hr Pre-dose																
Absolute value	38	4.83 (0.462)	4.8 (4.5, 5.1)	4.2, 6.1			41	4.62 (0.489)	4.7 (4.2, 5.0)	3.8, 5.9						
Change from baseline	38	-0.34 (0.477)	-0.4 (-0.7, 0.0)	-1.4, 0.8	-0.32 (0.072)	(-0.47, -0.18)	41	-0.47 (0.443)	-0.5 (-0.8, -0.2)	-1.4, 0.6	-0.48 (0.070)	(-0.62, -0.34)	-0.16 (-0.36, 0.04)	0.1194	-0.27 (-0.72, 0.17)	
Percent change from baseline	38	-6.40 (8.869)	-8.2 (-14.0, 0.0)	-24.1, 15.1			41	-9.15 (8.629)	-9.6 (-15.7, -4.0)	-26.9, 11.3						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Sex																0.3815
Male																
Baseline																
Absolute value	98	5.36 (0.386)	5.3 (5.1, 5.6)	4.5, 6.4			80	5.28 (0.373)	5.3 (5.0, 5.5)	4.5, 6.5						
Day 1 / 1-hr Post-dose 1																
Absolute value	98	5.40 (0.583)	5.3 (5.0, 5.9)	4.1, 6.7			80	5.19 (0.539)	5.2 (4.8, 5.5)	3.9, 6.7						
Change from baseline	98	0.04 (0.374)	0.0 (-0.2, 0.3)	-0.7, 1.2	0.05 (0.038)	(-0.03, 0.12)	80	-0.08 (0.341)	-0.1 (-0.3, 0.1)	-1.0, 0.9	-0.09 (0.042)	(-0.17, -0.01)	-0.14 (-0.25, -0.03)	0.0153	-0.35 (-0.65, -0.05)	
Percent change from baseline	98	0.71 (7.020)	0.0 (-3.8, 5.1)	-13.7, 21.8			80	-1.66 (6.490)	-1.7 (-5.4, 1.9)	-19.2, 16.7						
Day 1 / 2-hr Post-dose 1																
Absolute value	98	5.34 (0.554)	5.3 (4.9, 5.7)	3.8, 6.7			80	5.12 (0.477)	5.2 (4.8, 5.4)	4.0, 6.4						
Change from baseline	98	-0.01 (0.394)	0.0 (-0.3, 0.2)	-1.6, 0.8	-0.01 (0.038)	(-0.08, 0.07)	80	-0.15 (0.345)	-0.1 (-0.3, 0.0)	-1.1, 0.9	-0.16 (0.042)	(-0.24, -0.07)	-0.15 (-0.26, -0.04)	0.0091	-0.37 (-0.67, -0.07)	
Percent change from baseline	98	-0.26 (7.252)	0.0 (-5.5, 4.0)	-27.1, 15.4			80	-2.83 (6.485)	-2.0 (-6.1, 0.9)	-19.2, 17.3						
Day 1 / 4-hr Post-dose 1																
Absolute value	98	5.13 (0.533)	5.1 (4.8, 5.4)	3.9, 6.3			80	4.93 (0.496)	4.9 (4.5, 5.3)	3.8, 6.5						
Change from baseline	98	-0.23 (0.413)	-0.3 (-0.5, 0.0)	-1.3, 0.9	-0.22 (0.043)	(-0.30, -0.14)	80	-0.34 (0.442)	-0.3 (-0.6, 0.0)	-2.2, 0.7	-0.35 (0.047)	(-0.44, -0.25)	-0.13 (-0.25, -0.00)	0.0491	-0.27 (-0.57, 0.03)	
Percent change from baseline	98	-4.18 (7.594)	-4.7 (-9.1, 0.0)	-22.0, 17.3			80	-6.32 (8.071)	-5.4 (-11.5, 0.0)	-36.7, 13.7						
Day 2 / 0-hr Pre-dose																
Absolute value	98	5.13 (0.451)	5.1 (4.8, 5.4)	4.0, 6.3			78	4.74 (0.432)	4.7 (4.5, 5.1)	3.9, 6.0						
Change from baseline	98	-0.23 (0.325)	-0.3 (-0.4, 0.0)	-1.1, 0.8	-0.22 (0.034)	(-0.29, -0.16)	78	-0.53 (0.376)	-0.5 (-0.8, -0.3)	-1.7, 0.4	-0.54 (0.038)	(-0.61, -0.46)	-0.31 (-0.42, -0.21)	<.0001	-0.87 (-1.18, -0.56)	
Percent change from baseline	98	-4.20 (6.032)	-4.6 (-7.8, 0.0)	-18.6, 17.0			78	-9.97 (6.864)	-10.1 (-13.5, -5.8)	-30.4, 7.1						
Day 2 / 1-hr Post-dose 1																
Absolute value	97	5.09 (0.542)	5.0 (4.7, 5.5)	4.0, 6.3			78	4.67 (0.400)	4.7 (4.3, 5.0)	3.5, 5.4						
Change from baseline	97	-0.26 (0.494)	-0.2 (-0.5, 0.1)	-2.2, 1.1	-0.25 (0.046)	(-0.34, -0.16)	78	-0.60 (0.438)	-0.6 (-0.9, -0.3)	-2.1, 0.5	-0.61 (0.051)	(-0.71, -0.51)	-0.36 (-0.49, -0.22)	<.0001	-0.73 (-1.04, -0.42)	
Percent change from baseline	97	-4.74 (8.892)	-4.3 (-10.0, 1.9)	-35.5, 21.6			78	-11.18 (7.990)	-12.2 (-16.4, -5.7)	-37.5, 11.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	97	5.13 (0.485)	5.1 (4.8, 5.5)	4.0, 6.4			78	4.71 (0.460)	4.7 (4.3, 5.0)	4.0, 6.7						
Change from baseline	97	-0.22 (0.397)	-0.2 (-0.5, 0.0)	-1.4, 0.8	-0.22 (0.040)	(-0.30, -0.14)	78	-0.56 (0.413)	-0.5 (-0.8, -0.3)	-1.6, 0.5	-0.57 (0.045)	(-0.66, -0.48)	-0.35 (-0.47, -0.23)	<.0001	-0.84 (-1.15, -0.53)	
Percent change from baseline	97	-4.10 (7.304)	-3.4 (-9.8, 0.0)	-22.6, 16.3			78	-10.57 (7.430)	-10.2 (-15.4, -6.0)	-28.6, 8.1						
Day 3 / 0-hr Pre-dose																
Absolute value	97	5.05 (0.461)	5.1 (4.7, 5.3)	4.1, 6.3			78	4.55 (0.476)	4.4 (4.2, 4.9)	3.7, 6.2						
Change from baseline	97	-0.30 (0.395)	-0.3 (-0.6, 0.0)	-1.4, 0.8	-0.29 (0.044)	(-0.38, -0.21)	78	-0.72 (0.508)	-0.7 (-1.0, -0.5)	-1.9, 1.0	-0.72 (0.049)	(-0.82, -0.63)	-0.43 (-0.56, -0.30)	<.0001	-0.93 (-1.24, -0.61)	
Percent change from baseline	97	-5.53 (7.316)	-5.9 (-10.9, 0.0)	-24.1, 15.1			78	-13.41 (9.120)	-14.4 (-19.6, -8.6)	-33.9, 19.2						
Female																
Baseline																
Absolute value	60	5.21 (0.309)	5.2 (5.0, 5.5)	4.5, 5.8			63	5.23 (0.286)	5.2 (5.0, 5.4)	4.8, 6.1						
Day 1 / 1-hr Post-dose 1																
Absolute value	60	5.16 (0.557)	5.2 (4.8, 5.5)	3.8, 6.5			63	5.10 (0.441)	5.0 (4.8, 5.4)	4.0, 6.6						
Change from baseline	60	-0.05 (0.446)	0.0 (-0.3, 0.2)	-1.7, 1.0	-0.05 (0.055)	(-0.16, 0.06)	63	-0.14 (0.386)	-0.1 (-0.4, 0.1)	-1.3, 0.7	-0.14 (0.053)	(-0.24, -0.03)	-0.09 (-0.24, 0.07)	0.2662	-0.22 (-0.58, 0.13)	
Percent change from baseline	60	-0.93 (8.440)	0.0 (-4.9, 3.9)	-30.9, 18.9			63	-2.61 (7.348)	-2.0 (-7.4, 2.0)	-24.1, 14.3						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Sex *(contd.)*																
Female *(contd.)*																
Day 1 / 2-hr Post-dose 1																
Absolute value	60	5.23 (0.538)	5.2 (4.8, 5.6)	4.0, 6.4			63	5.01 (0.454)	5.0 (4.7, 5.3)	4.2, 6.7						
Change from baseline	60	0.02 (0.468)	0.0 (-0.3, 0.4)	-1.5, 1.0	0.02 (0.055)	(-0.09, 0.13)	63	-0.22 (0.377)	-0.2 (-0.5, 0.1)	-1.1, 0.6	-0.22 (0.054)	(-0.32, -0.11)	-0.24 (-0.39, -0.08)	0.0027	-0.58 (-0.94, -0.21)	
Percent change from baseline	60	0.50 (8.928)	0.0 (-4.6, 7.1)	-27.3, 22.2			63	-4.19 (7.116)	-3.8 (-8.6, 1.7)	-20.4, 9.8						
Day 1 / 4-hr Post-dose 1																
Absolute value	60	5.00 (0.461)	5.0 (4.7, 5.3)	4.0, 6.2			63	4.83 (0.453)	4.8 (4.5, 5.2)	3.8, 6.1						
Change from baseline	60	-0.21 (0.458)	-0.2 (-0.5, 0.0)	-1.4, 0.9	-0.21 (0.056)	(-0.32, -0.10)	63	-0.41 (0.450)	-0.5 (-0.6, 0.0)	-1.5, 0.6	-0.40 (0.055)	(-0.51, -0.29)	-0.19 (-0.35, -0.04)	0.0167	-0.44 (-0.79, -0.08)	
Percent change from baseline	60	-3.84 (8.735)	-3.9 (-9.4, 0.9)	-25.5, 20.0			63	-7.64 (8.478)	-8.6 (-12.2, 0.0)	-27.3, 11.3						
Day 2 / 0-hr Pre-dose																
Absolute value	60	5.10 (0.481)	5.1 (4.8, 5.5)	4.1, 6.2			62	4.73 (0.386)	4.7 (4.5, 5.0)	3.9, 6.2						
Change from baseline	60	-0.11 (0.411)	-0.1 (-0.4, 0.2)	-1.4, 0.8	-0.12 (0.048)	(-0.21, -0.02)	62	-0.51 (0.350)	-0.5 (-0.7, -0.3)	-1.3, 0.2	-0.51 (0.048)	(-0.60, -0.42)	-0.39 (-0.53, -0.26)	<.0001	-1.05 (-1.43, -0.67)	
Percent change from baseline	60	-2.08 (7.816)	-2.1 (-7.5, 3.6)	-25.5, 15.4			62	-9.69 (6.523)	-10.3 (-13.2, -5.7)	-24.5, 3.9						
Day 2 / 1-hr Post-dose 1																
Absolute value	60	5.00 (0.523)	5.0 (4.6, 5.5)	4.0, 6.0			62	4.47 (0.460)	4.4 (4.2, 4.8)	3.5, 5.6						
Change from baseline	60	-0.21 (0.470)	-0.2 (-0.5, 0.1)	-1.3, 0.9	-0.21 (0.057)	(-0.32, -0.10)	62	-0.77 (0.421)	-0.8 (-1.0, -0.5)	-1.9, 0.1	-0.77 (0.056)	(-0.88, -0.66)	-0.56 (-0.72, -0.40)	<.0001	-1.26 (-1.65, -0.87)	
Percent change from baseline	60	-3.90 (8.973)	-3.8 (-9.9, 2.0)	-23.6, 17.6			62	-14.62 (7.869)	-14.6 (-18.9, -9.8)	-34.5, 2.0						
Day 2 / 4-hr Post-dose 1																
Absolute value	60	4.99 (0.529)	5.0 (4.6, 5.4)	4.0, 6.2			62	4.55 (0.375)	4.6 (4.3, 4.8)	3.7, 5.3						
Change from baseline	60	-0.22 (0.506)	-0.3 (-0.5, 0.1)	-1.2, 1.0	-0.22 (0.057)	(-0.33, -0.11)	62	-0.68 (0.424)	-0.7 (-1.0, -0.4)	-1.8, 0.2	-0.68 (0.056)	(-0.79, -0.57)	-0.46 (-0.62, -0.30)	<.0001	-1.00 (-1.38, -0.62)	
Percent change from baseline	60	-4.05 (9.659)	-4.7 (-10.7, 2.8)	-21.6, 21.3			62	-12.85 (7.779)	-13.2 (-19.6, -8.0)	-32.7, 3.9						
Day 3 / 0-hr Pre-dose																
Absolute value	60	5.04 (0.499)	5.0 (4.7, 5.3)	3.9, 6.4			62	4.49 (0.447)	4.5 (4.2, 4.8)	3.4, 5.9						
Change from baseline	60	-0.17 (0.429)	-0.2 (-0.5, 0.1)	-1.0, 0.7	-0.17 (0.057)	(-0.28, -0.06)	62	-0.75 (0.484)	-0.8 (-1.1, -0.4)	-1.8, 0.6	-0.75 (0.056)	(-0.86, -0.64)	-0.58 (-0.74, -0.42)	<.0001	-1.28 (-1.67, -0.89)	
Percent change from baseline	60	-3.15 (8.258)	-3.8 (-9.7, 2.0)	-17.9, 15.6			62	-14.19 (9.001)	-15.1 (-20.8, -7.7)	-32.7, 11.3						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Age																0.6328
<65 years																
Baseline																
Absolute value	66	5.34 (0.367)	5.3 (5.1, 5.6)	4.5, 6.4			54	5.20 (0.340)	5.2 (5.0, 5.4)	4.5, 6.0						
Day 1 / 1-hr Post-dose 1																
Absolute value	66	5.39 (0.573)	5.3 (5.0, 5.9)	4.4, 6.6			54	5.10 (0.498)	5.1 (4.7, 5.4)	3.9, 6.3						
Change from baseline	66	0.05 (0.391)	0.0 (-0.2, 0.2)	-0.7, 1.1	0.06 (0.048)	(-0.04, 0.15)	54	-0.11 (0.361)	-0.1 (-0.4, 0.1)	-1.0, 0.9	-0.12 (0.053)	(-0.22, -0.01)	-0.18 (-0.32, -0.04)	0.0148	-0.42 (-0.78, -0.05)	
Percent change from baseline	66	0.86 (7.352)	0.0 (-4.0, 3.9)	-13.7, 20.0			54	-2.08 (6.933)	-2.0 (-7.4, 2.0)	-18.2, 16.7						
Day 1 / 2-hr Post-dose 1																
Absolute value	66	5.36 (0.545)	5.3 (5.0, 5.7)	4.4, 6.7			54	5.02 (0.466)	5.0 (4.7, 5.3)	4.0, 6.1						
Change from baseline	66	0.02 (0.411)	0.0 (-0.3, 0.3)	-0.9, 1.0	0.02 (0.048)	(-0.07, 0.12)	54	-0.19 (0.343)	-0.1 (-0.4, 0.0)	-1.0, 0.6	-0.20 (0.053)	(-0.30, -0.09)	-0.22 (-0.36, -0.08)	0.0023	-0.53 (-0.90, -0.16)	
Percent change from baseline	66	0.30 (7.570)	0.0 (-5.4, 5.7)	-14.5, 18.9			54	-3.58 (6.510)	-2.1 (-8.0, 0.0)	-18.2, 11.1						
Day 1 / 4-hr Post-dose 1																
Absolute value	66	5.18 (0.454)	5.1 (4.9, 5.4)	4.2, 6.3			54	4.90 (0.468)	4.9 (4.5, 5.3)	4.0, 5.8						
Change from baseline	66	-0.16 (0.402)	-0.1 (-0.4, 0.1)	-1.2, 0.6	-0.15 (0.051)	(-0.25, -0.05)	54	-0.30 (0.458)	-0.3 (-0.6, 0.1)	-1.5, 0.7	-0.31 (0.057)	(-0.42, -0.20)	-0.16 (-0.31, -0.01)	0.0403	-0.33 (-0.69, 0.04)	
Percent change from baseline	66	-2.87 (7.333)	-1.9 (-7.3, 2.0)	-20.7, 12.2			54	-5.60 (8.625)	-5.9 (-12.0, 1.9)	-27.3, 13.7						
Day 2 / 0-hr Pre-dose																
Absolute value	66	5.20 (0.515)	5.1 (4.9, 5.6)	4.1, 6.3			52	4.70 (0.385)	4.7 (4.5, 5.0)	3.9, 6.0						
Change from baseline	66	-0.15 (0.371)	-0.2 (-0.4, 0.1)	-1.4, 0.8	-0.14 (0.045)	(-0.23, -0.05)	52	-0.51 (0.373)	-0.6 (-0.7, -0.3)	-1.3, 0.4	-0.52 (0.051)	(-0.62, -0.42)	-0.38 (-0.52, -0.24)	<.0001	-0.97 (-1.35, -0.58)	
Percent change from baseline	66	-2.73 (6.922)	-3.5 (-6.9, 1.9)	-25.5, 15.4			52	-9.56 (6.845)	-10.7 (-13.3, -5.9)	-25.0, 7.1						
Day 2 / 1-hr Post-dose 1																
Absolute value	65	5.09 (0.513)	5.1 (4.6, 5.5)	4.1, 6.0			52	4.61 (0.429)	4.6 (4.3, 5.0)	3.8, 5.6						
Change from baseline	65	-0.24 (0.450)	-0.2 (-0.5, 0.1)	-1.6, 0.6	-0.23 (0.053)	(-0.34, -0.12)	52	-0.60 (0.425)	-0.6 (-0.9, -0.3)	-1.7, 0.5	-0.61 (0.060)	(-0.73, -0.49)	-0.38 (-0.54, -0.22)	<.0001	-0.80 (-1.18, -0.42)	
Percent change from baseline	65	-4.50 (8.230)	-3.8 (-9.1, 2.0)	-25.8, 11.3			52	-11.29 (7.926)	-12.4 (-17.3, -5.0)	-30.9, 11.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	65	5.10 (0.462)	5.1 (4.8, 5.4)	4.0, 6.2			52	4.62 (0.420)	4.6 (4.3, 5.0)	3.7, 6.0						
Change from baseline	65	-0.24 (0.442)	-0.2 (-0.5, 0.1)	-1.4, 0.8	-0.22 (0.054)	(-0.33, -0.11)	52	-0.58 (0.464)	-0.5 (-0.8, -0.3)	-1.8, 0.4	-0.60 (0.060)	(-0.72, -0.48)	-0.37 (-0.54, -0.21)	<.0001	-0.76 (-1.14, -0.39)	
Percent change from baseline	65	-4.25 (8.051)	-3.4 (-10.7, 1.9)	-22.6, 15.1			52	-10.93 (8.380)	-10.1 (-16.7, -5.8)	-32.7, 7.1						
Day 3 / 0-hr Pre-dose																
Absolute value	65	5.10 (0.510)	5.1 (4.8, 5.5)	4.1, 6.4			52	4.60 (0.464)	4.7 (4.2, 4.9)	3.8, 6.2						
Change from baseline	65	-0.24 (0.434)	-0.2 (-0.6, 0.1)	-1.4, 0.6	-0.22 (0.057)	(-0.33, -0.11)	52	-0.61 (0.515)	-0.5 (-1.0, -0.3)	-1.7, 1.0	-0.62 (0.064)	(-0.74, -0.49)	-0.40 (-0.57, -0.23)	<.0001	-0.79 (-1.16, -0.41)	
Percent change from baseline	65	-4.33 (7.985)	-3.4 (-10.5, 2.0)	-24.1, 11.5			52	-11.40 (9.454)	-10.8 (-18.2, -4.9)	-28.8, 19.2						
>= 65 years																
Baseline																
Absolute value	92	5.27 (0.363)	5.2 (5.0, 5.5)	4.5, 6.2			89	5.29 (0.332)	5.3 (5.0, 5.4)	4.8, 6.5						
Day 1 / 1-hr Post-dose 1																
Absolute value	92	5.25 (0.587)	5.2 (4.9, 5.7)	3.8, 6.7			89	5.18 (0.500)	5.1 (4.9, 5.4)	4.0, 6.7						
Change from baseline	92	-0.02 (0.413)	0.0 (-0.2, 0.3)	-1.7, 1.2	-0.02 (0.042)	(-0.11, 0.06)	89	-0.11 (0.364)	-0.1 (-0.3, 0.1)	-1.3, 0.9	-0.11 (0.043)	(-0.19, -0.02)	-0.08 (-0.20, 0.03)	0.1578	-0.23 (-0.52, 0.07)	
Percent change from baseline	92	-0.46 (7.775)	0.0 (-4.0, 4.7)	-30.9, 21.8			89	-2.07 (6.875)	-1.9 (-5.6, 1.9)	-24.1, 15.5						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

Lokelma

Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Age *(contd.)*																
>= 65 years *(contd.)*																
Day 1 / 2-hr Post-dose 1																
Absolute value	92	5.26 (0.552)	5.3 (4.9, 5.7)	3.8, 6.4			89	5.11 (0.469)	5.1 (4.8, 5.4)	4.2, 6.7						
Change from baseline	92	-0.01 (0.432)	0.0 (-0.3, 0.3)	-1.6, 1.0	-0.01 (0.042)	(-0.09, 0.07)	89	-0.18 (0.372)	-0.2 (-0.4, 0.1)	-1.1, 0.9	-0.18 (0.043)	(-0.26, -0.09)	-0.17 (-0.28, -0.05)	0.0066	-0.42 (-0.71, -0.12)	
Percent change from baseline	92	-0.16 (8.183)	0.8 (-4.8, 5.3)	-27.3, 22.2			89	-3.34 (6.972)	-3.7 (-6.8, 1.8)	-20.4, 17.3						
Day 1 / 4-hr Post-dose 1																
Absolute value	92	5.01 (0.537)	4.9 (4.6, 5.4)	3.9, 6.3			89	4.88 (0.487)	4.9 (4.5, 5.2)	3.8, 6.5						
Change from baseline	92	-0.26 (0.445)	-0.3 (-0.6, 0.0)	-1.4, 0.9	-0.26 (0.045)	(-0.35, -0.17)	89	-0.41 (0.435)	-0.4 (-0.6, -0.1)	-2.2, 0.6	-0.41 (0.046)	(-0.50, -0.32)	-0.15 (-0.27, -0.02)	0.0241	-0.34 (-0.64, -0.05)	
Percent change from baseline	92	-4.90 (8.417)	-6.0 (-10.3, 0.0)	-25.5, 20.0			89	-7.70 (7.958)	-7.5 (-12.0, -1.8)	-36.7, 11.3						
Day 2 / 0-hr Pre-dose																
Absolute value	92	5.06 (0.412)	5.0 (4.8, 5.3)	4.0, 6.2			88	4.76 (0.426)	4.7 (4.5, 5.0)	3.9, 6.2						
Change from baseline	92	-0.21 (0.357)	-0.2 (-0.4, 0.0)	-1.1, 0.8	-0.21 (0.036)	(-0.28, -0.14)	88	-0.53 (0.360)	-0.5 (-0.8, -0.3)	-1.7, 0.1	-0.53 (0.037)	(-0.60, -0.46)	-0.32 (-0.42, -0.22)	<.0001	-0.90 (-1.20, -0.59)	
Percent change from baseline	92	-3.88 (6.741)	-3.8 (-7.8, 0.0)	-18.6, 17.0			88	-10.01 (6.635)	-9.7 (-13.6, -5.7)	-30.4, 2.0						
Day 2 / 1-hr Post-dose 1																
Absolute value	92	5.04 (0.551)	5.0 (4.6, 5.5)	4.0, 6.3			88	4.57 (0.444)	4.6 (4.3, 4.9)	3.5, 5.5						
Change from baseline	92	-0.24 (0.509)	-0.2 (-0.5, 0.1)	-2.2, 1.1	-0.24 (0.048)	(-0.33, -0.14)	88	-0.72 (0.439)	-0.8 (-1.0, -0.5)	-2.1, 0.3	-0.72 (0.049)	(-0.82, -0.62)	-0.48 (-0.62, -0.35)	<.0001	-1.02 (-1.33, -0.71)	
Percent change from baseline	92	-4.37 (9.395)	-4.1 (-10.4, 1.8)	-35.5, 21.6			88	-13.53 (8.117)	-14.3 (-18.6, -8.9)	-37.5, 6.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	92	5.06 (0.535)	5.0 (4.6, 5.5)	4.0, 6.4			88	4.65 (0.438)	4.6 (4.3, 5.0)	3.9, 6.7						
Change from baseline	92	-0.21 (0.441)	-0.2 (-0.5, 0.0)	-1.1, 1.0	-0.21 (0.043)	(-0.30, -0.13)	88	-0.64 (0.393)	-0.6 (-0.9, -0.4)	-1.6, 0.5	-0.64 (0.044)	(-0.72, -0.55)	-0.42 (-0.54, -0.30)	<.0001	-1.02 (-1.33, -0.71)	
Percent change from baseline	92	-3.97 (8.435)	-3.9 (-9.7, 0.0)	-21.6, 21.3			88	-11.97 (7.197)	-12.2 (-17.1, -7.3)	-28.6, 8.1						
Day 3 / 0-hr Pre-dose																
Absolute value	92	5.01 (0.447)	5.1 (4.7, 5.3)	3.9, 6.2			88	4.48 (0.459)	4.4 (4.2, 4.8)	3.4, 5.9						
Change from baseline	92	-0.26 (0.399)	-0.3 (-0.6, 0.0)	-1.0, 0.8	-0.26 (0.043)	(-0.35, -0.18)	88	-0.81 (0.472)	-0.8 (-1.2, -0.5)	-1.9, 0.6	-0.81 (0.044)	(-0.90, -0.72)	-0.54 (-0.67, -0.42)	<.0001	-1.25 (-1.57, -0.93)	
Percent change from baseline	92	-4.83 (7.619)	-6.0 (-10.7, 0.0)	-18.2, 15.6			88	-15.15 (8.543)	-15.8 (-21.1, -9.8)	-33.9, 11.3						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Lokelma

Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Region																0.5869
USA																
Baseline																
Absolute value	148	5.28 (0.360)	5.2 (5.0, 5.5)	4.5, 6.4			133	5.23 (0.326)	5.2 (5.0, 5.4)	4.5, 6.5						
Day 1 / 1-hr Post-dose 1																
Absolute value	148	5.29 (0.588)	5.2 (4.9, 5.8)	3.8, 6.7			133	5.12 (0.489)	5.1 (4.8, 5.4)	3.9, 6.7						
Change from baseline	148	0.01 (0.413)	0.0 (-0.2, 0.3)	-1.7, 1.2	0.02 (0.033)	(-0.05, 0.08)	133	-0.11 (0.362)	-0.1 (-0.3, 0.1)	-1.3, 0.9	-0.11 (0.035)	(-0.18, -0.04)	-0.13 (-0.22, -0.03)	0.0075	-0.31 (-0.54, -0.07)	
Percent change from baseline	148	0.15 (7.783)	0.0 (-4.0, 4.7)	-30.9, 21.8			133	-2.08 (6.925)	-1.9 (-6.0, 1.9)	-24.1, 16.7						
Day 1 / 2-hr Post-dose 1																
Absolute value	148	5.28 (0.551)	5.3 (4.9, 5.7)	3.8, 6.7			133	5.05 (0.444)	5.0 (4.7, 5.3)	4.0, 6.4						
Change from baseline	148	0.00 (0.431)	0.0 (-0.3, 0.3)	-1.6, 1.0	0.01 (0.033)	(-0.06, 0.07)	133	-0.19 (0.351)	-0.2 (-0.4, 0.0)	-1.1, 0.9	-0.19 (0.034)	(-0.26, -0.12)	-0.20 (-0.29, -0.10)	<.0001	-0.47 (-0.71, -0.24)	
Percent change from baseline	148	0.04 (8.075)	0.0 (-5.4, 5.5)	-27.3, 22.2			133	-3.51 (6.668)	-3.6 (-6.8, 0.0)	-20.4, 17.3						
Day 1 / 4-hr Post-dose 1																
Absolute value	148	5.07 (0.521)	5.0 (4.7, 5.4)	3.9, 6.3			133	4.89 (0.462)	4.9 (4.5, 5.2)	3.8, 6.5						
Change from baseline	148	-0.21 (0.436)	-0.2 (-0.5, 0.1)	-1.4, 0.9	-0.20 (0.034)	(-0.27, -0.13)	133	-0.34 (0.413)	-0.3 (-0.6, 0.0)	-1.5, 0.7	-0.35 (0.036)	(-0.42, -0.28)	-0.14 (-0.24, -0.05)	0.0042	-0.32 (-0.55, -0.08)	
Percent change from baseline	148	-3.85 (8.176)	-3.9 (-9.3, 1.7)	-25.5, 20.0			133	-6.45 (7.799)	-6.1 (-11.5, 0.0)	-27.3, 13.7						
Day 2 / 0-hr Pre-dose																
Absolute value	148	5.11 (0.468)	5.0 (4.8, 5.4)	4.0, 6.3			131	4.71 (0.389)	4.7 (4.4, 5.0)	3.9, 6.0						
Change from baseline	148	-0.17 (0.365)	-0.2 (-0.4, 0.0)	-1.4, 0.8	-0.17 (0.029)	(-0.22, -0.11)	131	-0.52 (0.365)	-0.5 (-0.8, -0.3)	-1.7, 0.4	-0.53 (0.031)	(-0.59, -0.47)	-0.36 (-0.45, -0.28)	<.0001	-0.97 (-1.22, -0.72)	
Percent change from baseline	148	-3.16 (6.891)	-3.8 (-7.5, 0.0)	-25.5, 17.0			131	-9.89 (6.723)	-10.2 (-13.2, -5.8)	-30.4, 7.1						
Day 2 / 1-hr Post-dose 1																
Absolute value	147	5.03 (0.511)	5.0 (4.6, 5.4)	4.0, 6.2			131	4.56 (0.433)	4.6 (4.2, 4.9)	3.5, 5.6						
Change from baseline	147	-0.25 (0.456)	-0.2 (-0.5, 0.1)	-1.6, 1.1	-0.24 (0.036)	(-0.31, -0.17)	131	-0.67 (0.439)	-0.7 (-0.9, -0.4)	-2.1, 0.5	-0.68 (0.038)	(-0.75, -0.60)	-0.44 (-0.54, -0.33)	<.0001	-0.94 (-1.19, -0.69)	
Percent change from baseline	147	-4.59 (8.527)	-4.0 (-10.0, 1.8)	-25.8, 21.6			131	-12.66 (8.177)	-13.5 (-17.6, -7.5)	-37.5, 11.1						
Day 2 / 4-hr Post-dose 1																
Absolute value	147	5.06 (0.499)	5.0 (4.7, 5.4)	4.0, 6.3			131	4.63 (0.430)	4.6 (4.3, 5.0)	3.7, 6.7						
Change from baseline	147	-0.21 (0.439)	-0.2 (-0.5, 0.1)	-1.4, 1.0	-0.21 (0.034)	(-0.28, -0.14)	131	-0.60 (0.418)	-0.6 (-0.9, -0.3)	-1.8, 0.5	-0.61 (0.036)	(-0.68, -0.53)	-0.40 (-0.50, -0.30)	<.0001	-0.89 (-1.14, -0.65)	
Percent change from baseline	147	-3.95 (8.262)	-3.8 (-9.8, 1.9)	-22.6, 21.3			131	-11.29 (7.642)	-11.3 (-16.7, -6.1)	-32.7, 8.1						
Day 3 / 0-hr Pre-dose																
Absolute value	147	5.04 (0.481)	5.1 (4.7, 5.3)	3.9, 6.4			131	4.51 (0.465)	4.4 (4.2, 4.8)	3.4, 6.2						
Change from baseline	147	-0.24 (0.415)	-0.2 (-0.6, 0.1)	-1.4, 0.8	-0.23 (0.037)	(-0.31, -0.16)	131	-0.72 (0.505)	-0.8 (-1.1, -0.4)	-1.9, 1.0	-0.73 (0.039)	(-0.81, -0.65)	-0.50 (-0.60, -0.39)	<.0001	-1.05 (-1.30, -0.80)	
Percent change from baseline	147	-4.45 (7.828)	-4.3 (-10.6, 2.0)	-24.1, 15.6			131	-13.63 (9.232)	-14.5 (-20.0, -7.7)	-33.9, 19.2						
Rest of world																
Baseline																
Absolute value	10	5.62 (0.305)	5.6 (5.5, 5.8)	5.2, 6.2			10	5.59 (0.307)	5.5 (5.4, 5.9)	5.2, 6.1						
Day 1 / 1-hr Post-dose 1																
Absolute value	10	5.58 (0.449)	5.7 (5.2, 6.0)	4.9, 6.2			10	5.48 (0.547)	5.4 (5.0, 5.9)	4.8, 6.6						
Change from baseline	10	-0.04 (0.241)	-0.1 (-0.2, 0.1)	-0.3, 0.4	-0.04 (0.101)	(-0.26, 0.18)	10	-0.11 (0.367)	-0.1 (-0.4, 0.1)	-0.6, 0.5	-0.11 (0.102)	(-0.33, 0.11)	-0.07 (-0.38, 0.24)	0.6241	-0.23 (-1.10, 0.65)	
Percent change from baseline	10	-0.79 (4.326)	-1.8 (-3.8, 1.8)	-5.8, 7.1			10	-2.07 (6.480)	-2.8 (-7.4, 1.8)	-11.1, 8.2						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 2.1.2.1 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)						Lokelma 10g QD (N=143)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Region *(contd.)*																
Rest of world *(contd.)*																
Day 1 / 2-hr Post-dose 1																
Absolute value	10	5.61 (0.425)	5.6 (5.3, 6.1)	4.8, 6.1			10	5.46 (0.628)	5.5 (5.2, 5.8)	4.5, 6.7						
Change from baseline	10	-0.01 (0.288)	0.0 (-0.1, 0.1)	-0.5, 0.5	-0.01 (0.127)	(-0.28, 0.26)	10	-0.13 (0.476)	-0.1 (-0.5, 0.2)	-0.9, 0.6	-0.13 (0.127)	(-0.40, 0.14)	-0.12 (-0.50, 0.26)	0.5053	-0.30 (-1.19, 0.58)	
Percent change from baseline	10	-0.19 (5.166)	0.9 (-1.8, 1.9)	-8.6, 8.9			10	-2.43 (8.479)	-2.6 (-9.6, 3.8)	-16.7, 9.8						
Day 1 / 4-hr Post-dose 1																
Absolute value	10	5.22 (0.253)	5.3 (5.1, 5.4)	4.6, 5.5			10	4.86 (0.700)	4.9 (4.3, 5.3)	3.8, 6.1						
Change from baseline	10	-0.40 (0.271)	-0.4 (-0.5, -0.2)	-1.0, -0.1	-0.40 (0.164)	(-0.74, -0.06)	10	-0.73 (0.683)	-0.8 (-1.1, -0.1)	-2.2, 0.0	-0.73 (0.164)	(-1.08, -0.39)	-0.33 (-0.82, 0.16)	0.1692	-0.64 (-1.53, 0.26)	
Percent change from baseline	10	-7.00 (4.472)	-6.1 (-8.9, -3.6)	-16.1, -1.8			10	-13.00 (11.714)	-13.8 (-20.4, -1.8)	-36.7, 0.0						
Day 2 / 0-hr Pre-dose																
Absolute value	10	5.23 (0.343)	5.2 (5.0, 5.3)	4.8, 6.0			9	5.11 (0.549)	5.0 (4.6, 5.4)	4.5, 6.2						
Change from baseline	10	-0.39 (0.264)	-0.4 (-0.5, -0.2)	-0.8, 0.0	-0.39 (0.103)	(-0.61, -0.17)	9	-0.51 (0.369)	-0.6 (-0.8, -0.2)	-1.0, 0.1	-0.49 (0.108)	(-0.72, -0.26)	-0.10 (-0.41, 0.21)	0.5109	-0.38 (-1.29, 0.53)	
Percent change from baseline	10	-6.89 (4.575)	-6.4 (-8.9, -3.6)	-14.3, 0.0			9	-9.21 (6.588)	-10.7 (-14.8, -3.6)	-16.9, 1.6						
Day 2 / 1-hr Post-dose 1																
Absolute value	10	5.49 (0.706)	5.8 (5.0, 5.9)	4.0, 6.3			9	4.87 (0.427)	5.0 (4.5, 5.1)	4.3, 5.5						
Change from baseline	10	-0.13 (0.825)	-0.0 (-0.2, 0.3)	-2.2, 0.7	-0.13 (0.209)	(-0.57, 0.31)	9	-0.76 (0.413)	-0.7 (-1.0, -0.5)	-1.5, -0.2	-0.71 (0.222)	(-1.18, -0.24)	-0.58 (-1.23, 0.06)	0.0745	-0.94 (-1.89, 0.01)	
Percent change from baseline	10	-1.96 (13.695)	-0.9 (-3.8, 5.5)	-35.5, 12.7			9	-13.36 (7.104)	-13.5 (-17.9, -9.1)	-25.4, -3.6						
Day 2 / 4-hr Post-dose 1																
Absolute value	10	5.28 (0.583)	5.3 (4.6, 5.7)	4.6, 6.4			9	4.73 (0.450)	4.7 (4.5, 5.0)	4.0, 5.3						
Change from baseline	10	-0.34 (0.467)	-0.4 (-0.6, 0.0)	-1.0, 0.5	-0.34 (0.136)	(-0.63, -0.05)	9	-0.89 (0.372)	-0.8 (-1.2, -0.7)	-1.4, -0.2	-0.86 (0.144)	(-1.17, -0.56)	-0.52 (-0.94, -0.11)	0.0170	-1.29 (-2.28, -0.30)	
Percent change from baseline	10	-6.10 (8.281)	-6.2 (-11.5, 0.0)	-17.9, 8.5			9	-15.81 (6.698)	-14.5 (-20.3, -13.1)	-25.9, -3.6						
Day 3 / 0-hr Pre-dose																
Absolute value	10	5.21 (0.335)	5.3 (4.9, 5.5)	4.7, 5.6			9	4.74 (0.388)	4.8 (4.5, 4.9)	4.2, 5.5						
Change from baseline	10	-0.41 (0.354)	-0.5 (-0.6, -0.2)	-0.9, 0.3	-0.41 (0.107)	(-0.64, -0.18)	9	-0.88 (0.331)	-0.9 (-1.2, -0.6)	-1.3, -0.5	-0.88 (0.115)	(-1.13, -0.64)	-0.47 (-0.81, -0.14)	0.0091	-1.36 (-2.36, -0.36)	
Percent change from baseline	10	-7.16 (6.315)	-9.6 (-10.7, -3.4)	-15.8, 5.8			9	-15.58 (5.648)	-17.3 (-20.3, -10.9)	-22.2, -8.3						

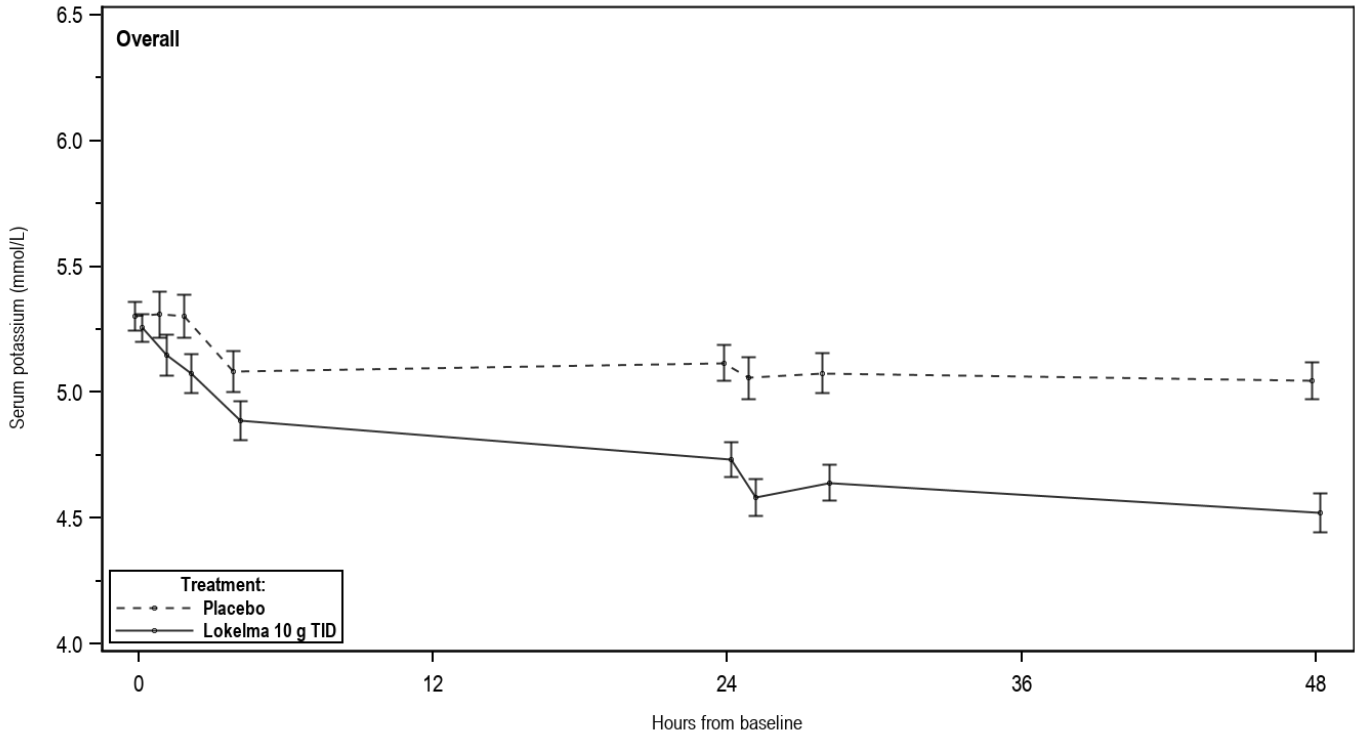
CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
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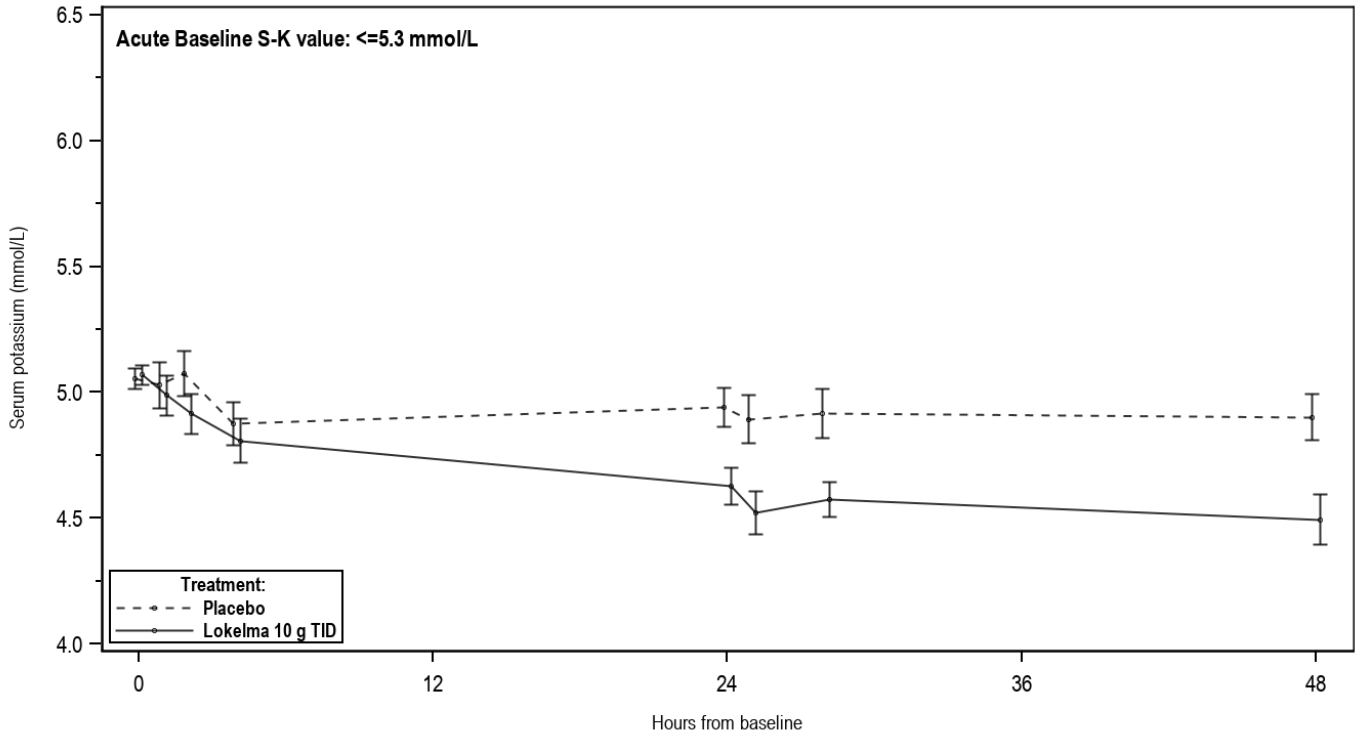
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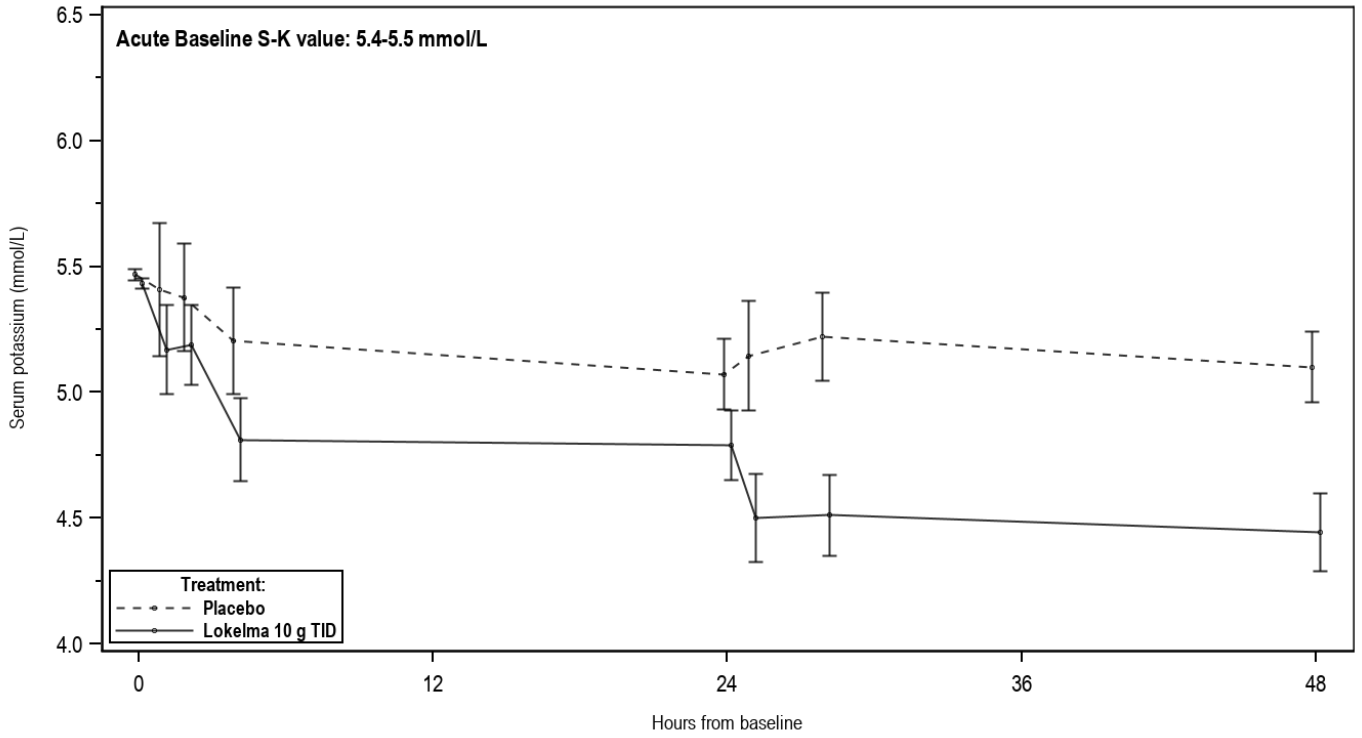
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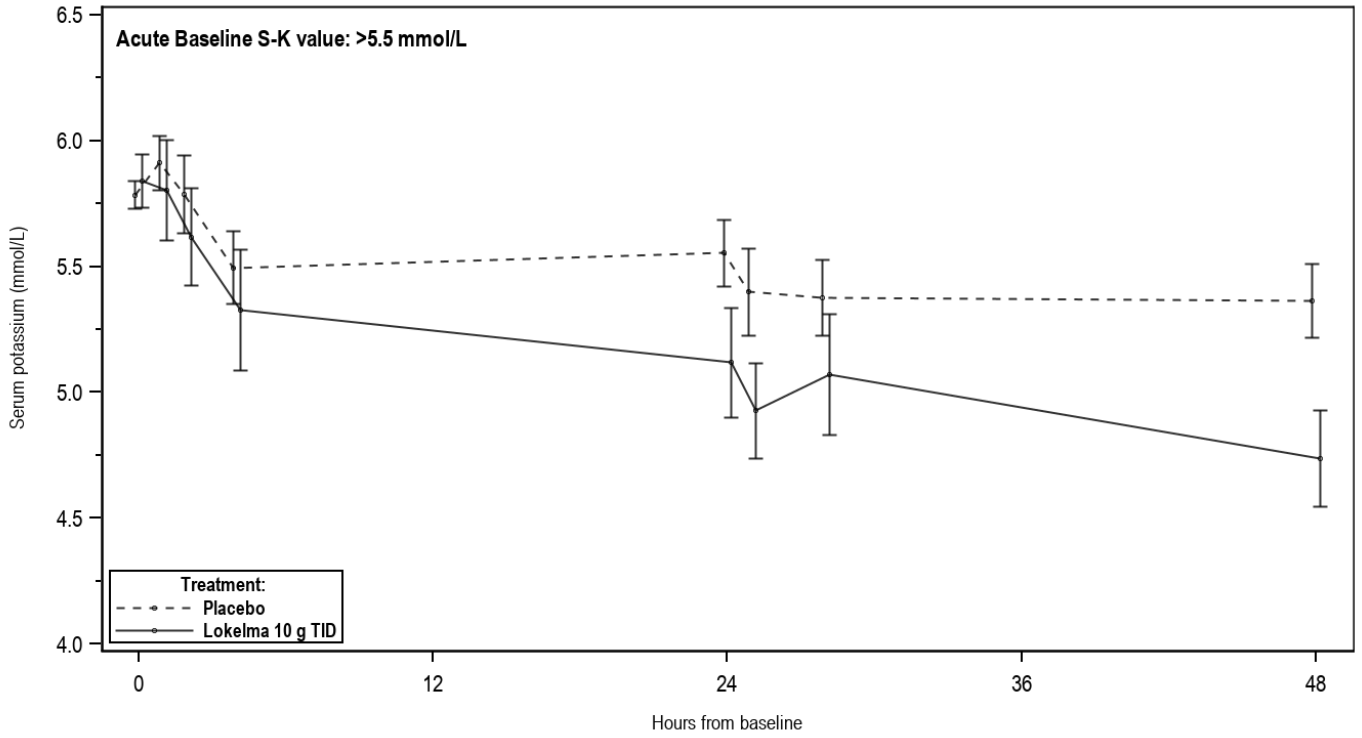
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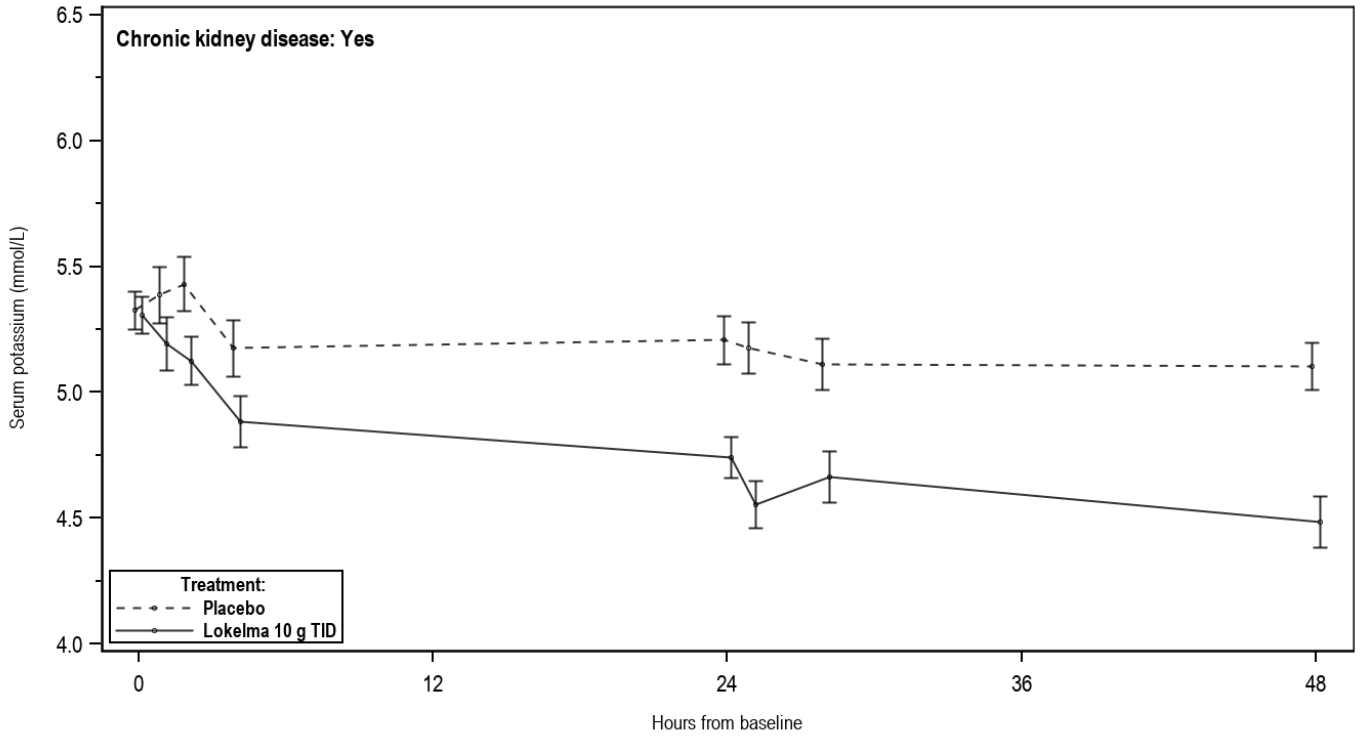
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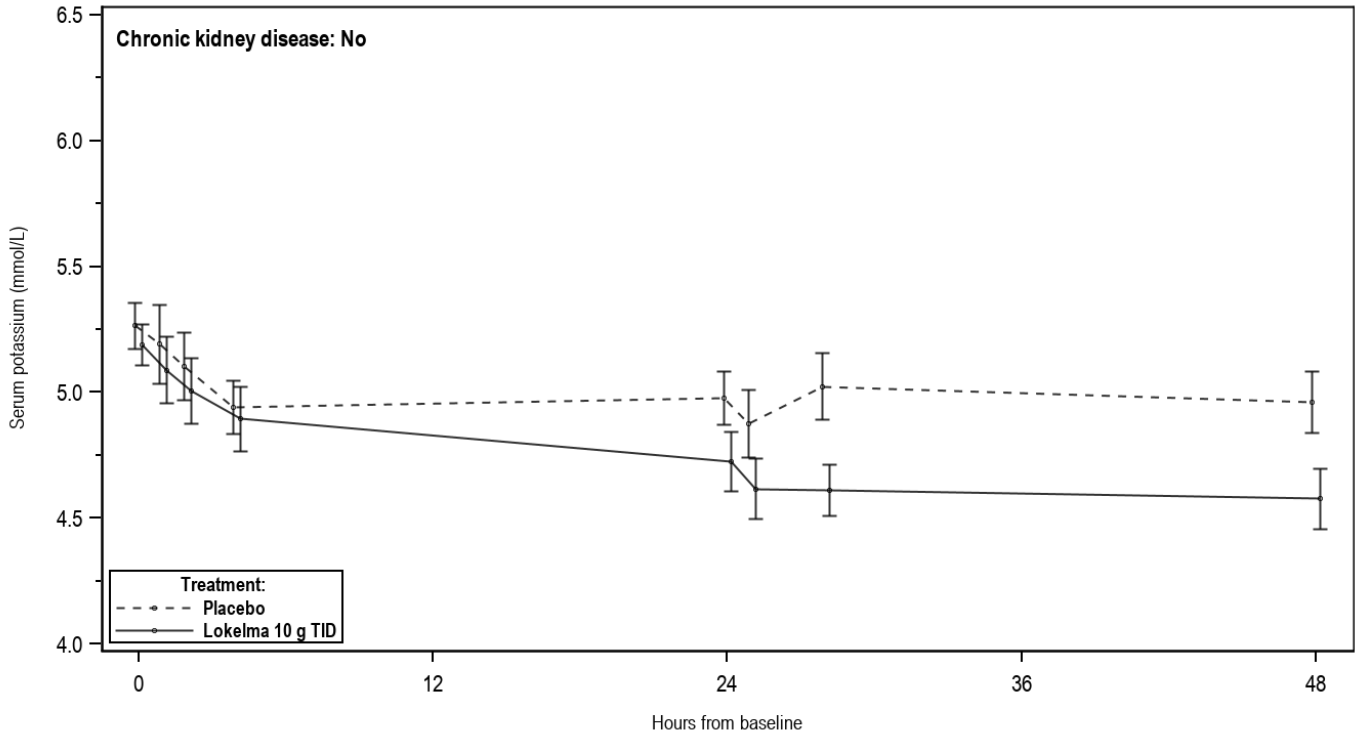
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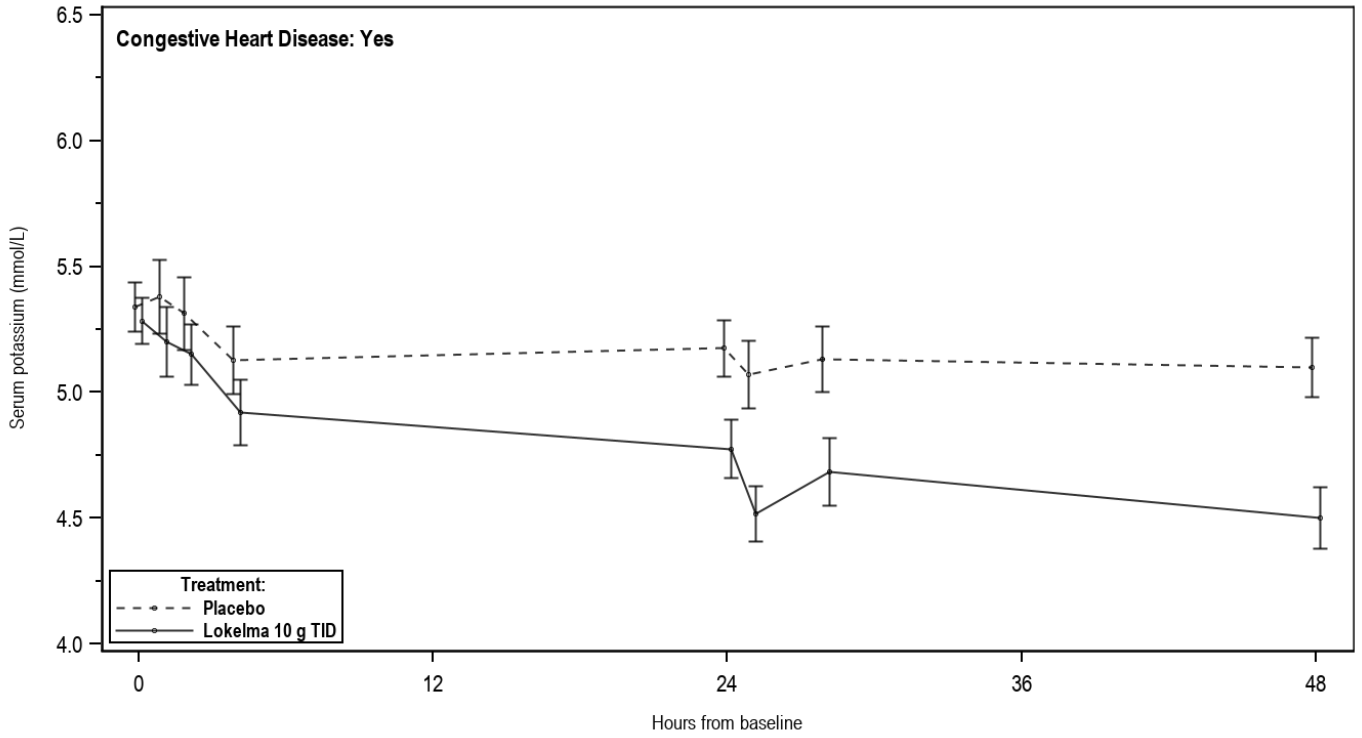
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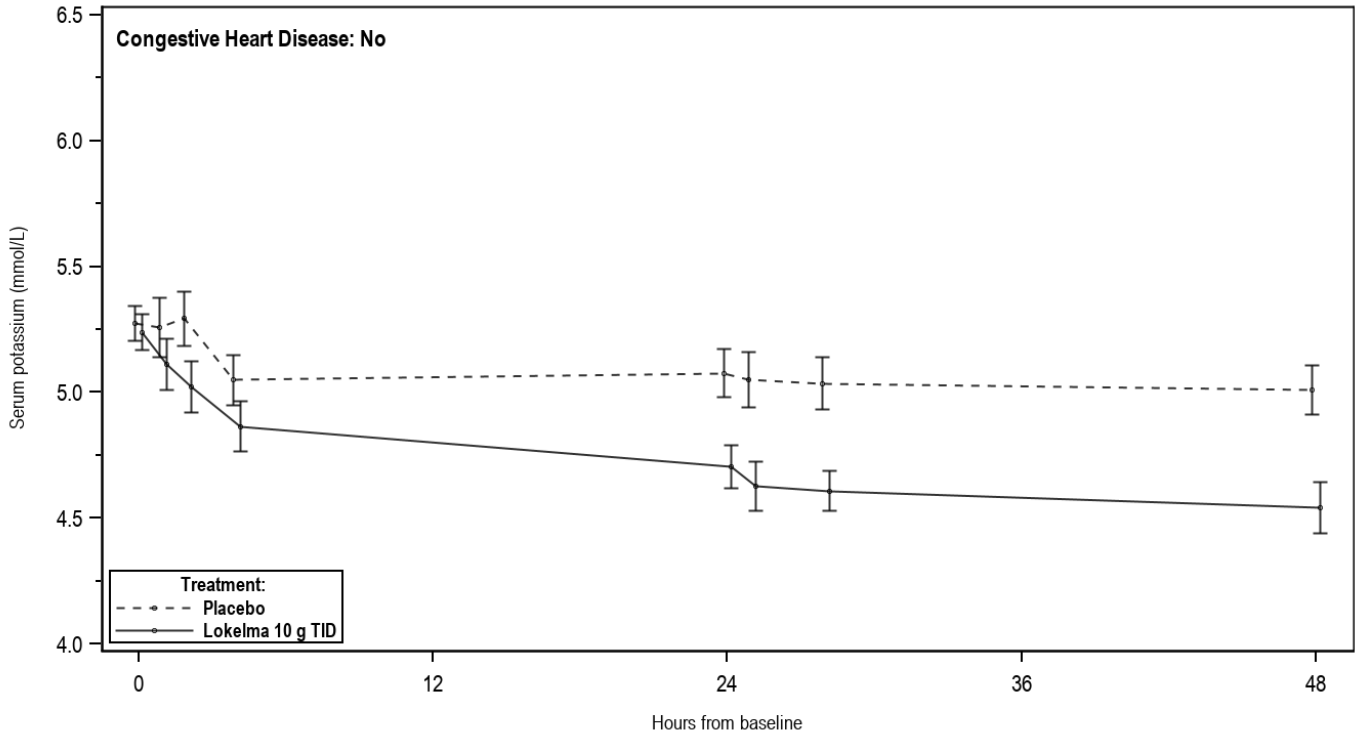
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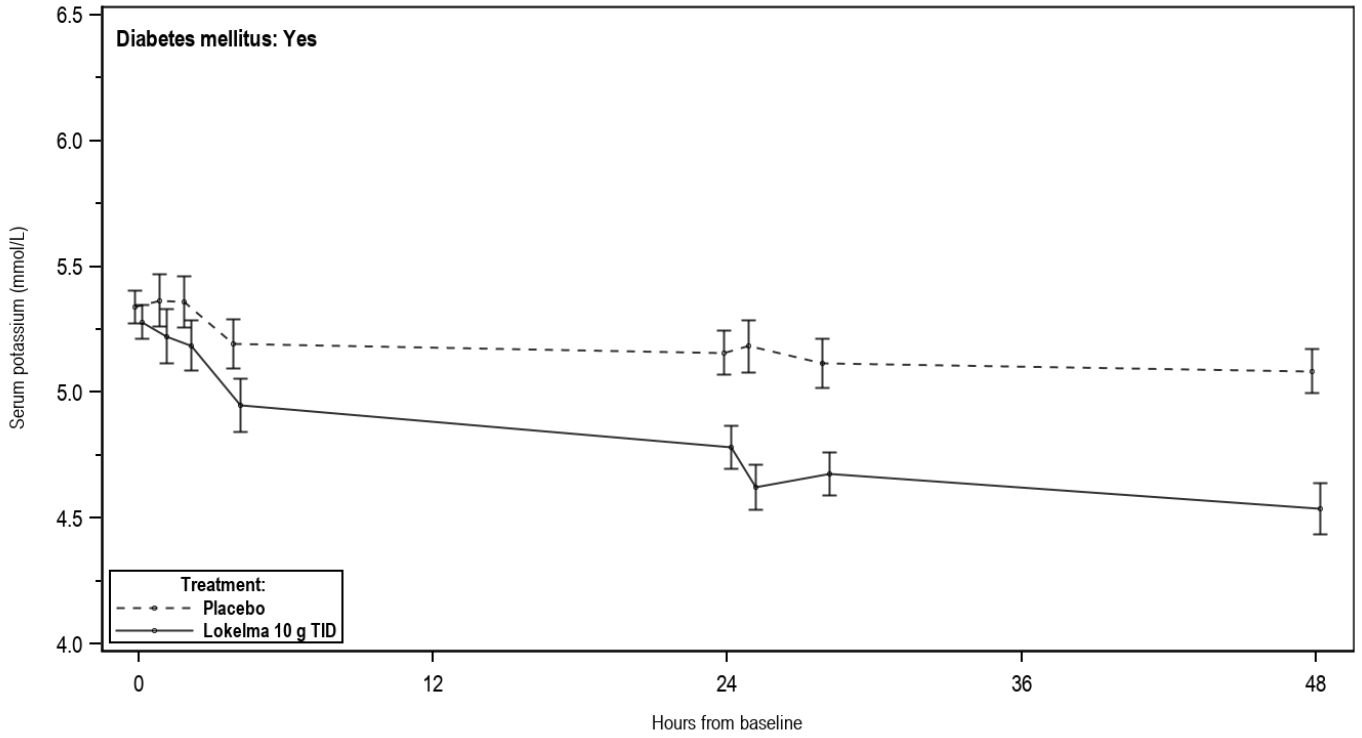
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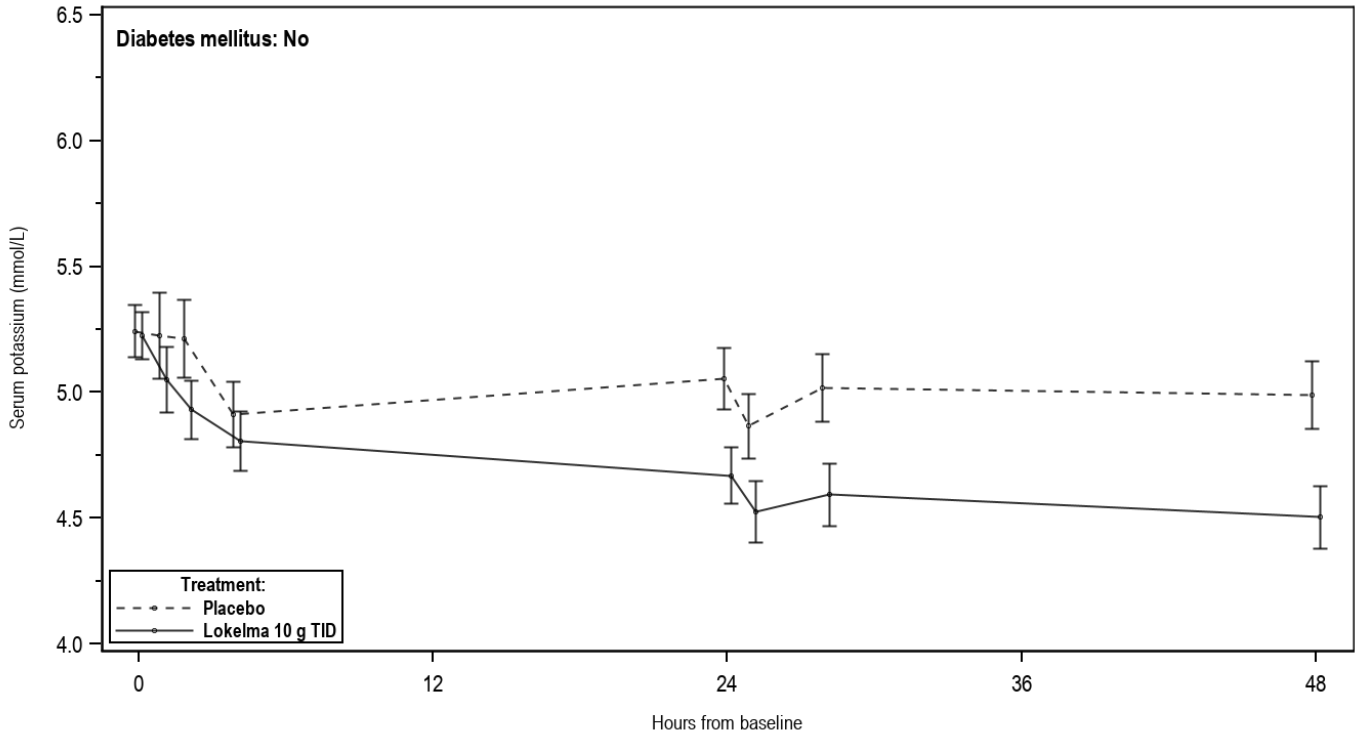
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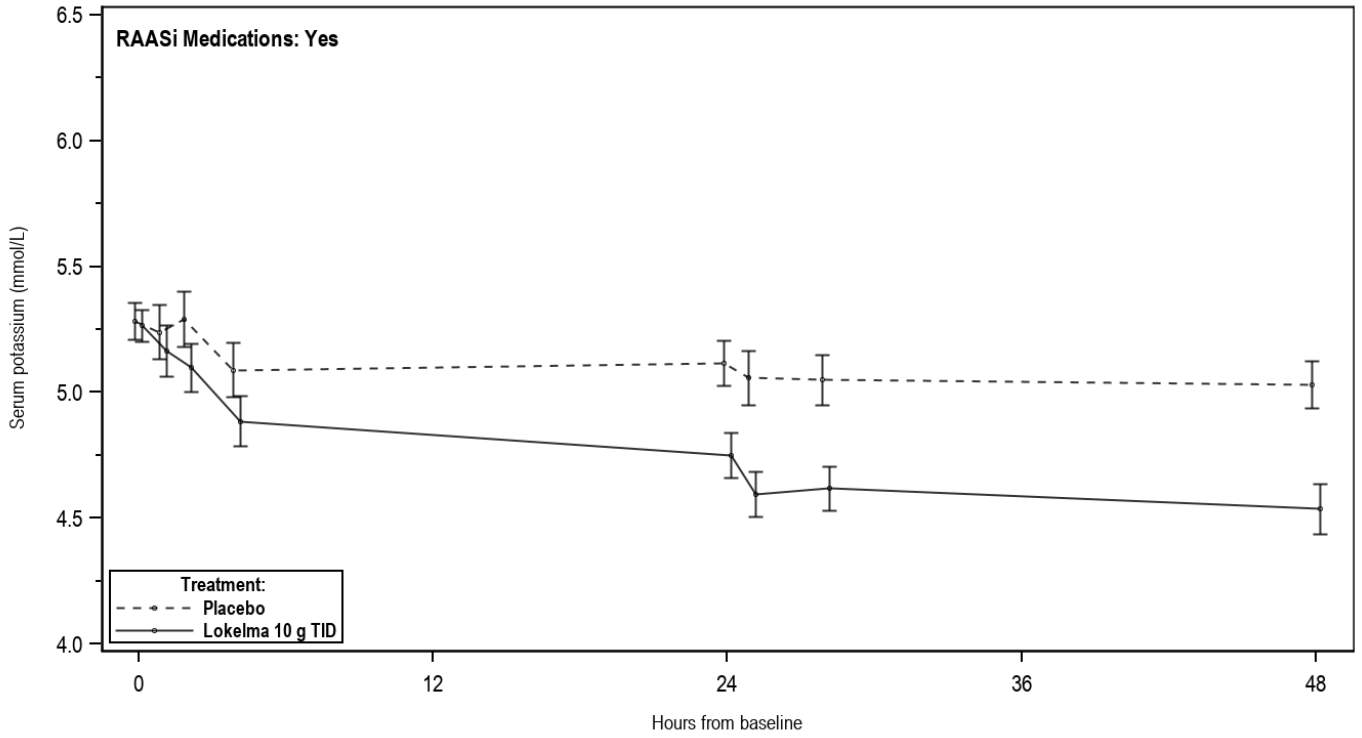
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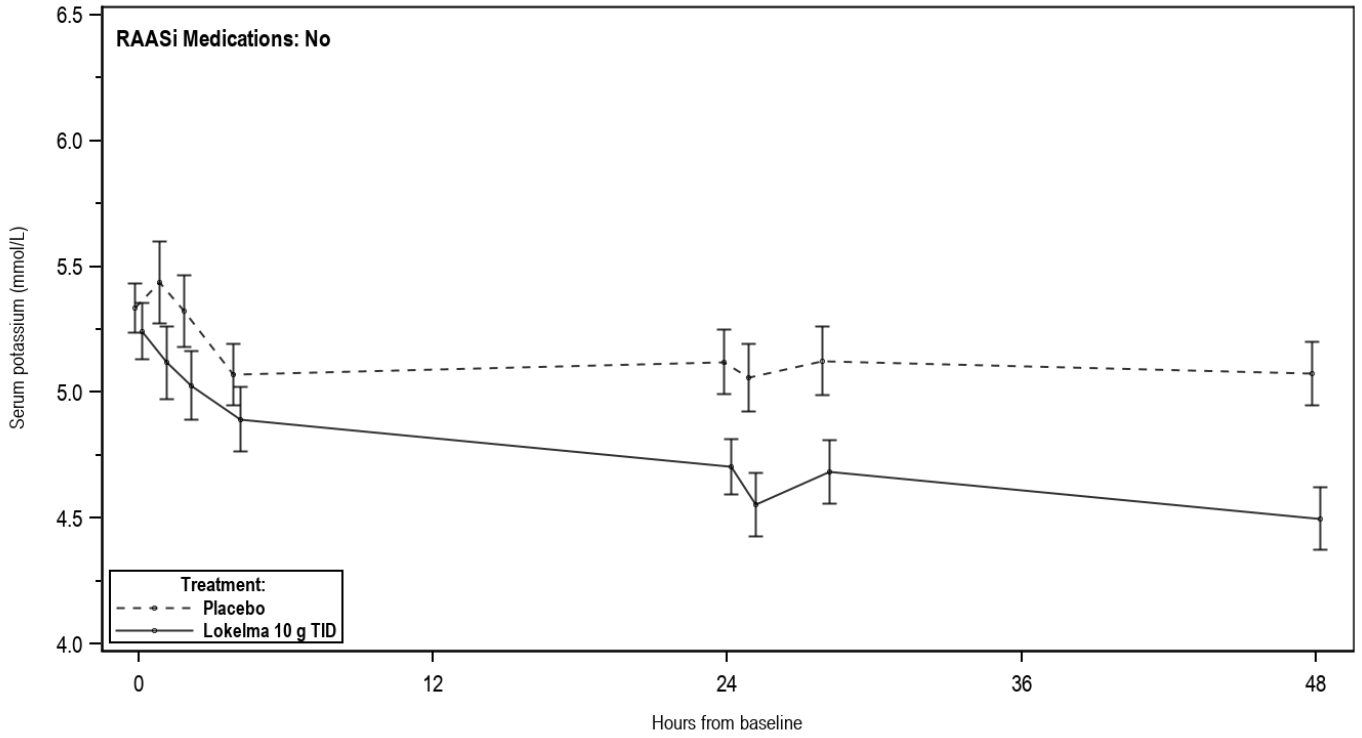
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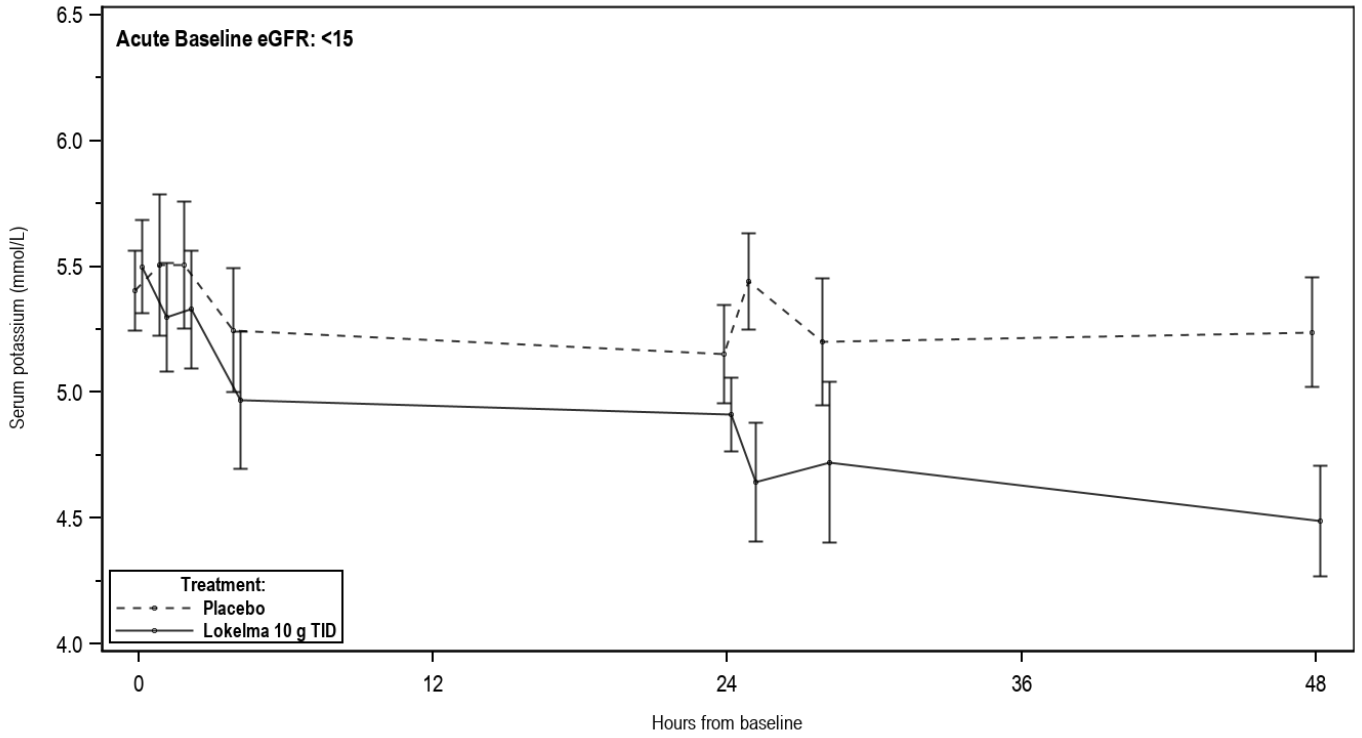
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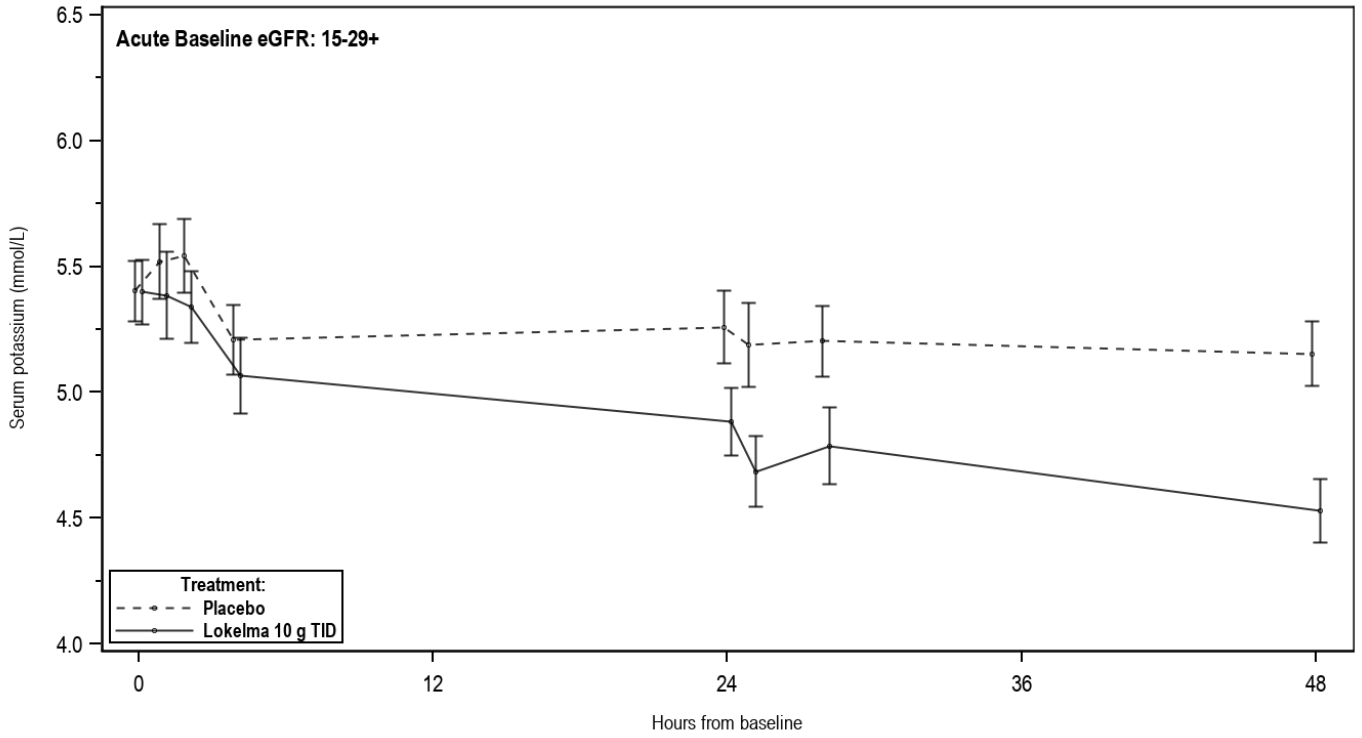
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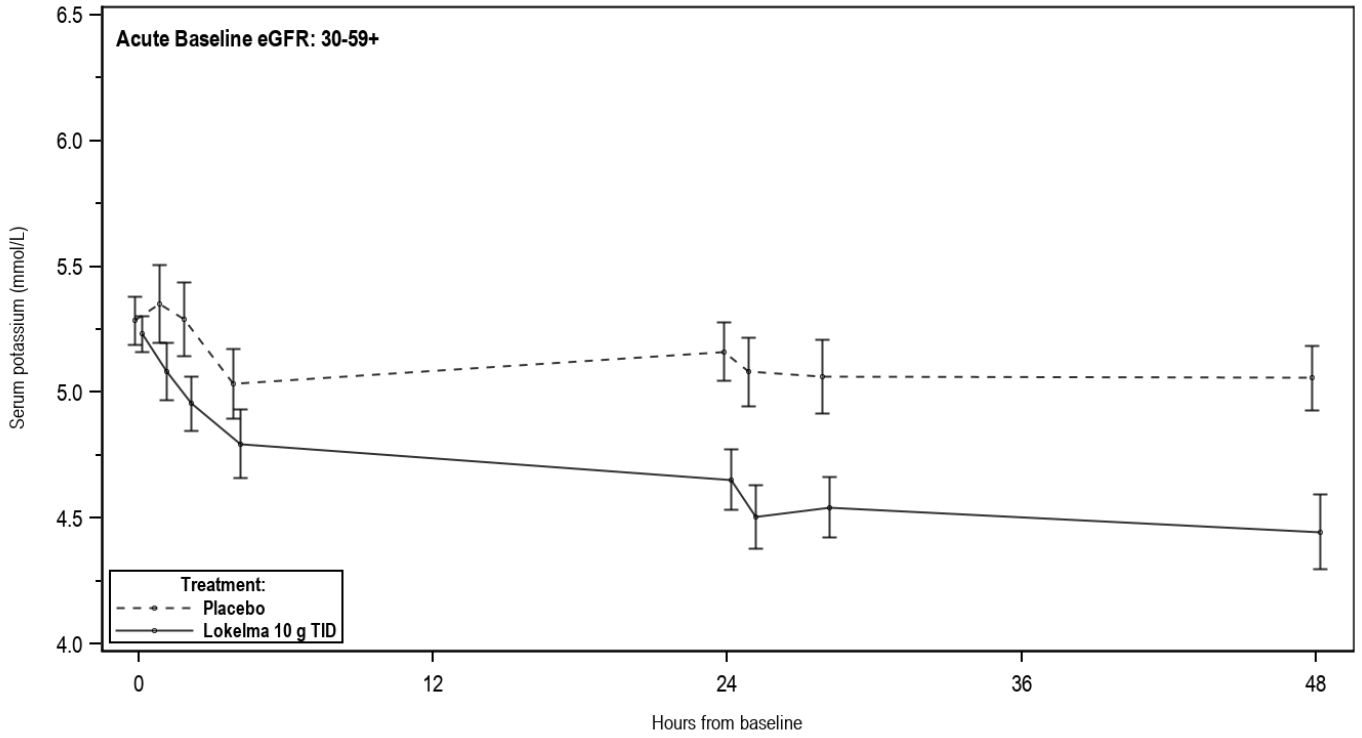
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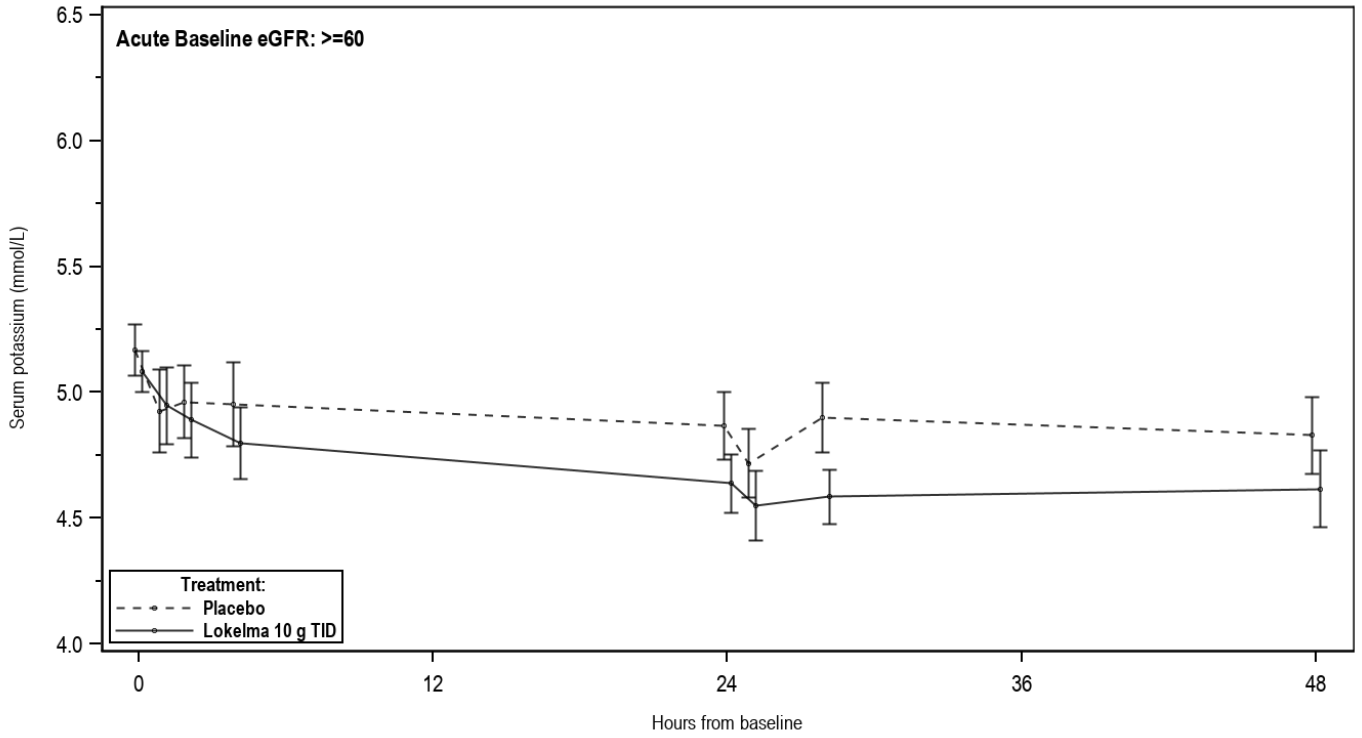
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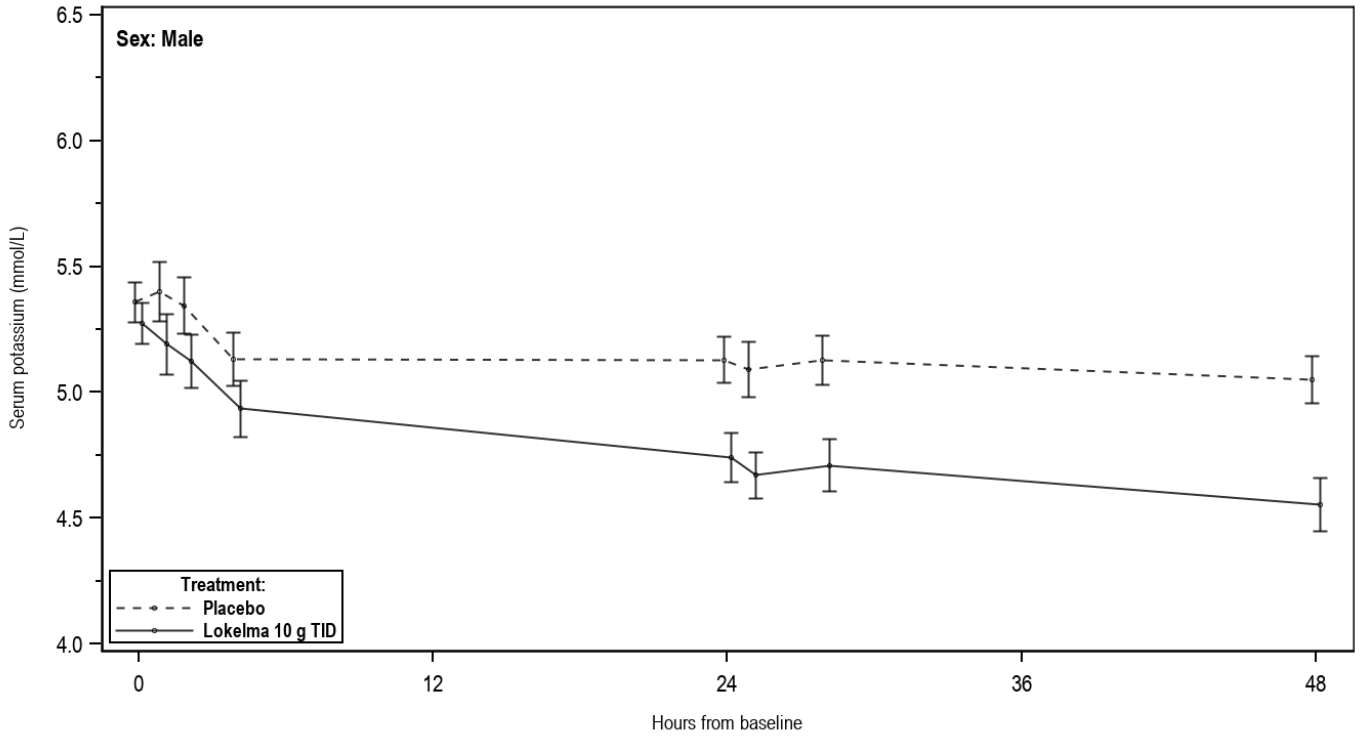
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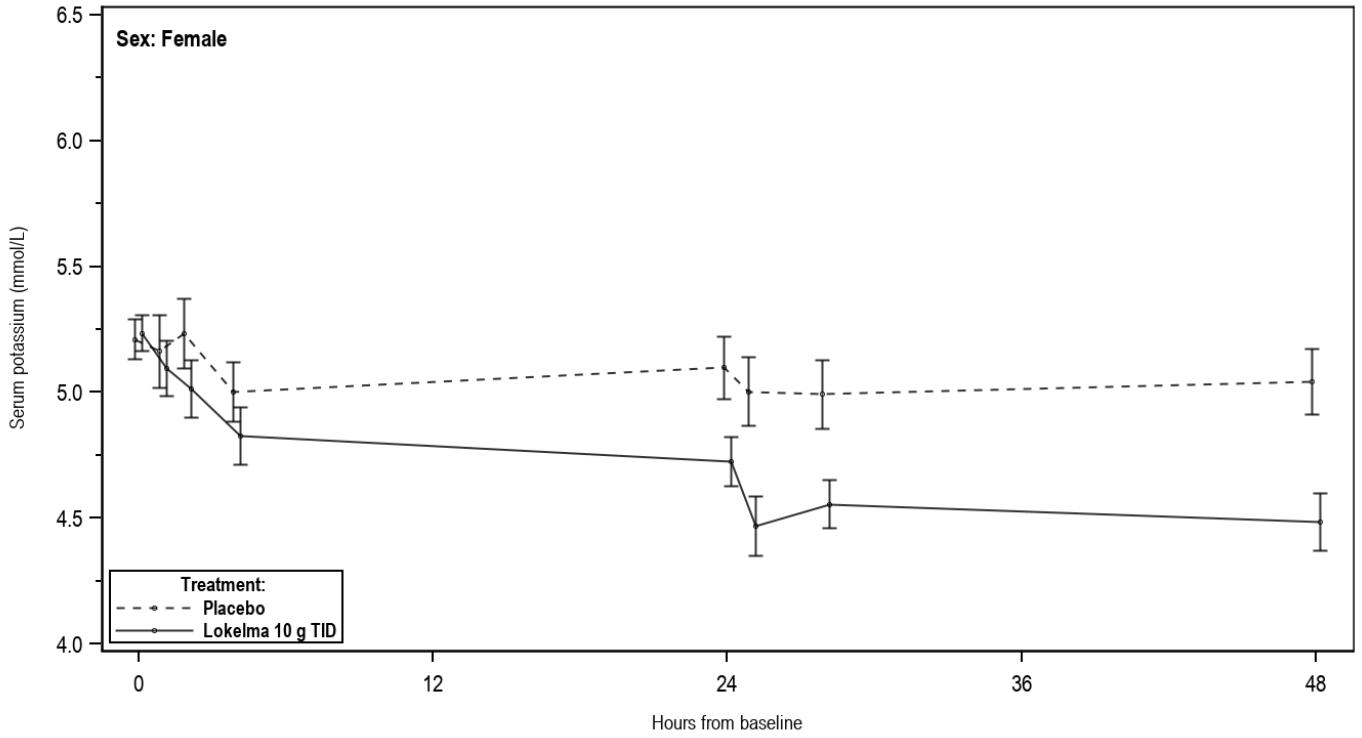
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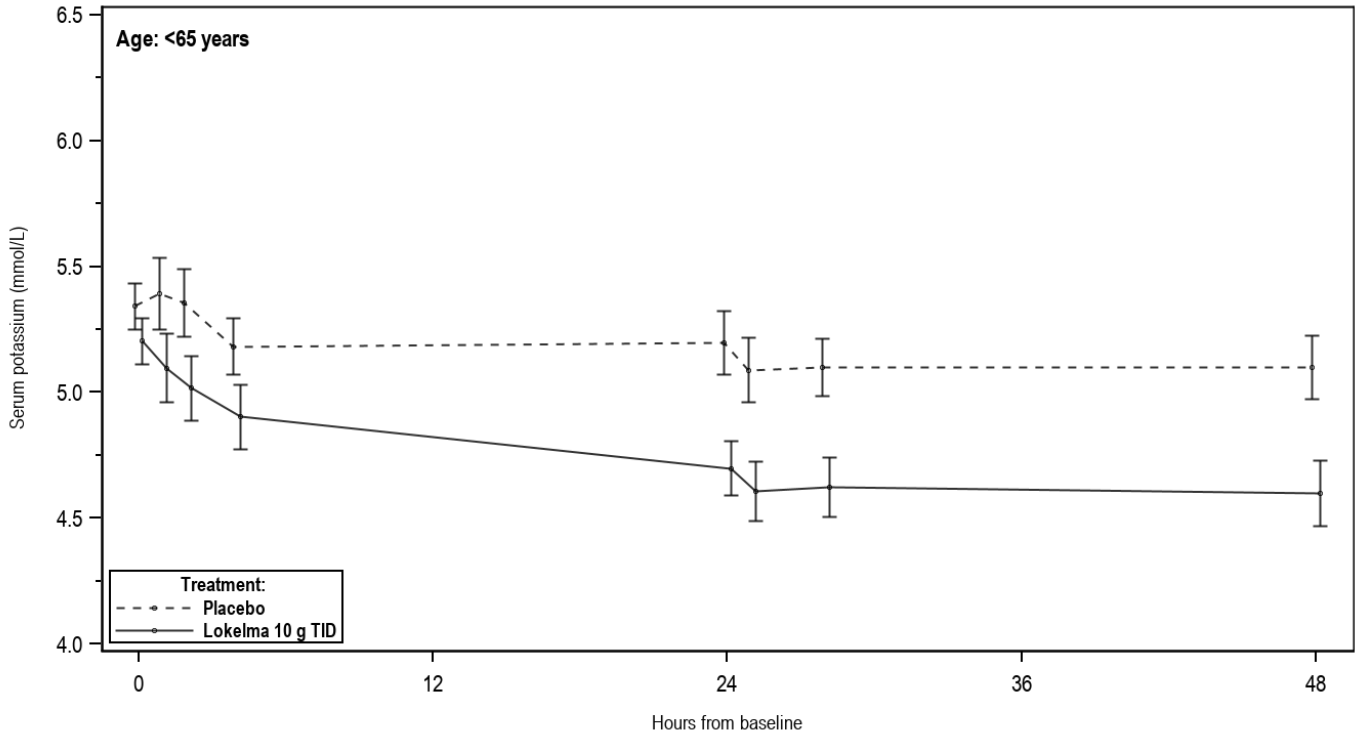
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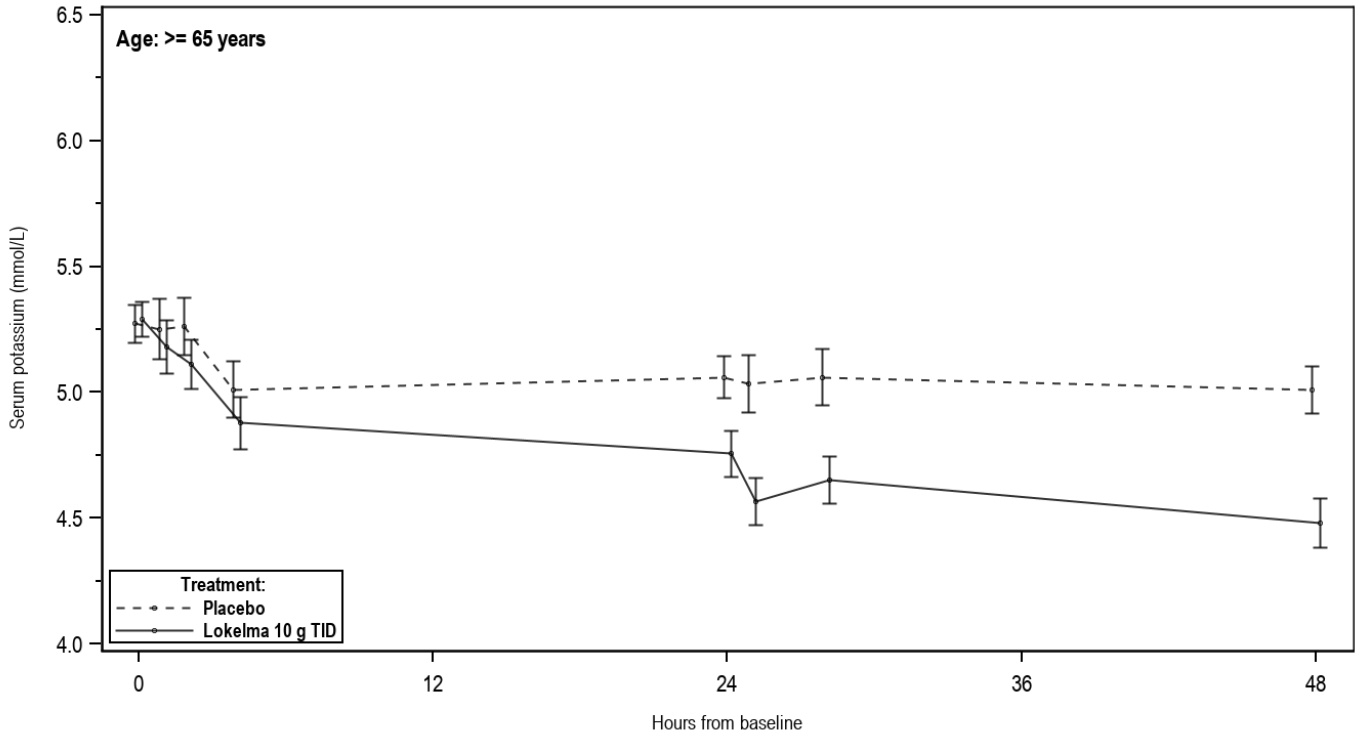
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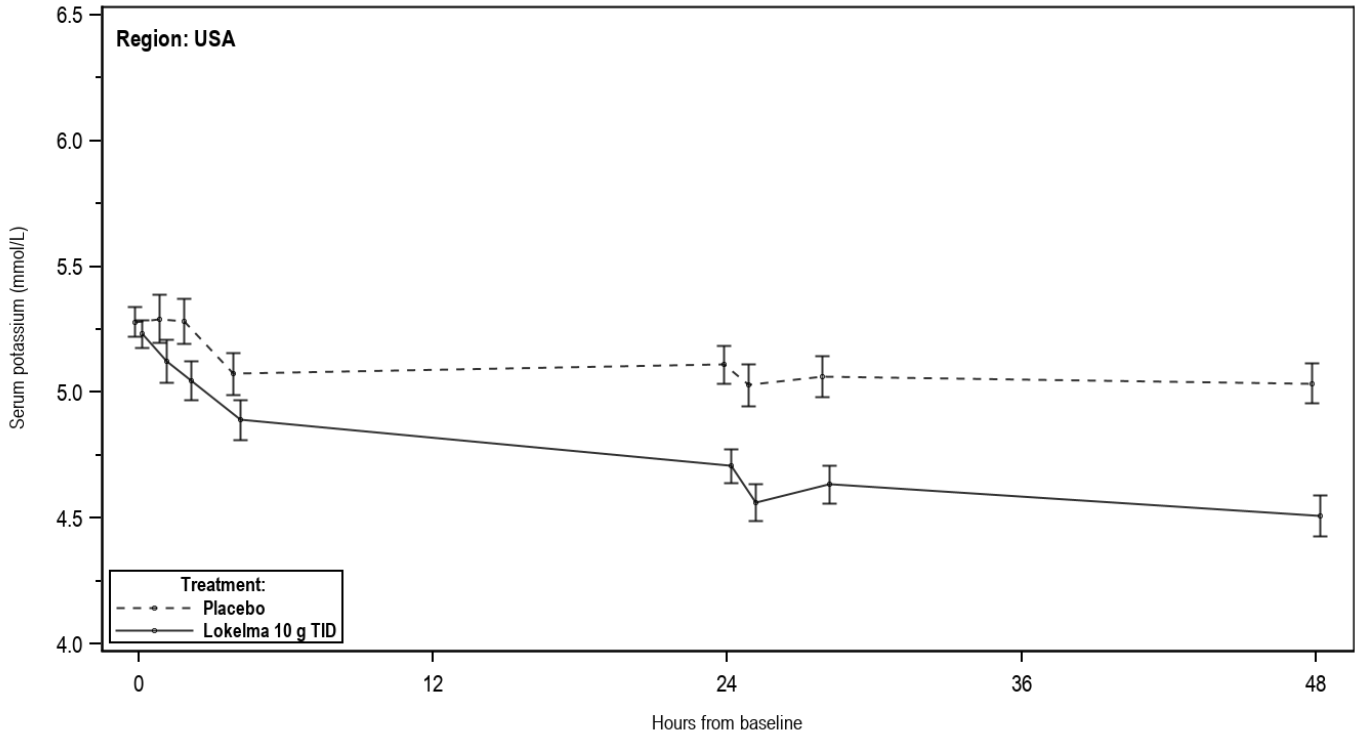
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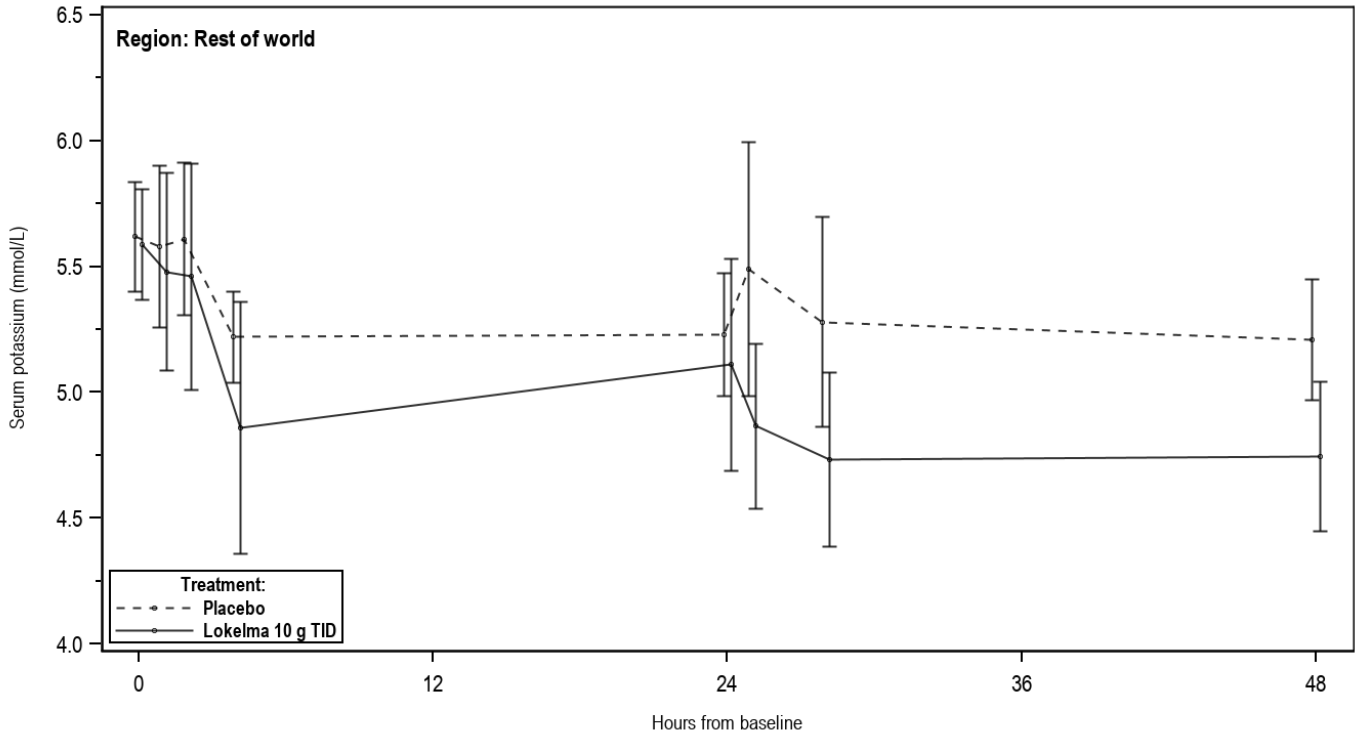
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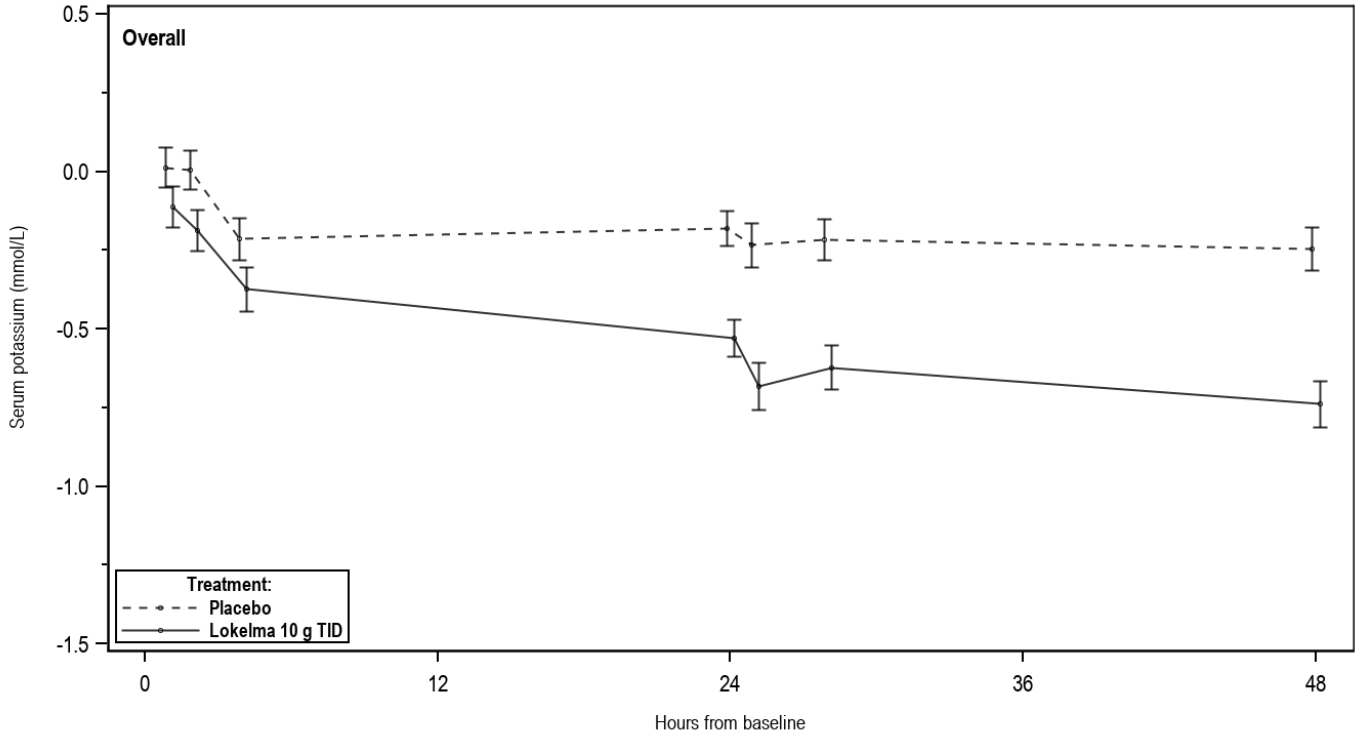
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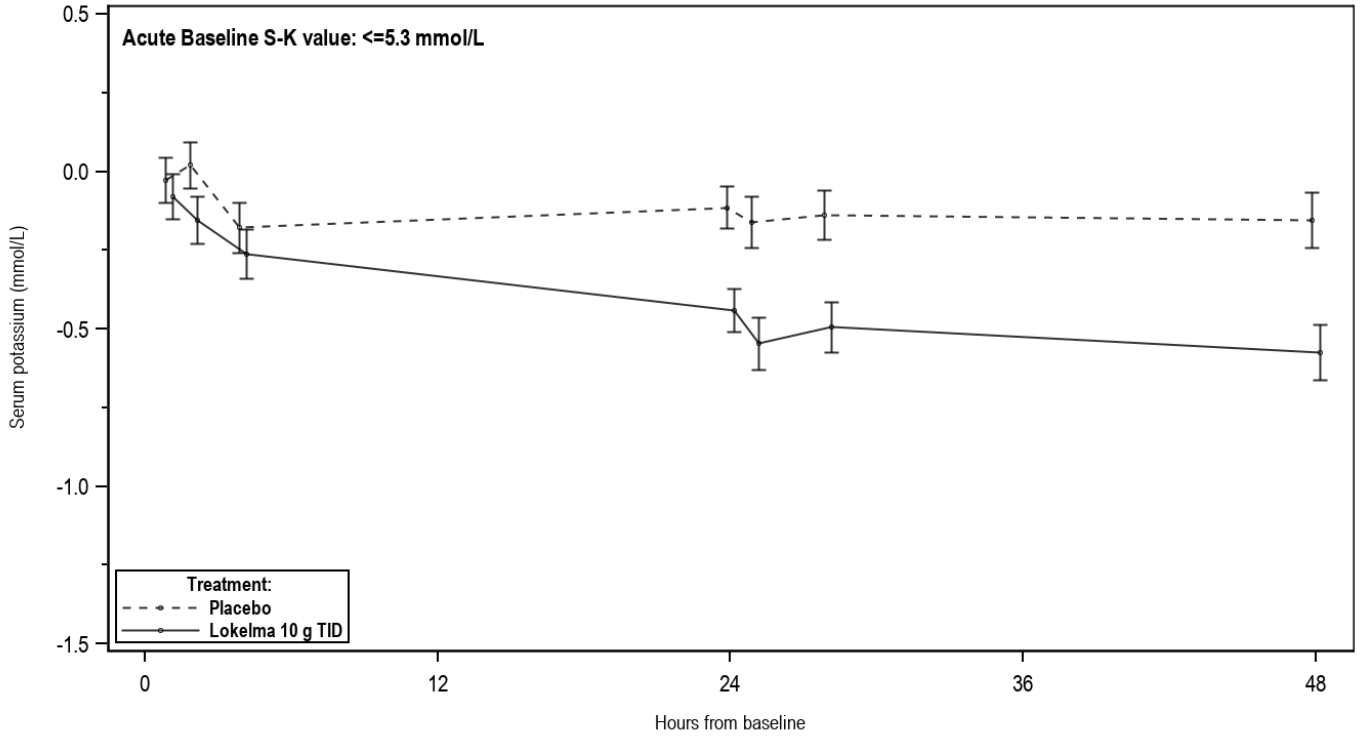
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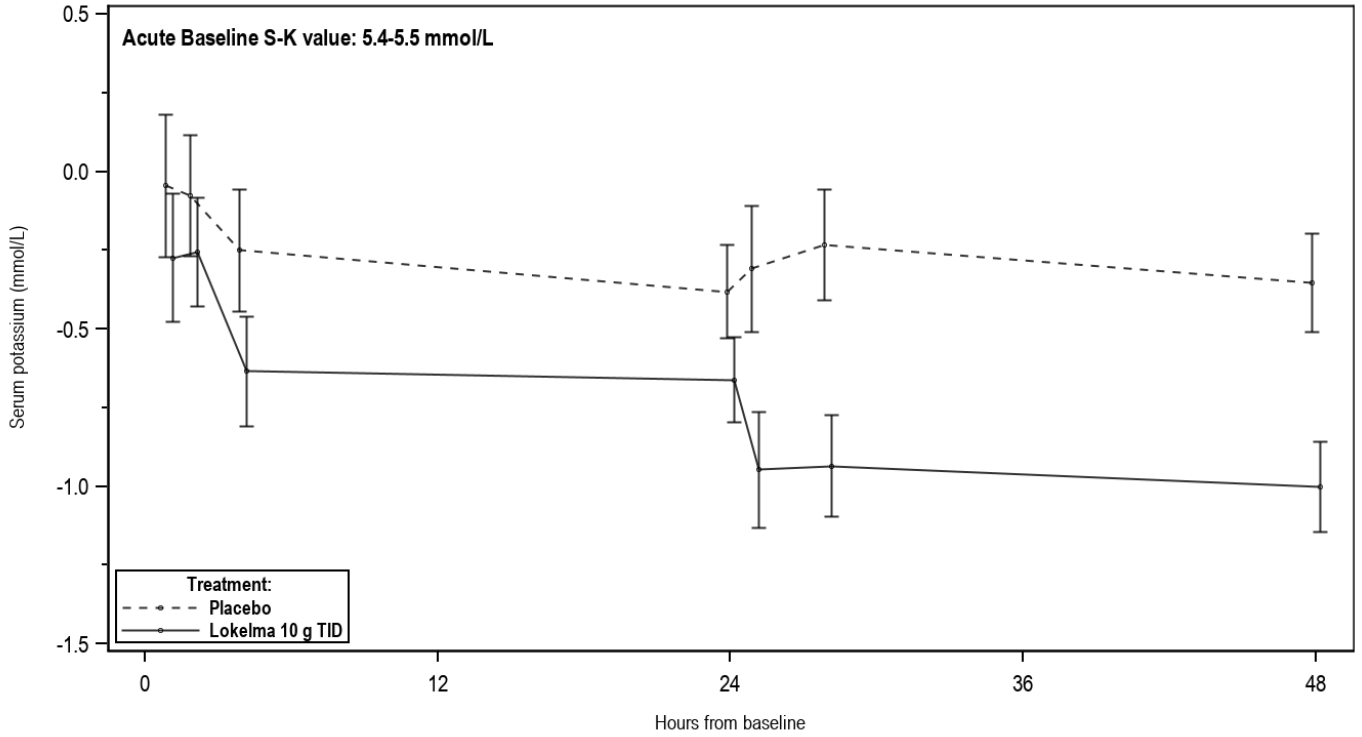
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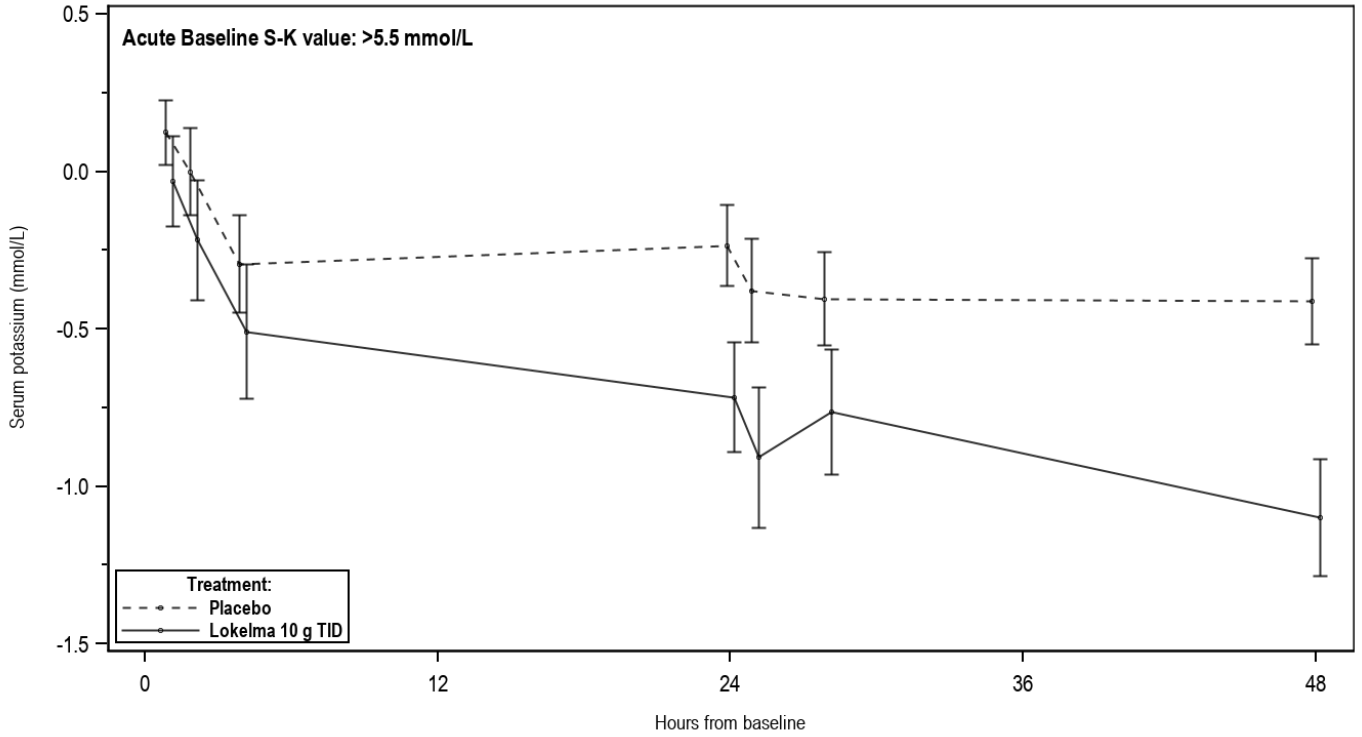
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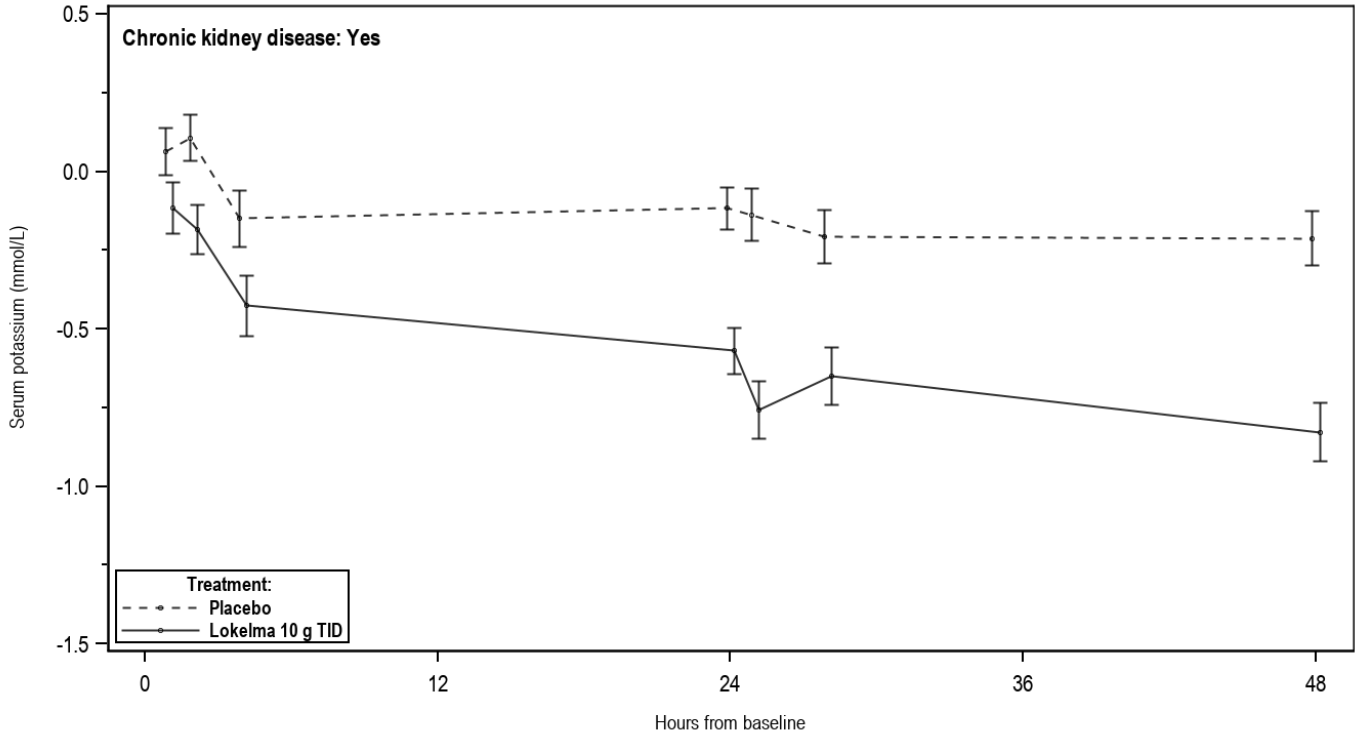
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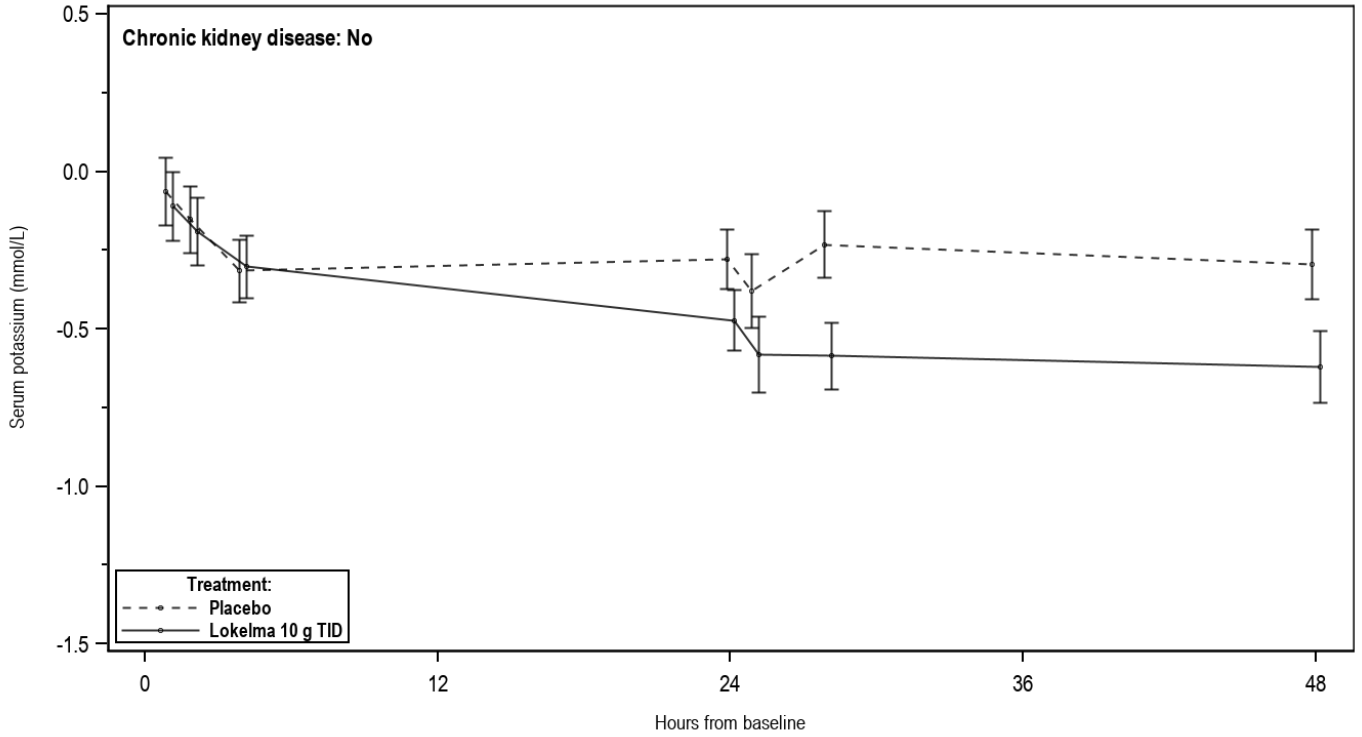
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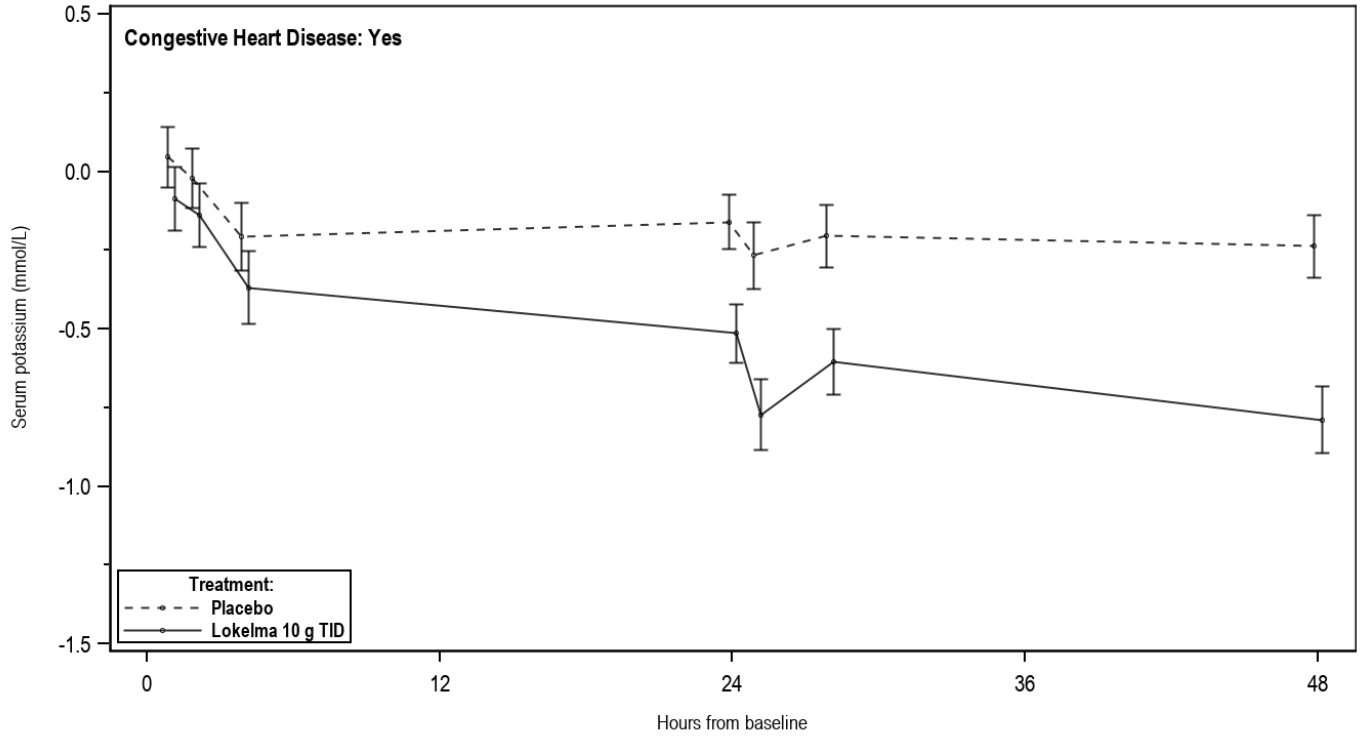
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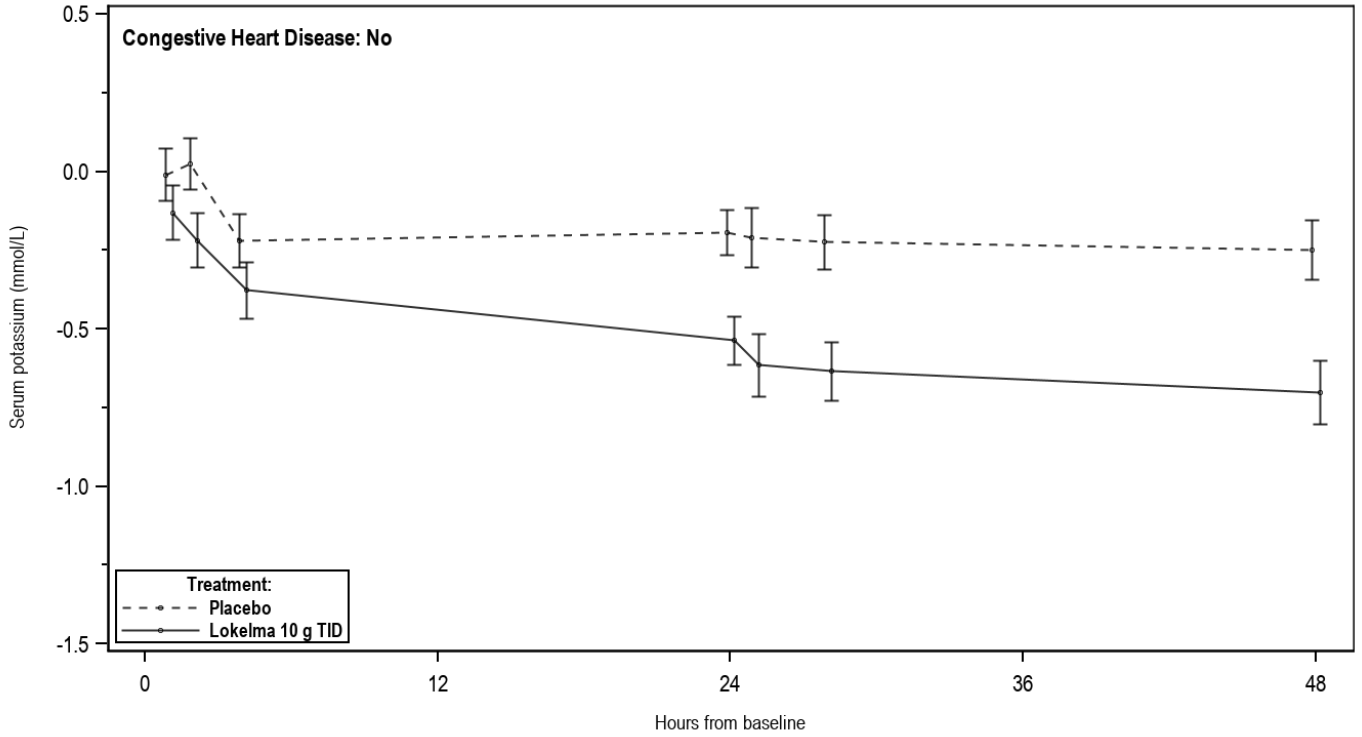
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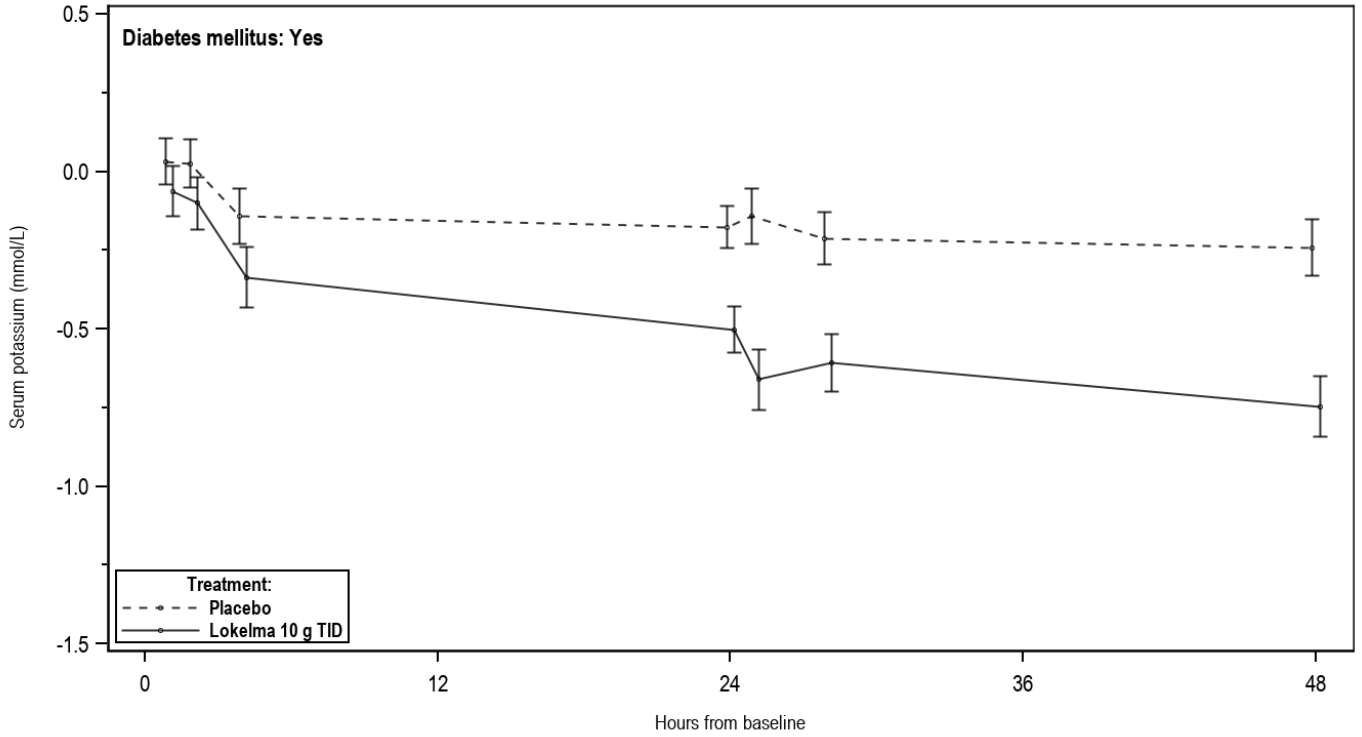
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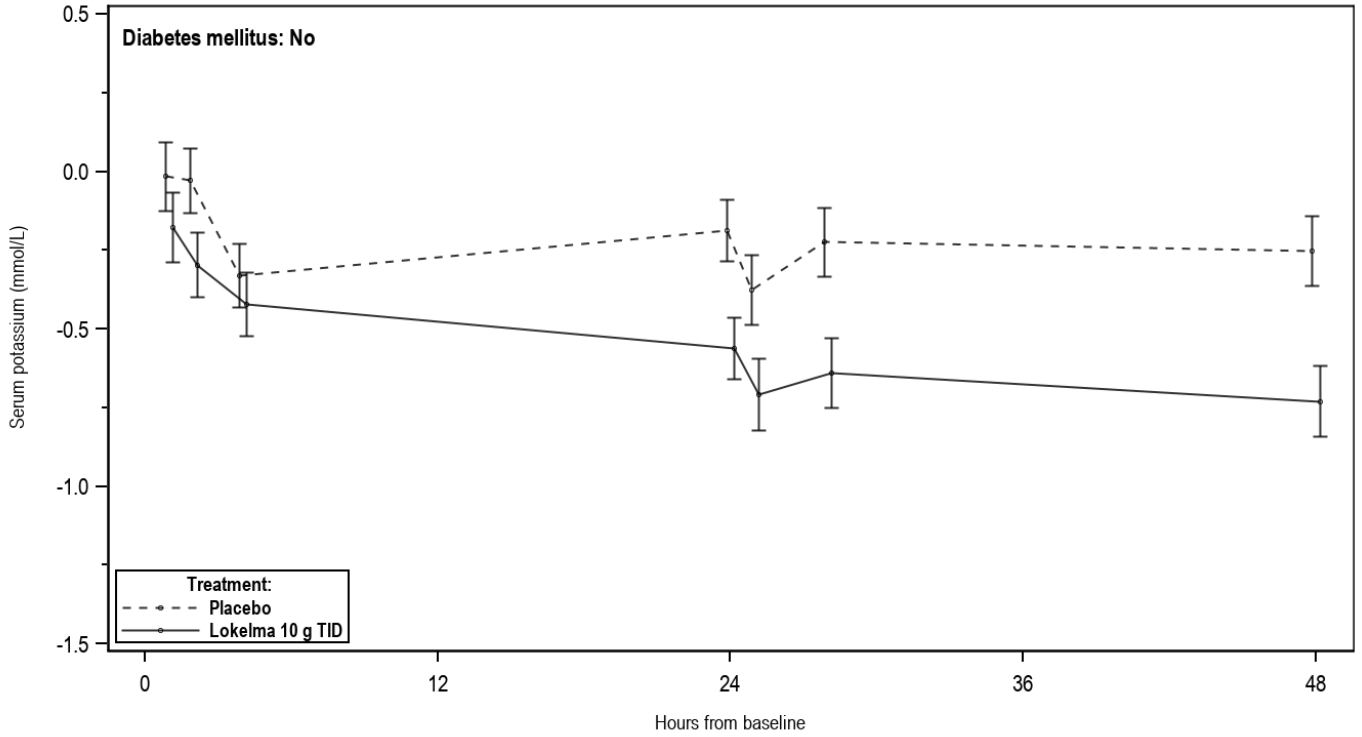
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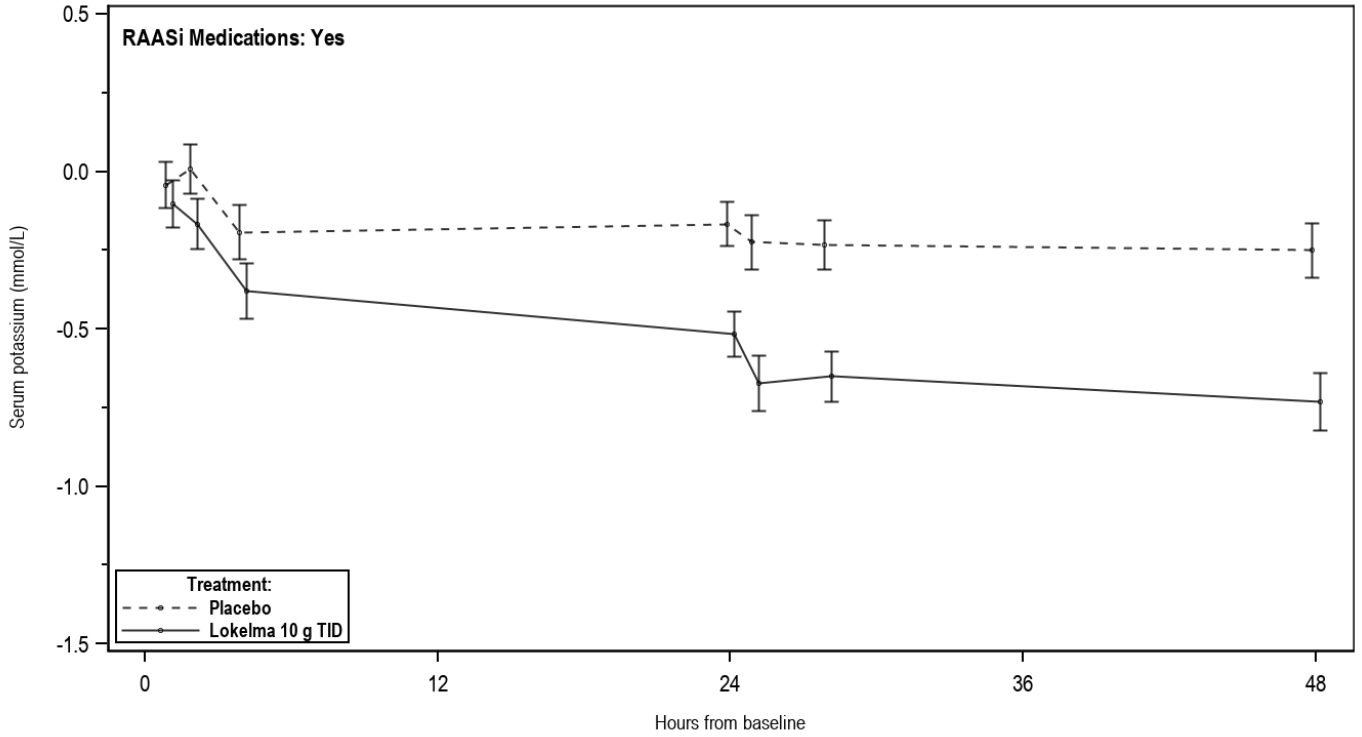
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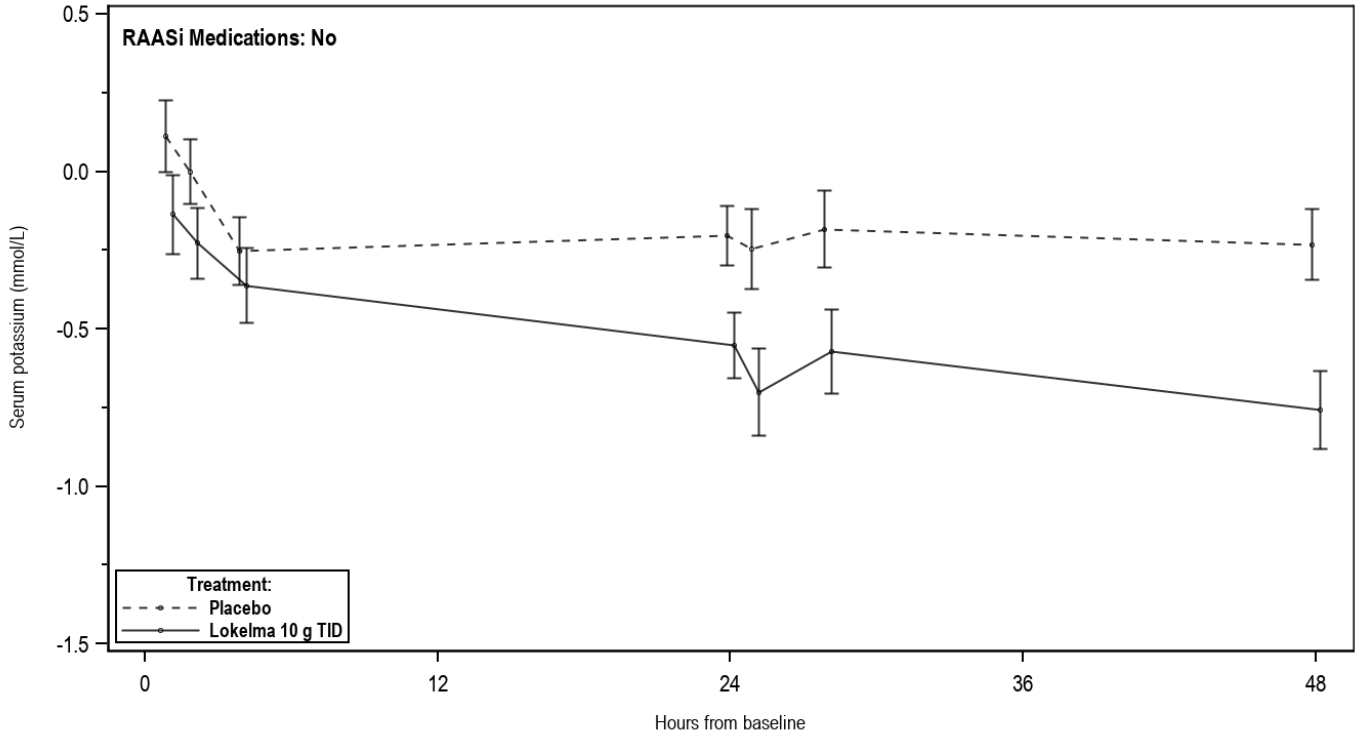
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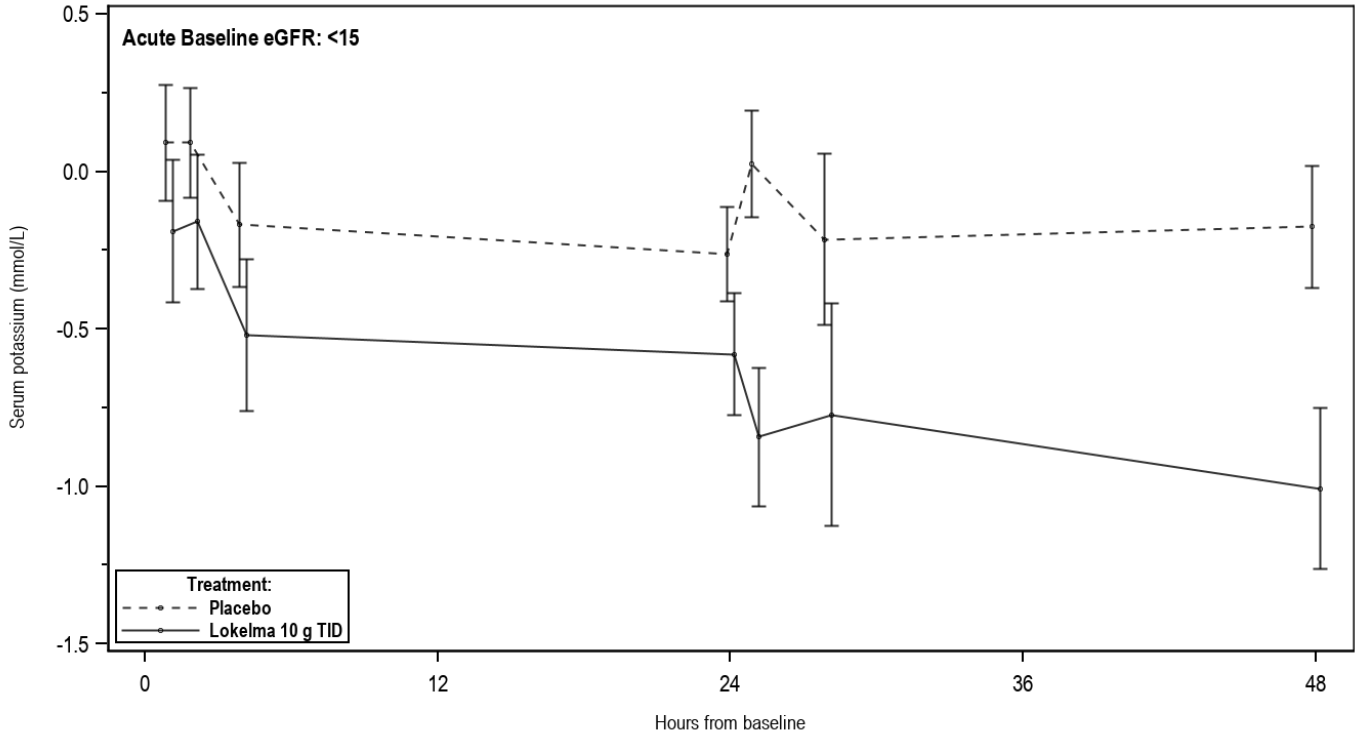
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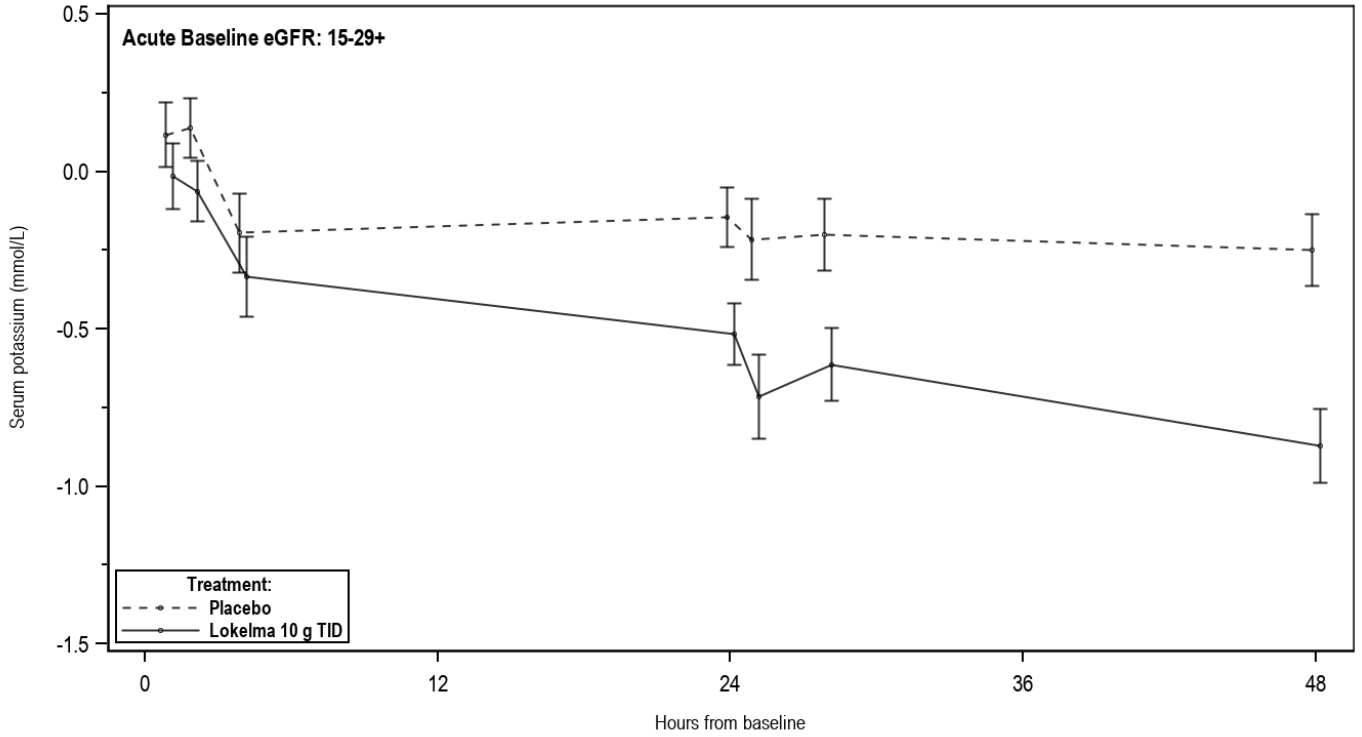
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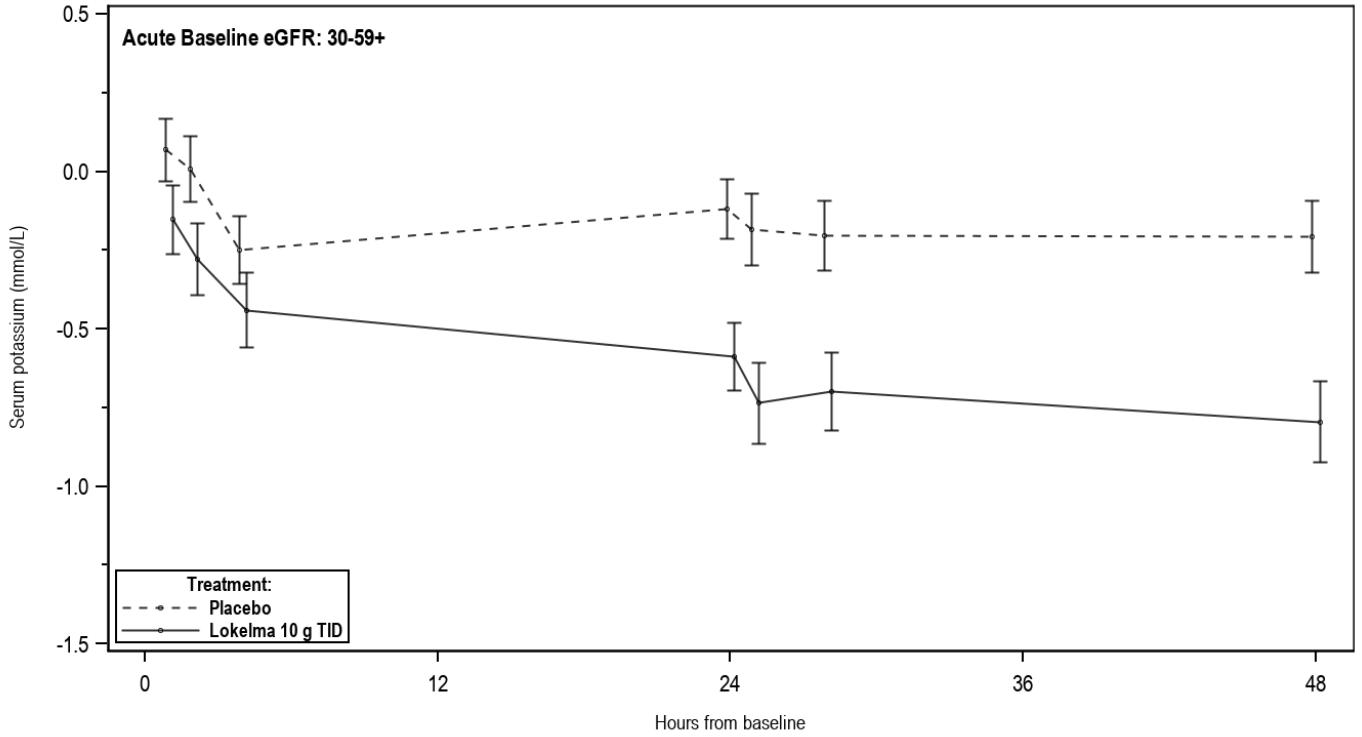
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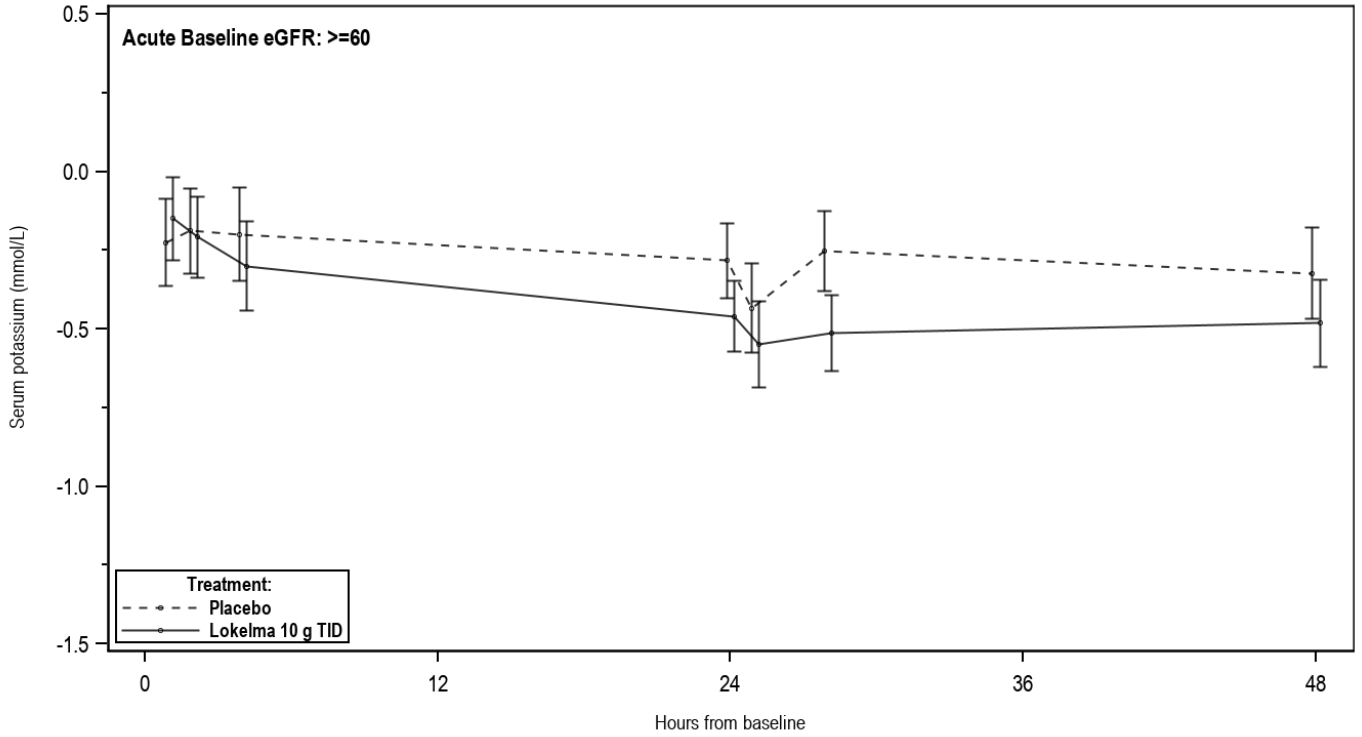
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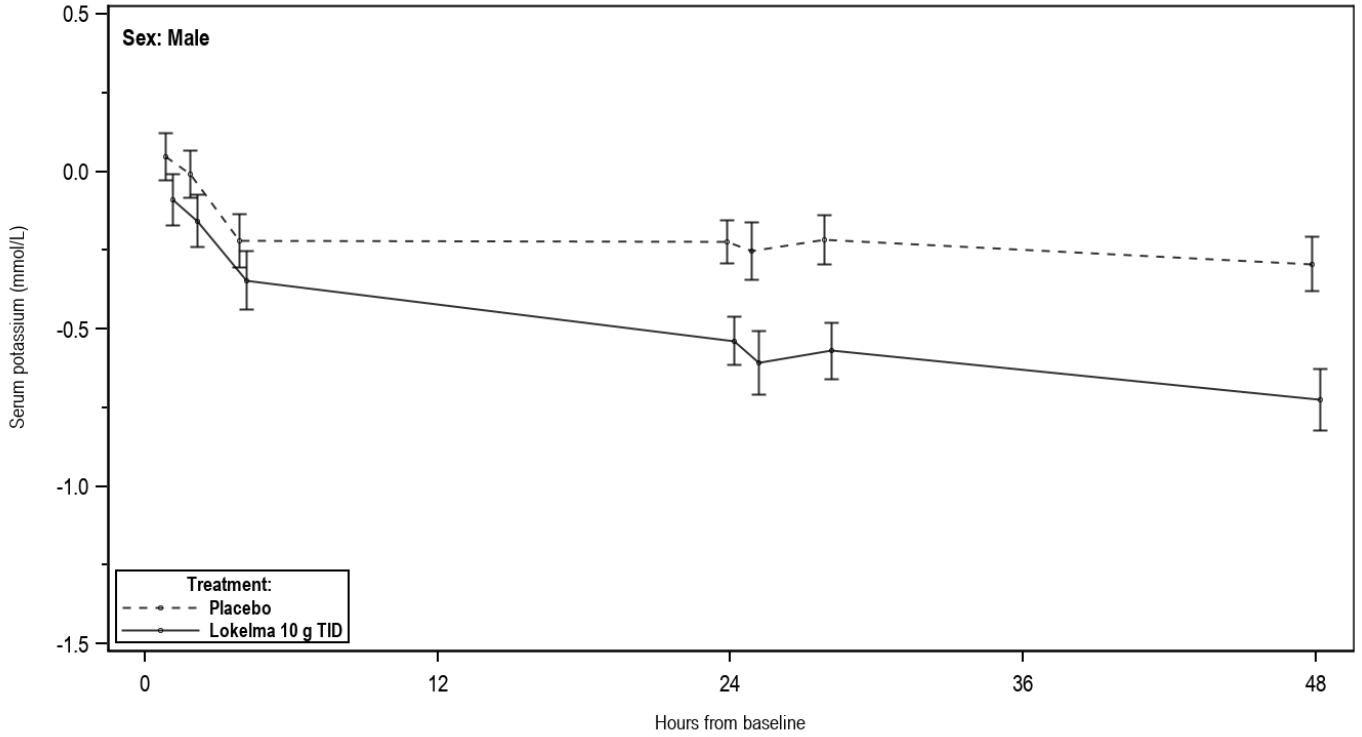
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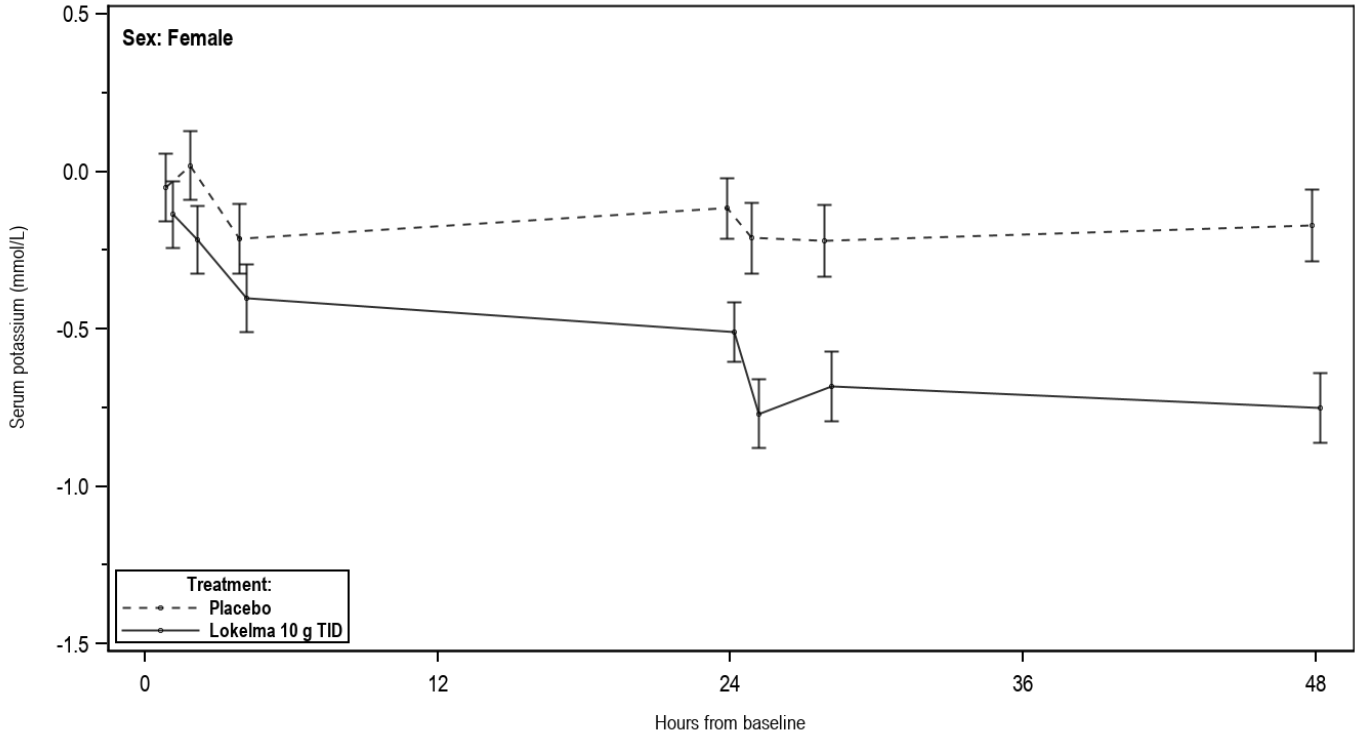
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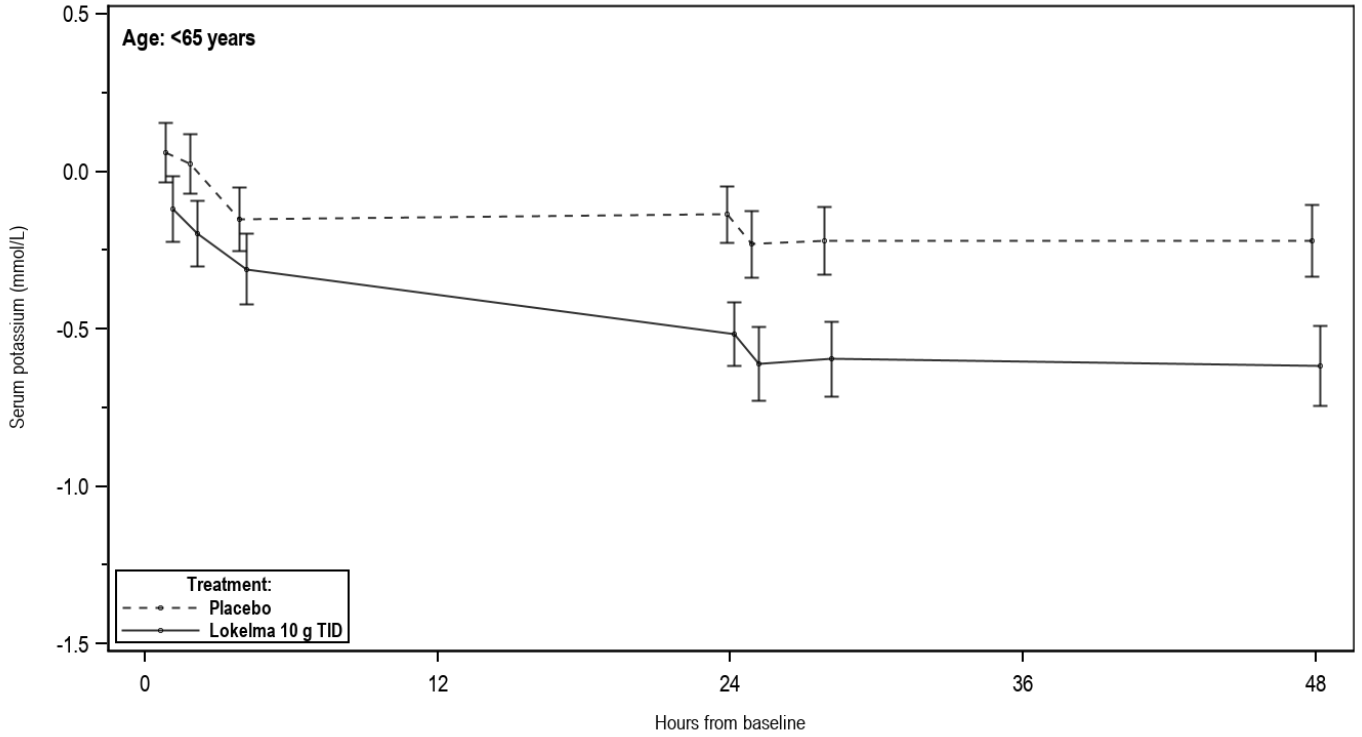
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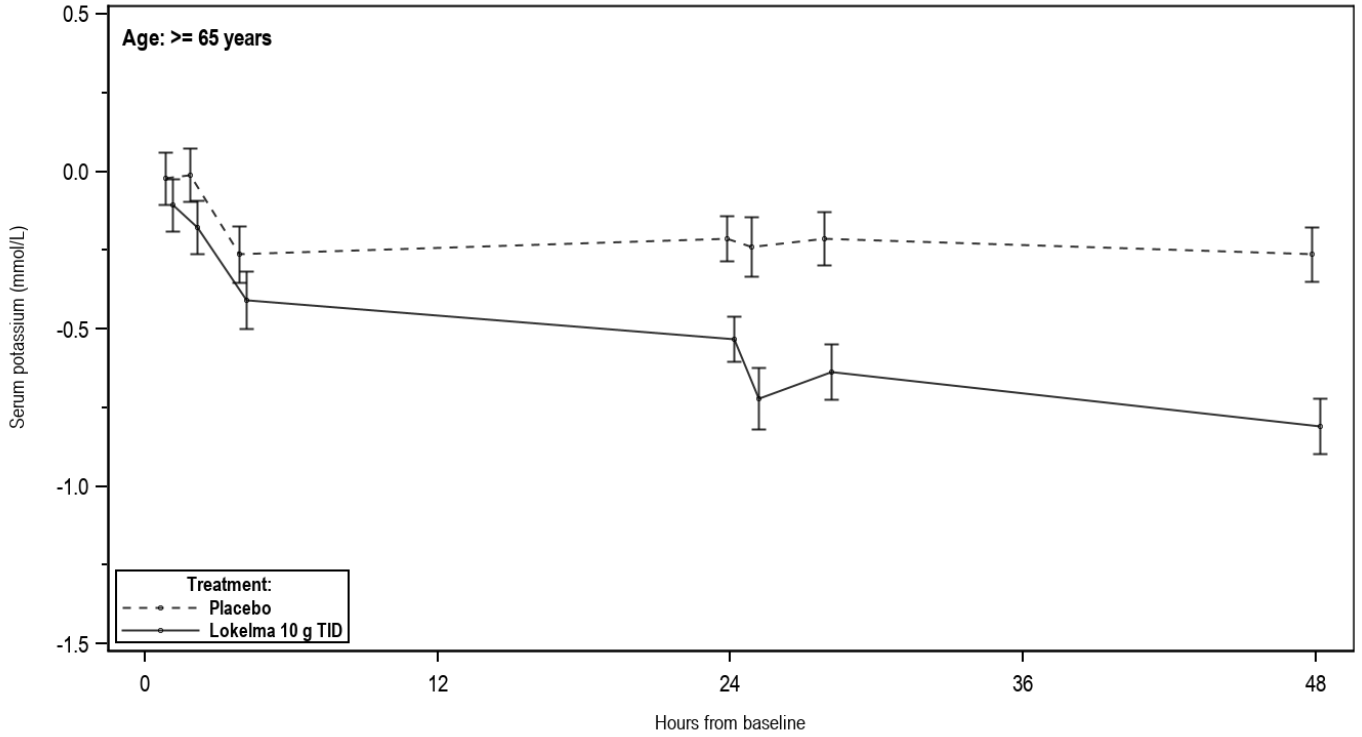
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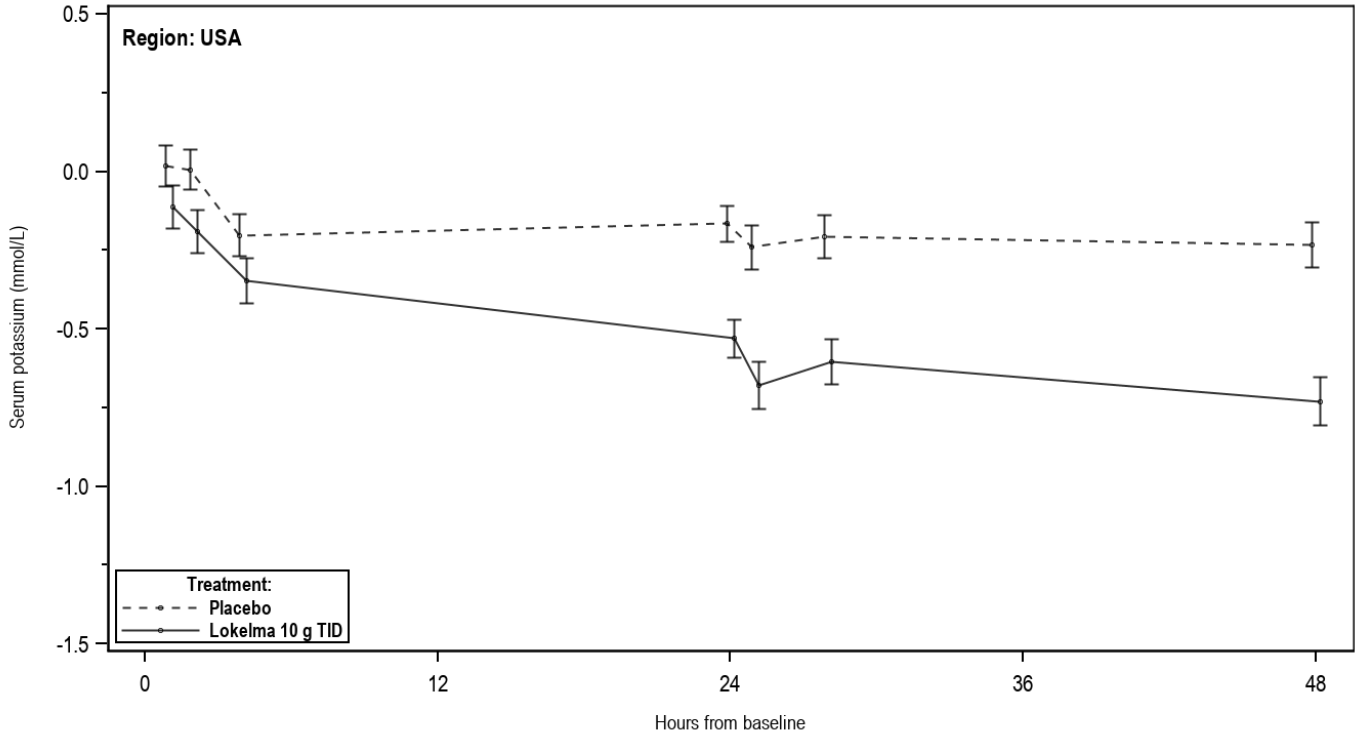
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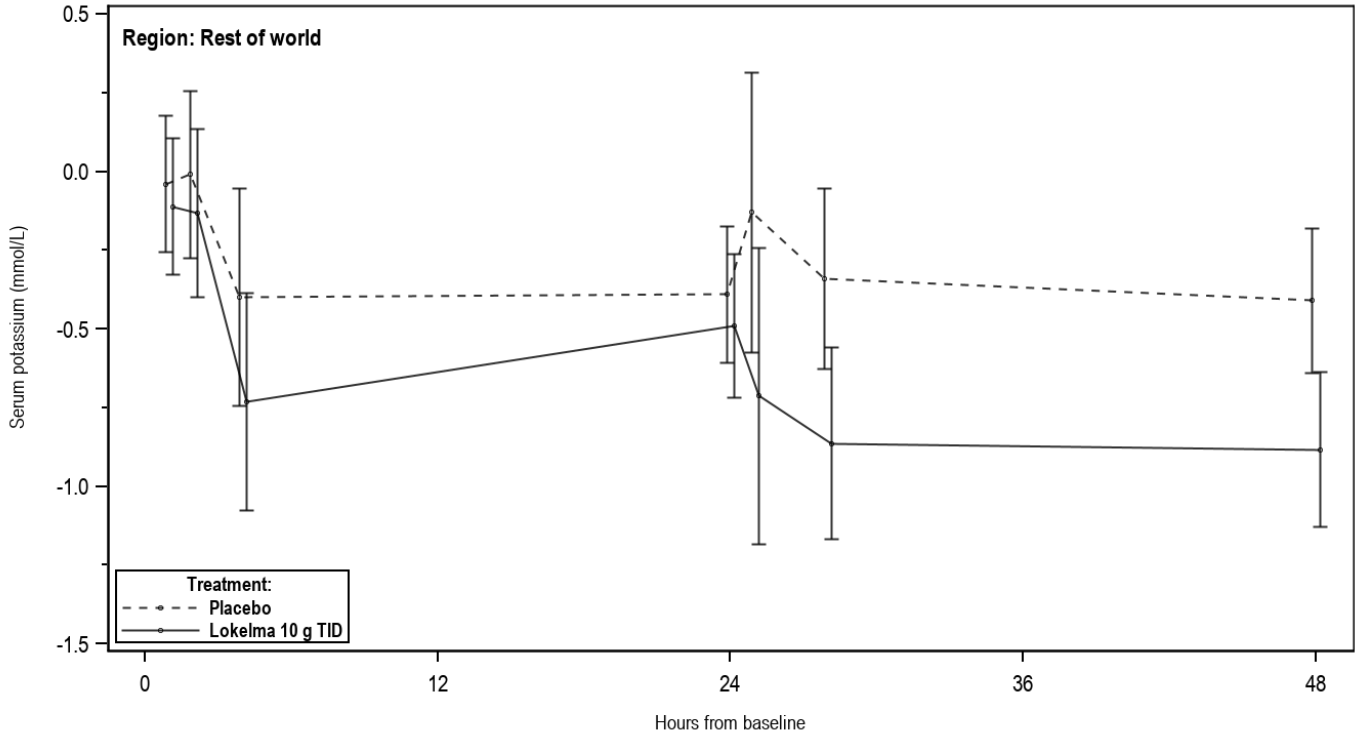
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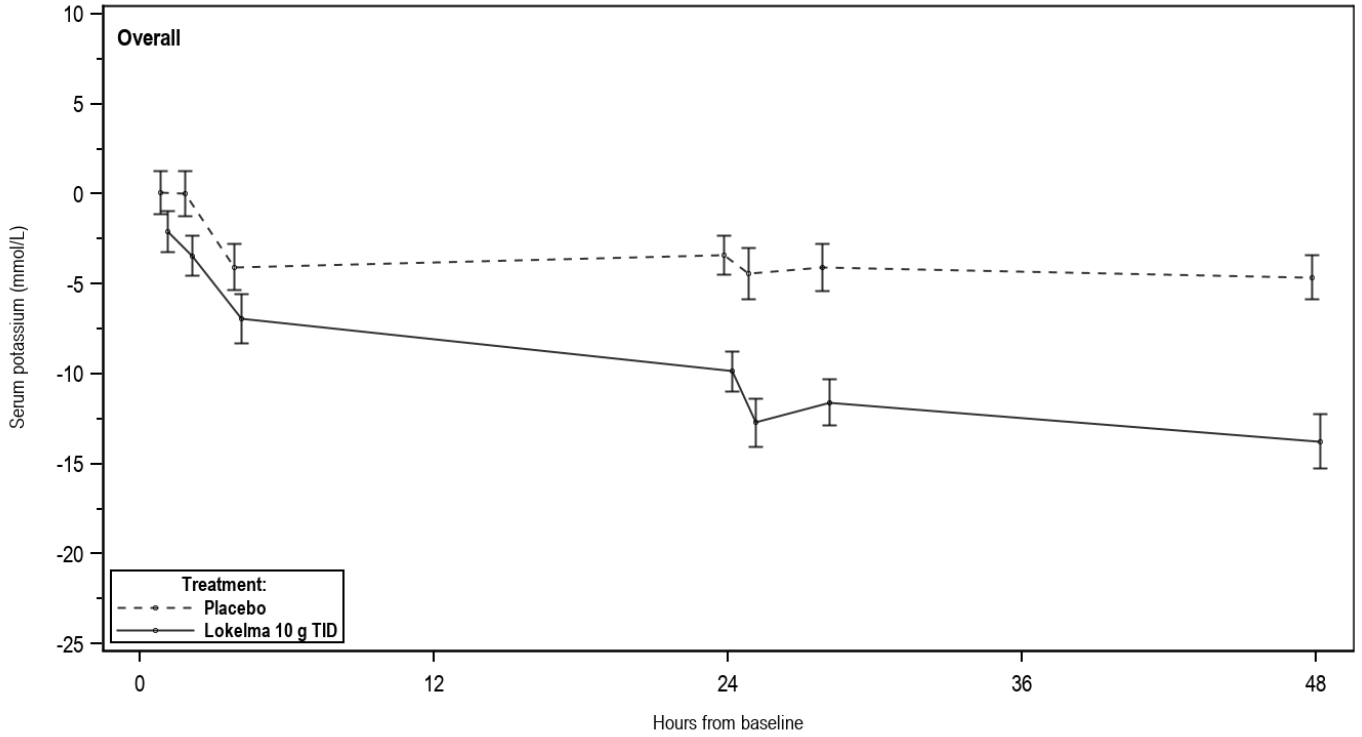
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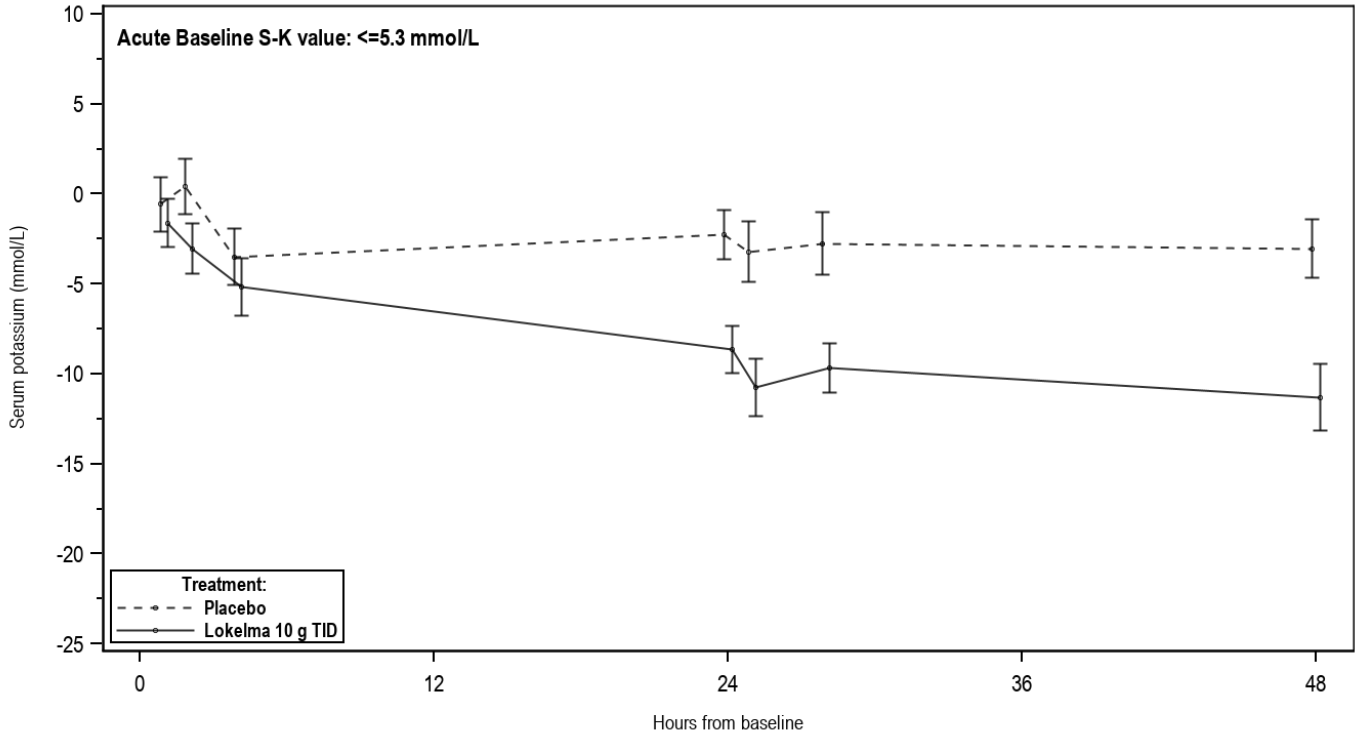
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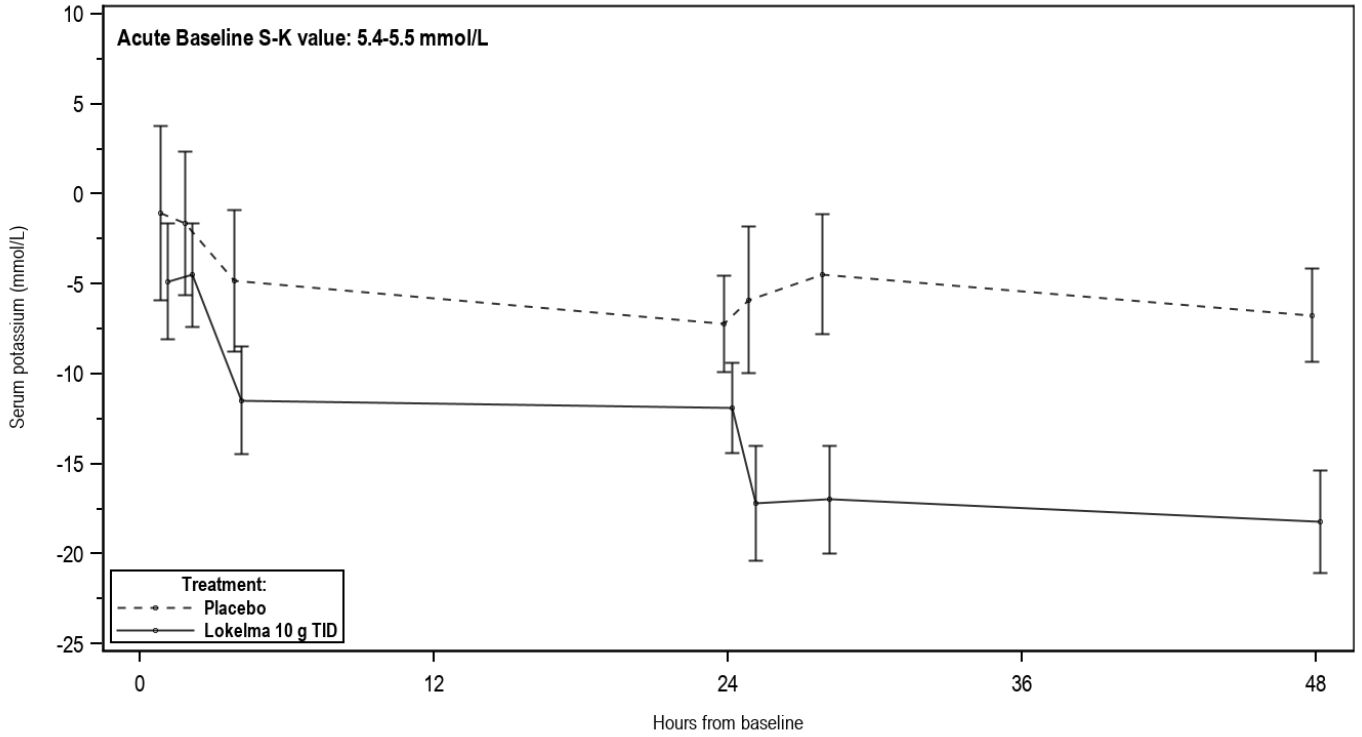
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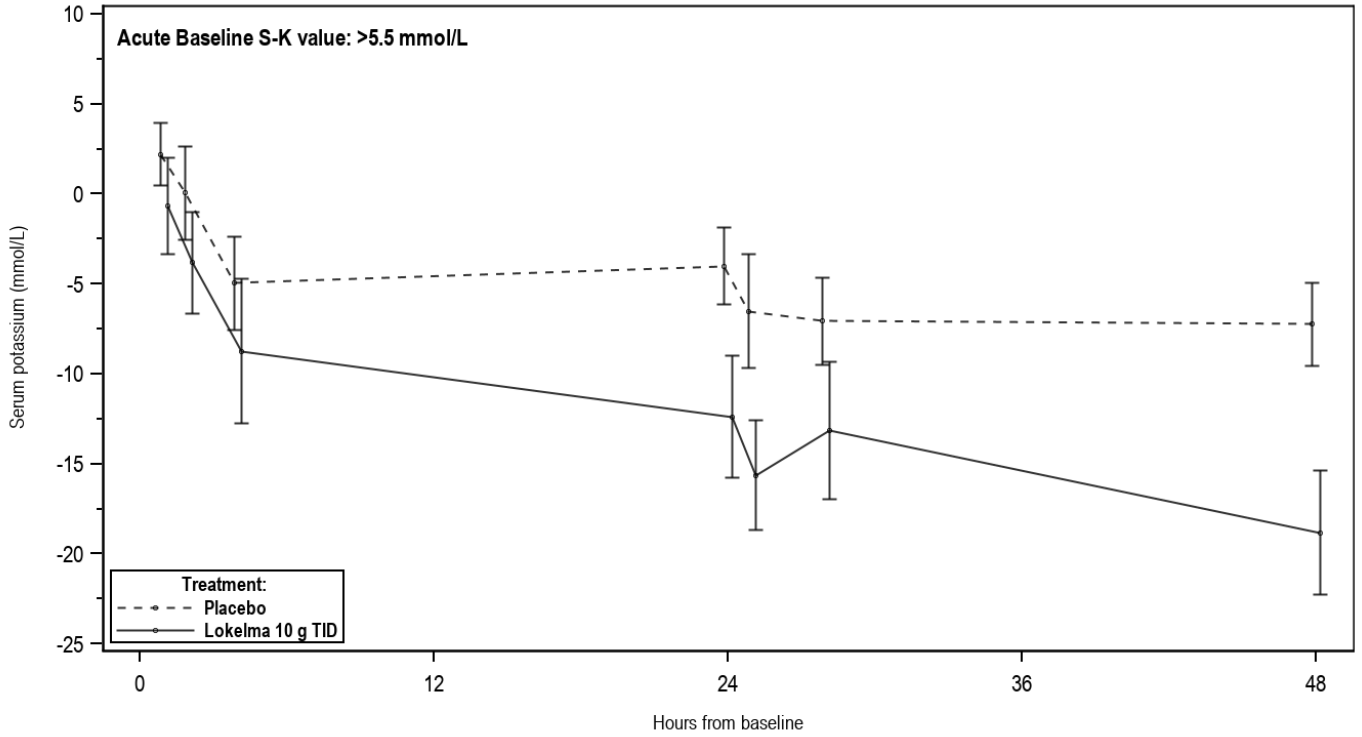
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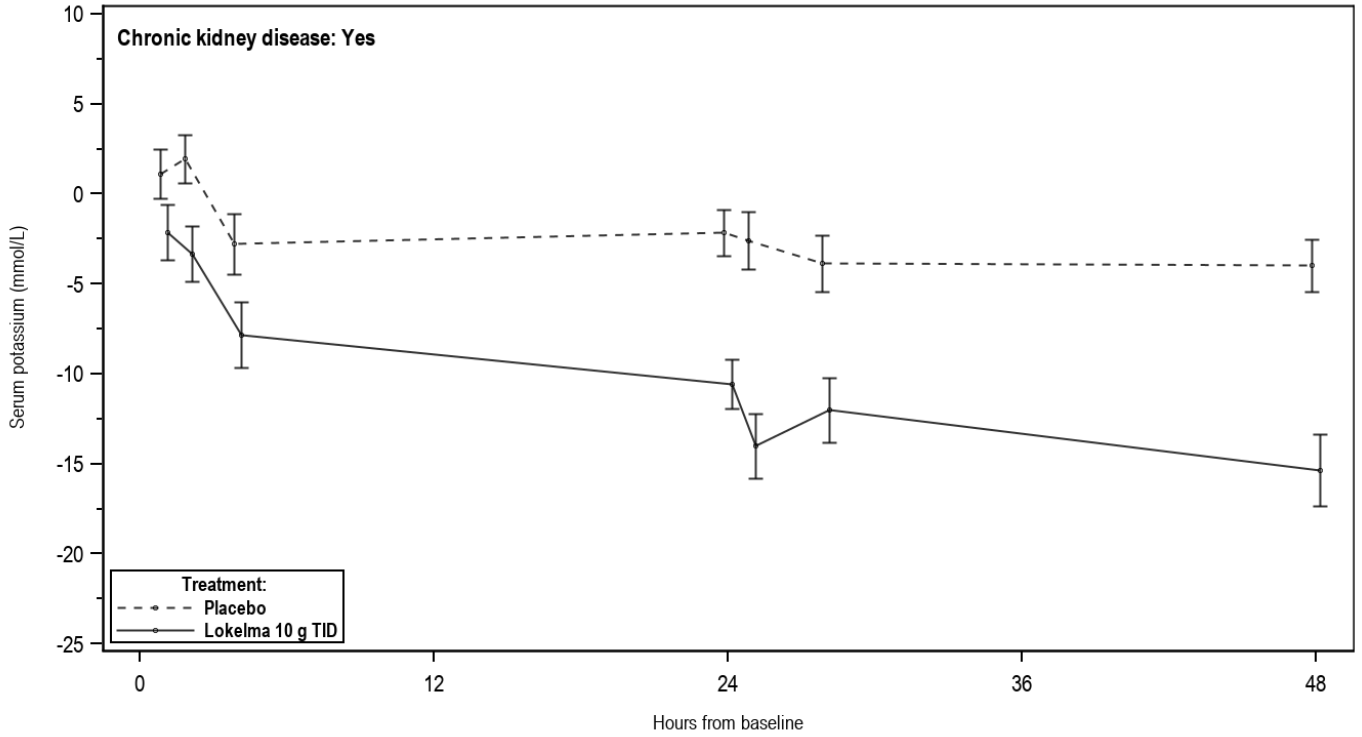
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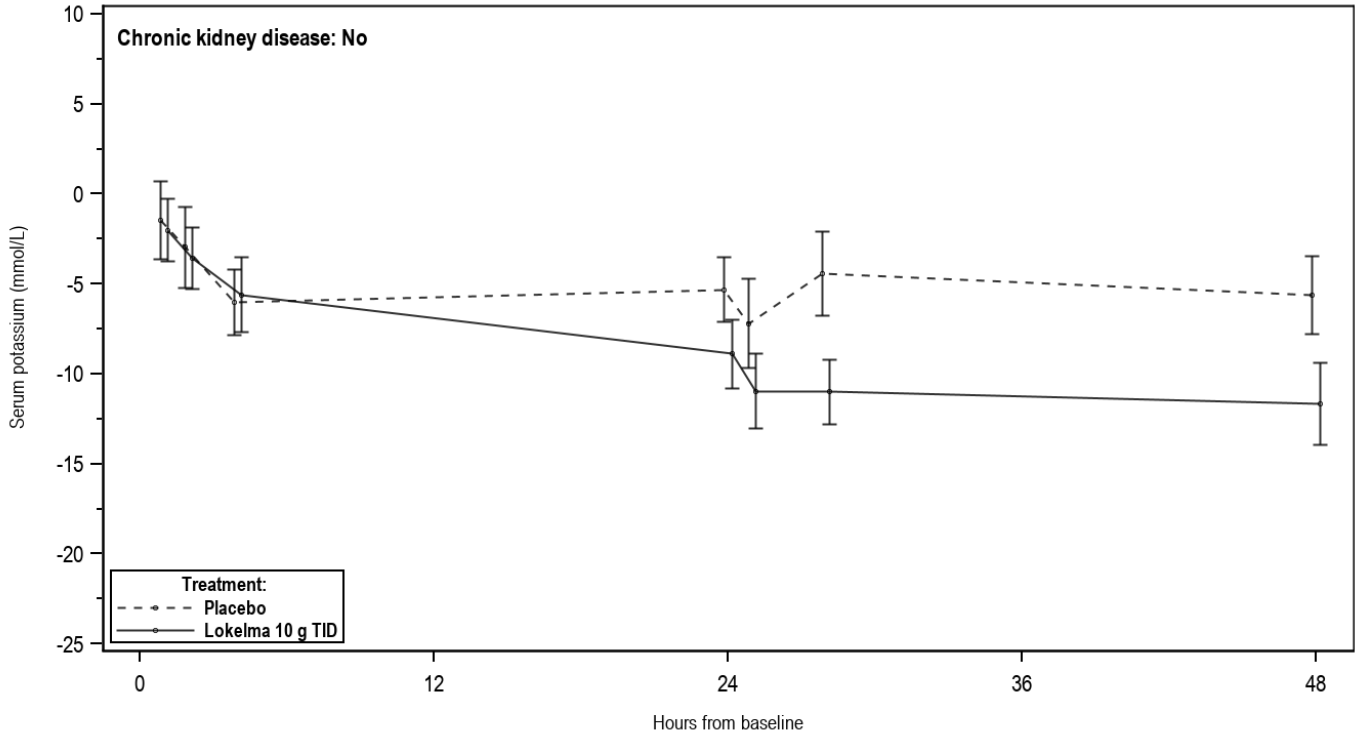
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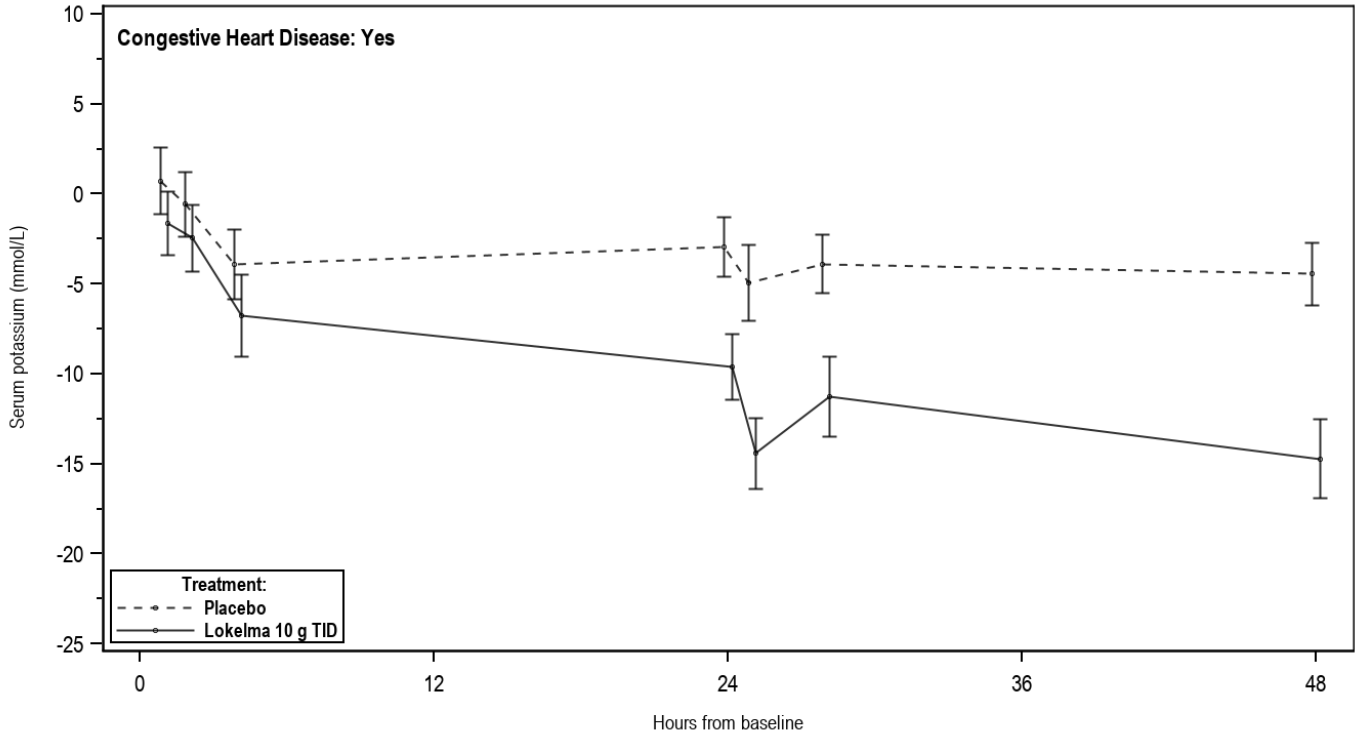
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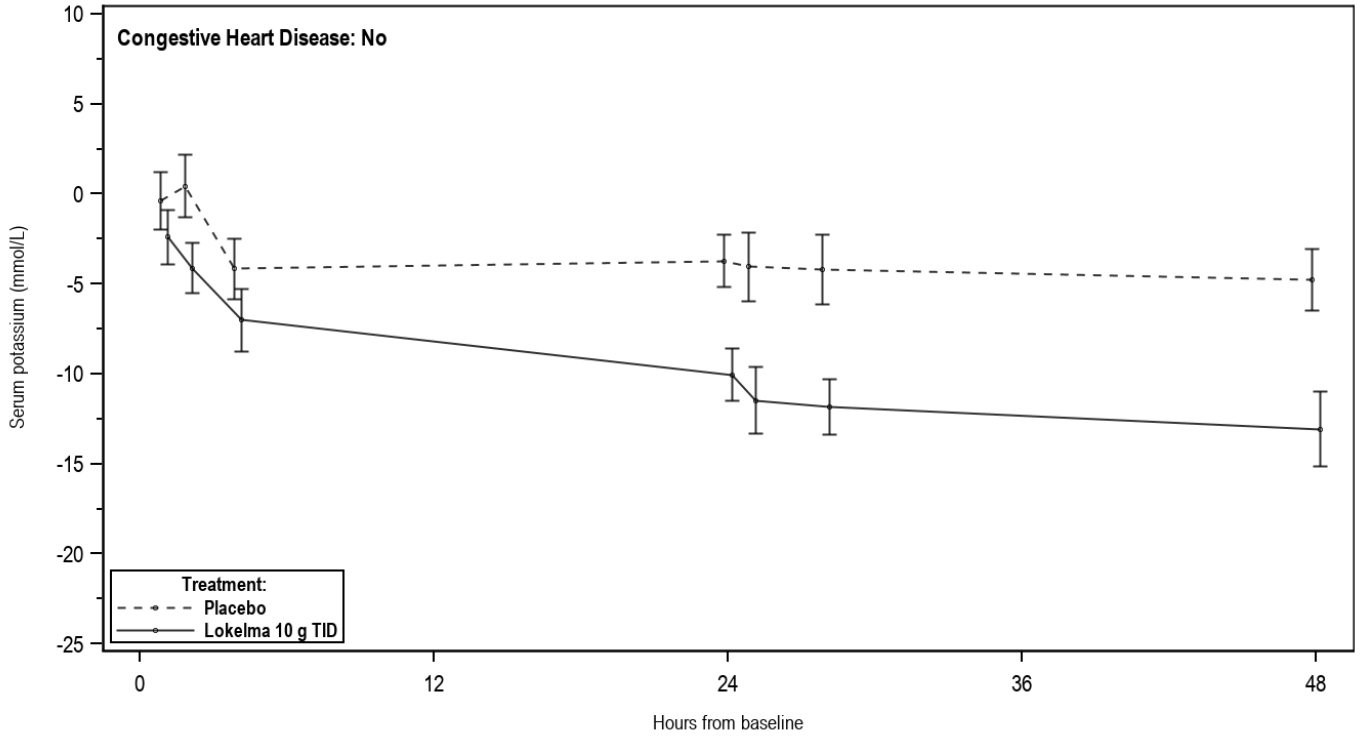
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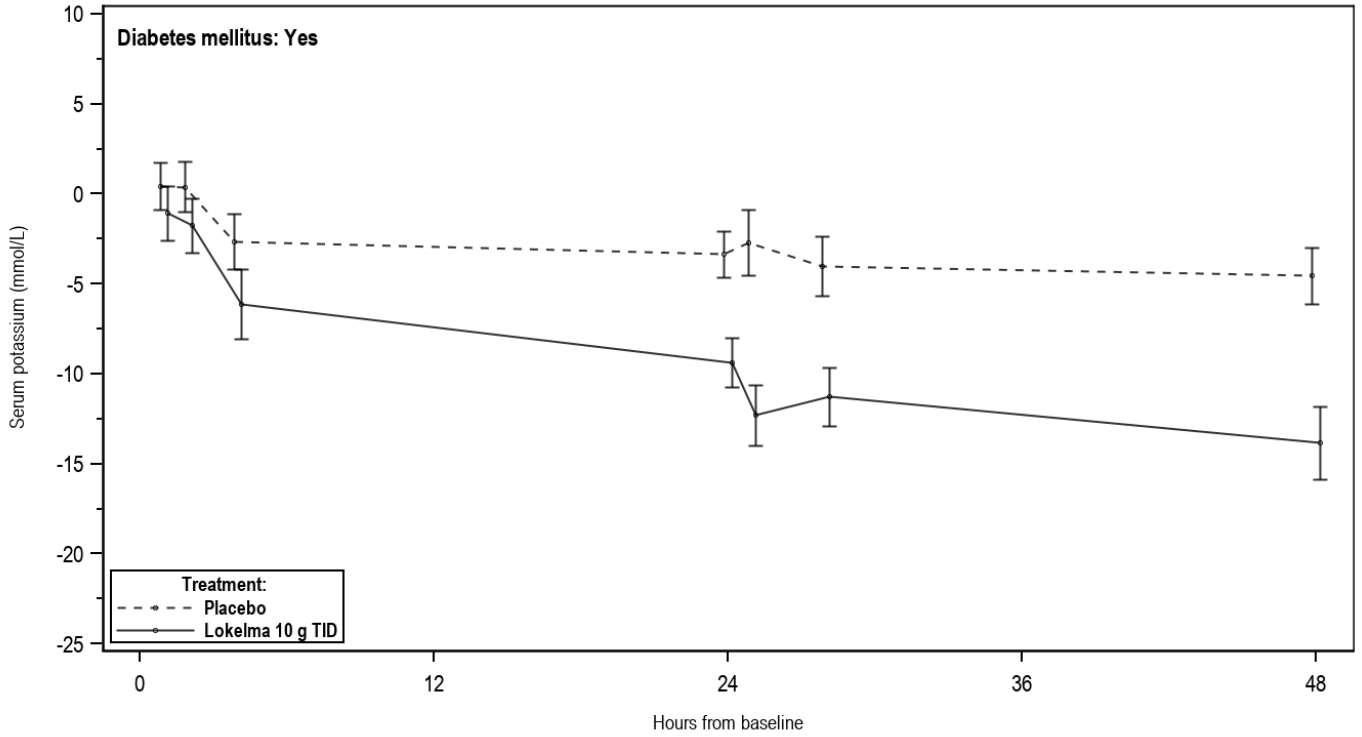
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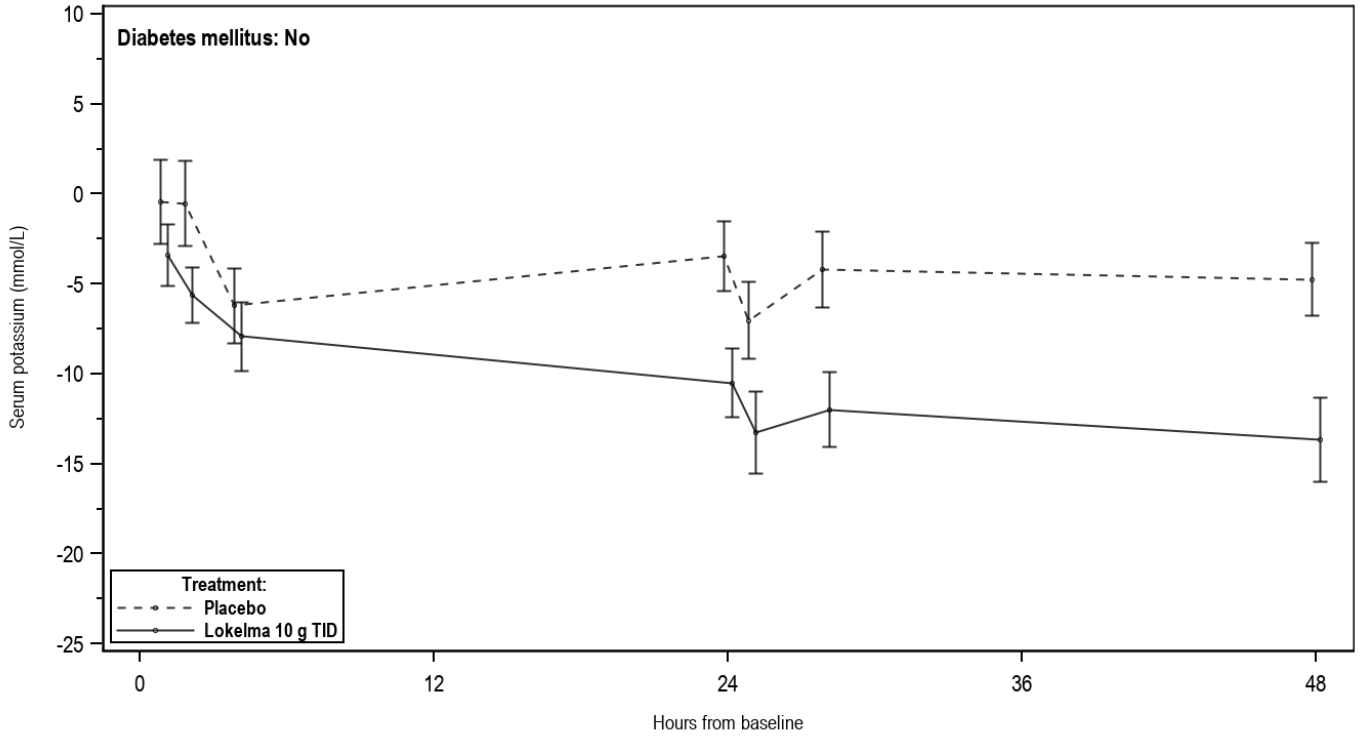
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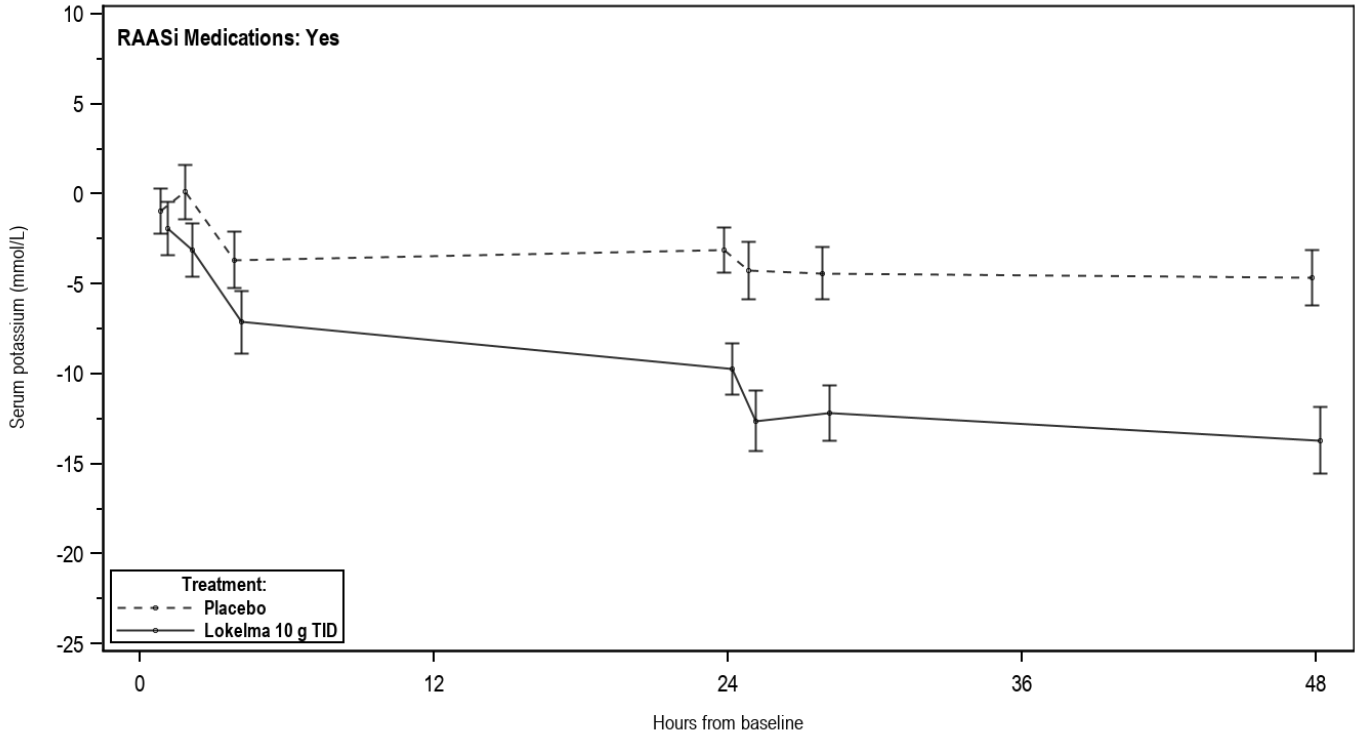
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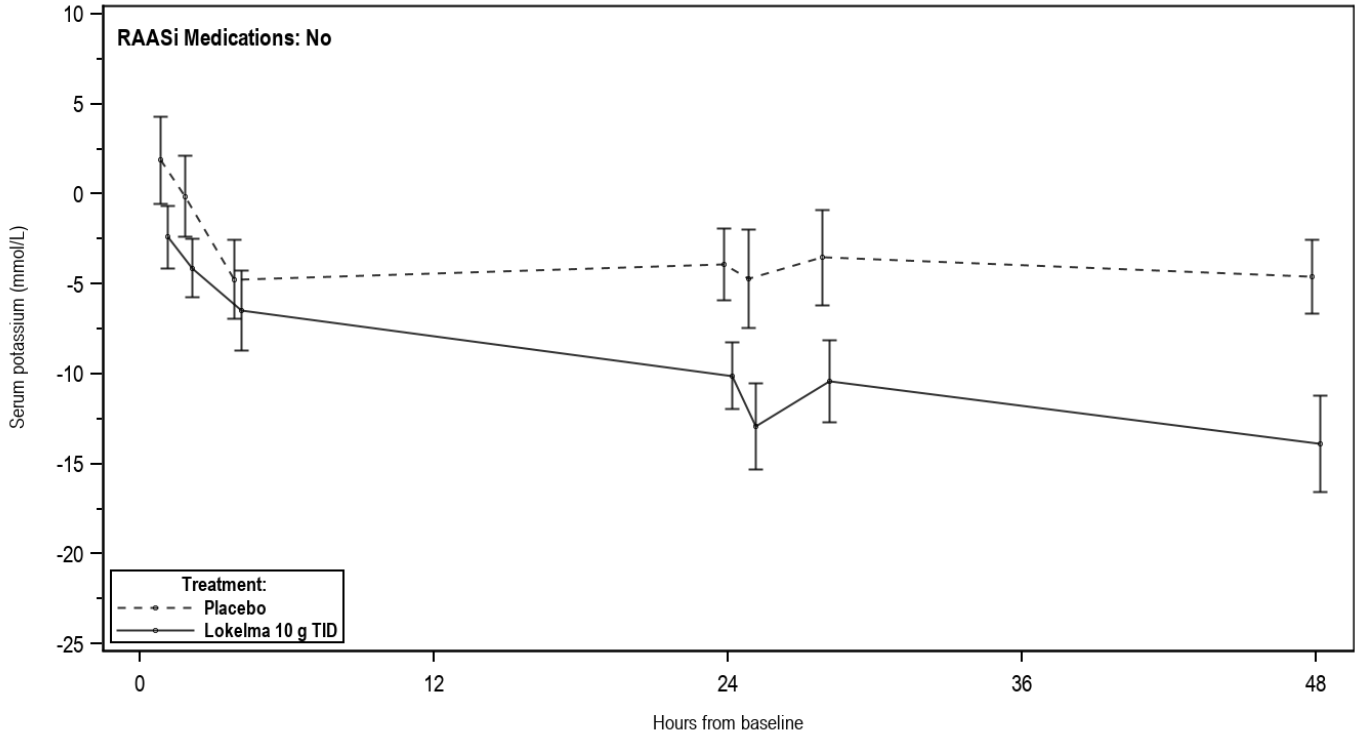
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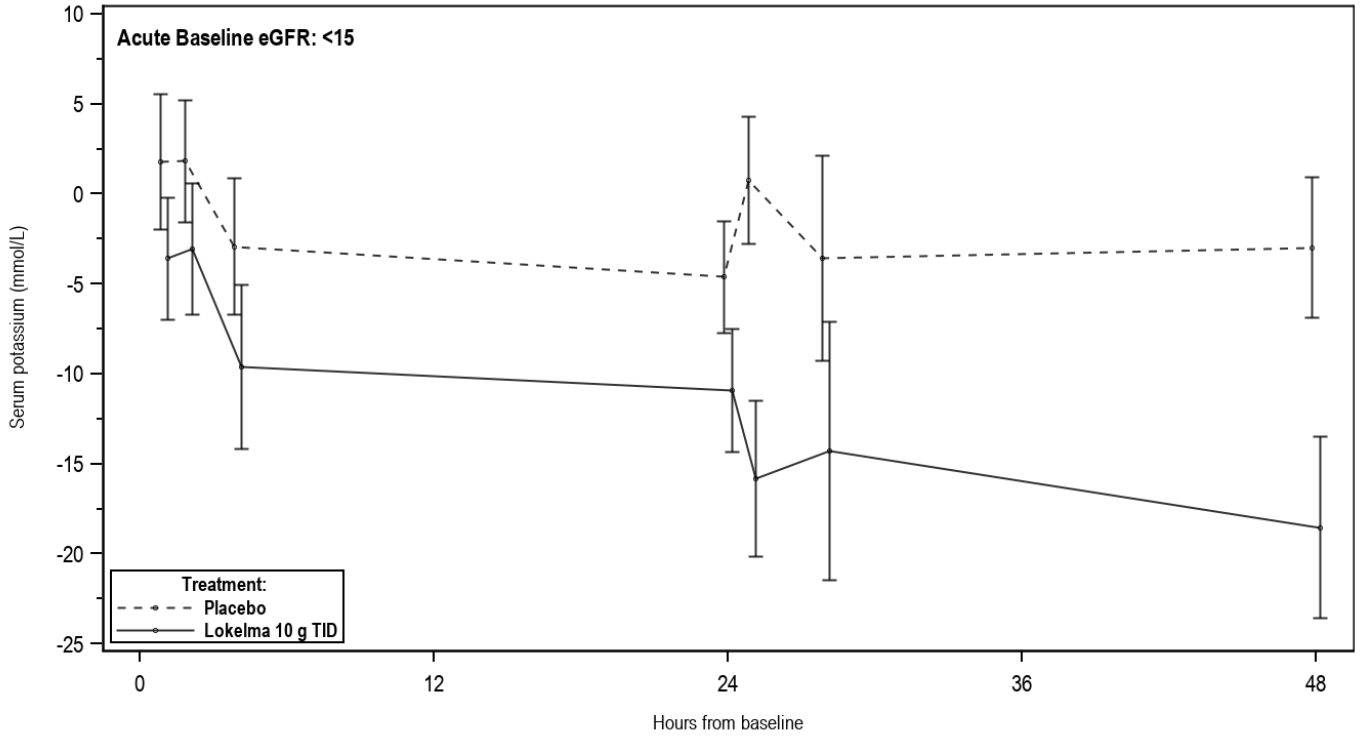
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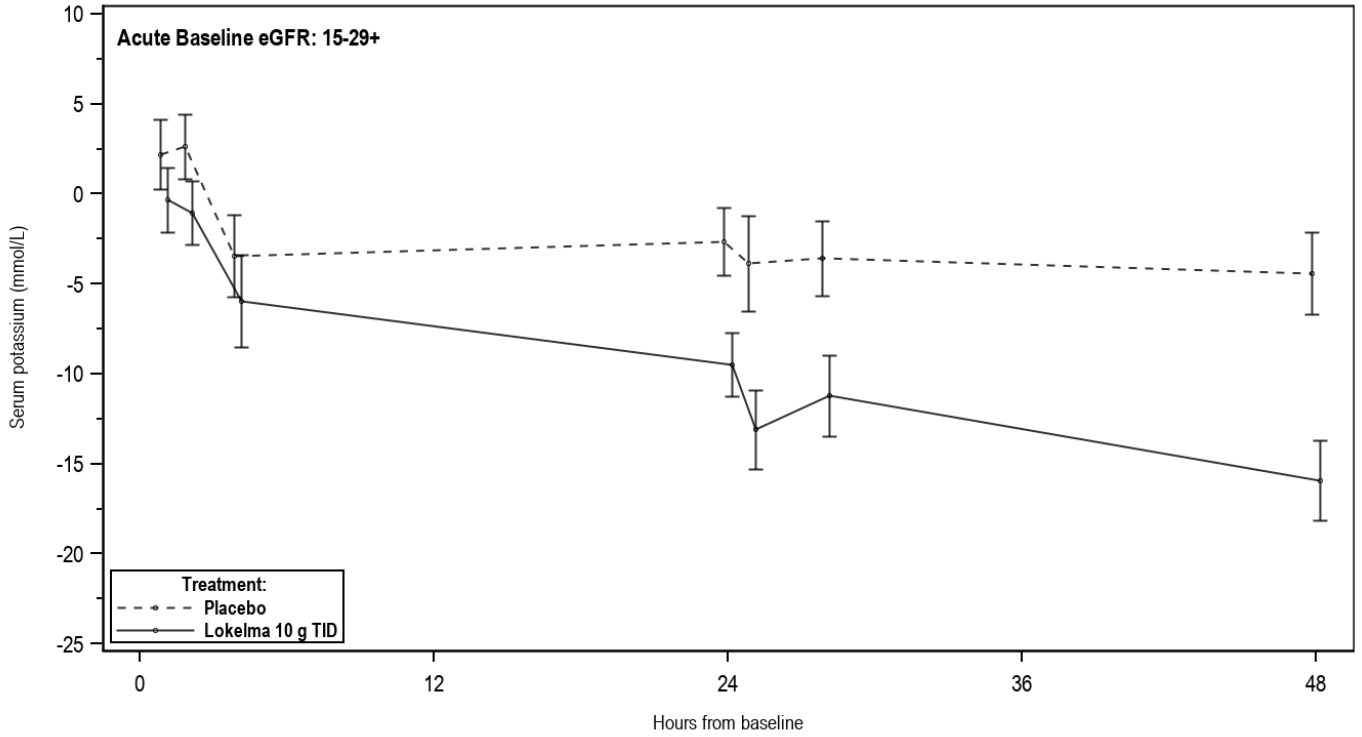
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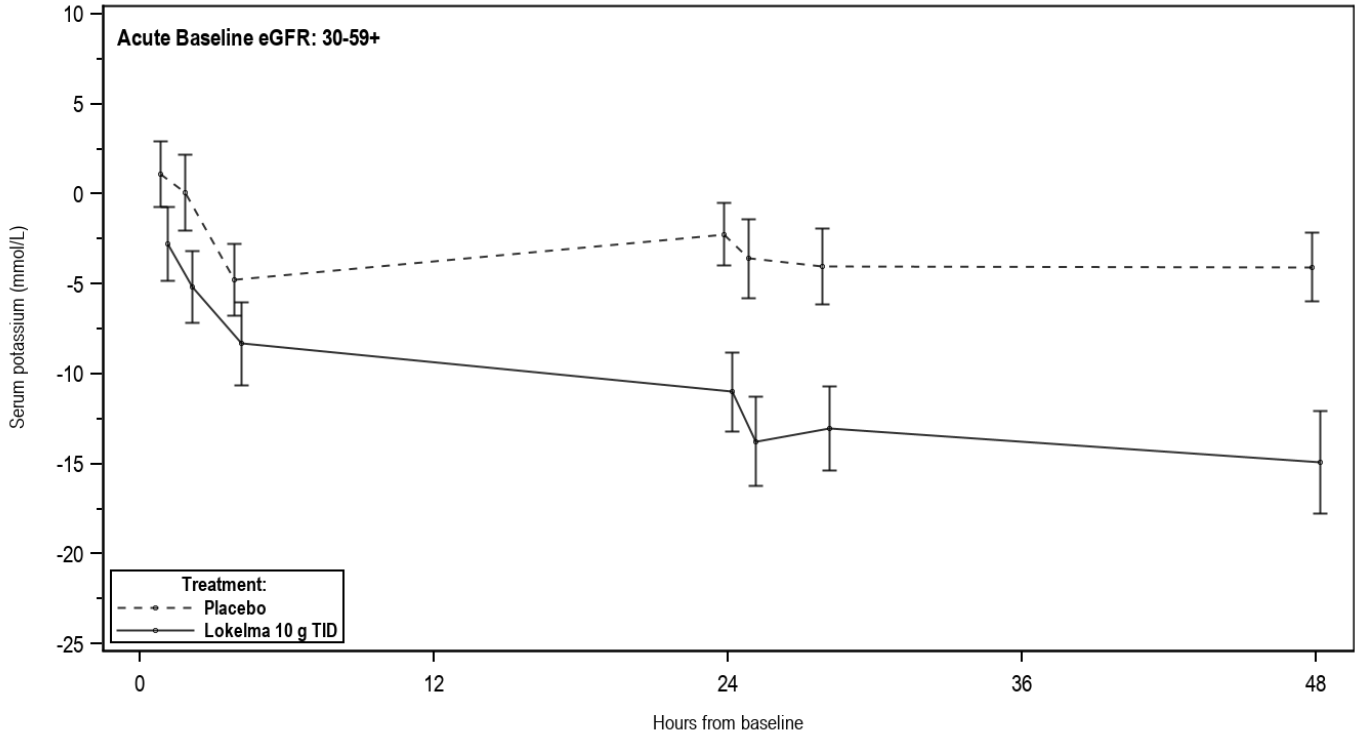
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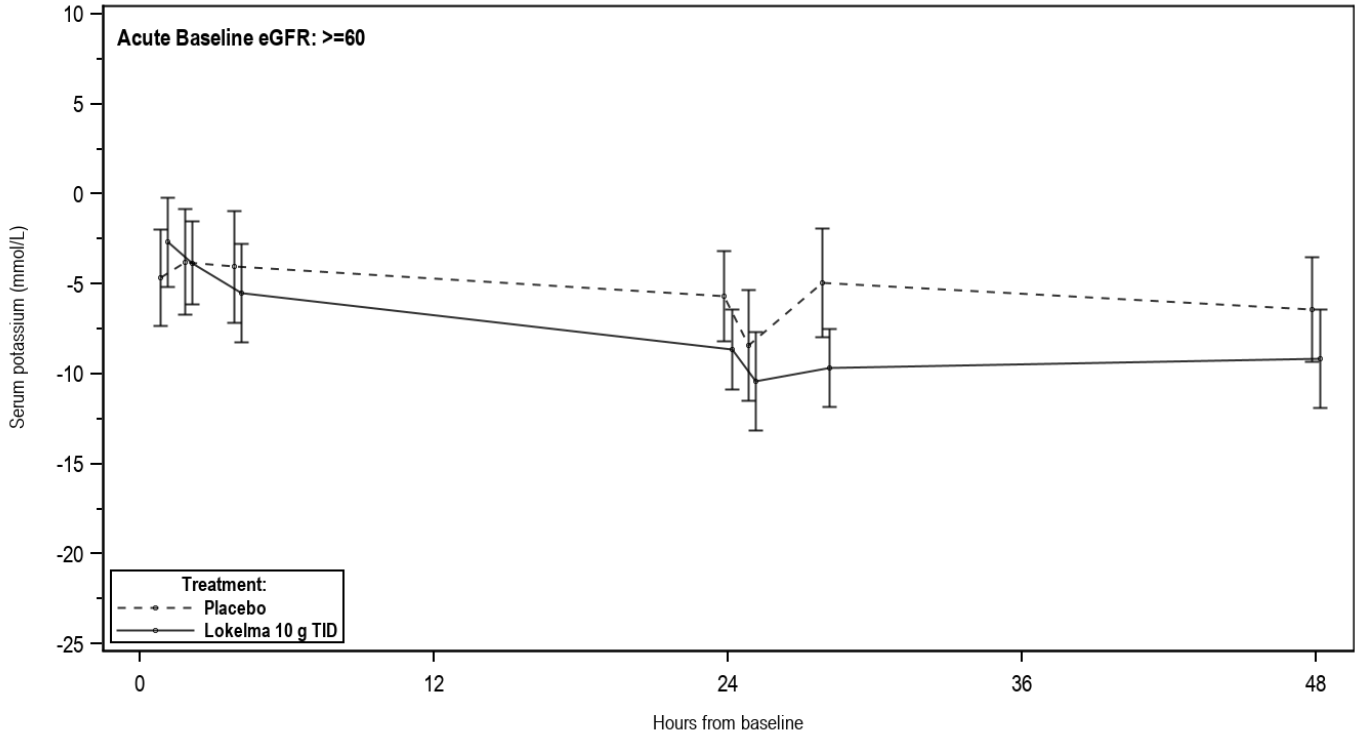
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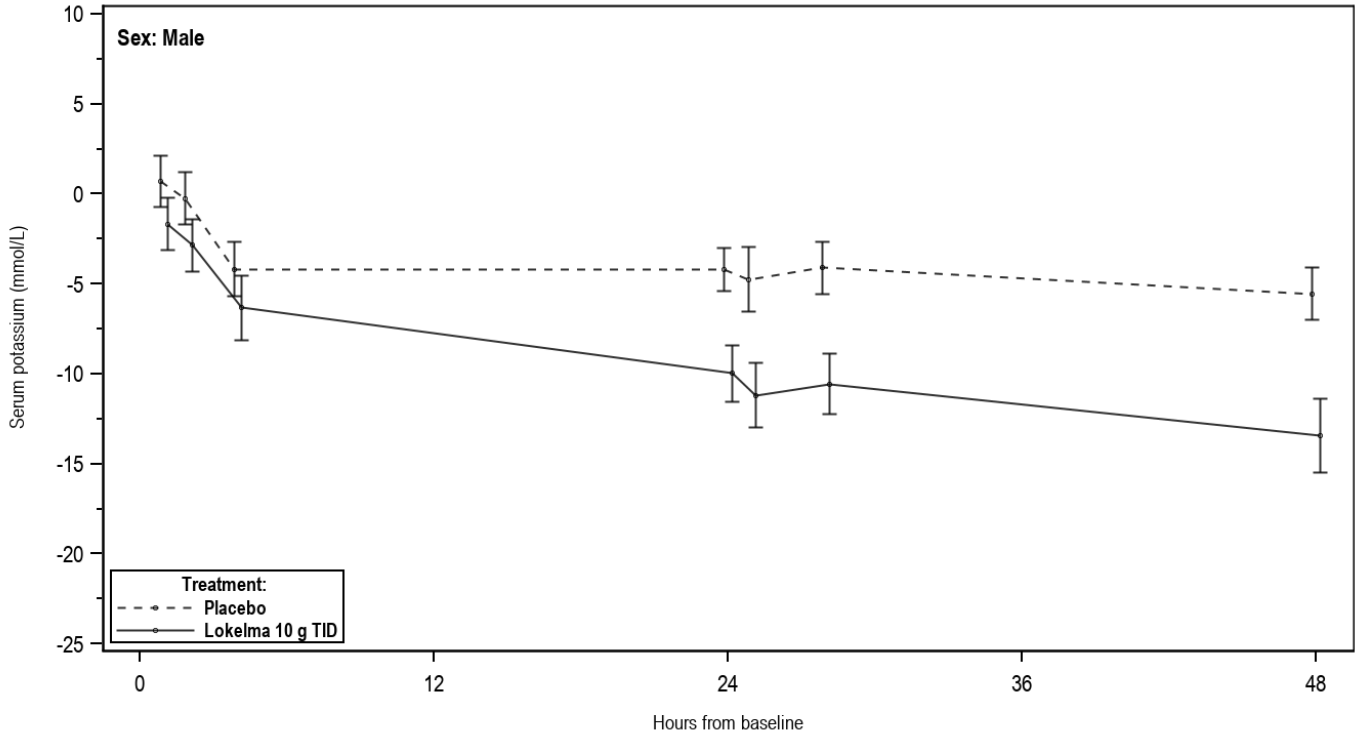
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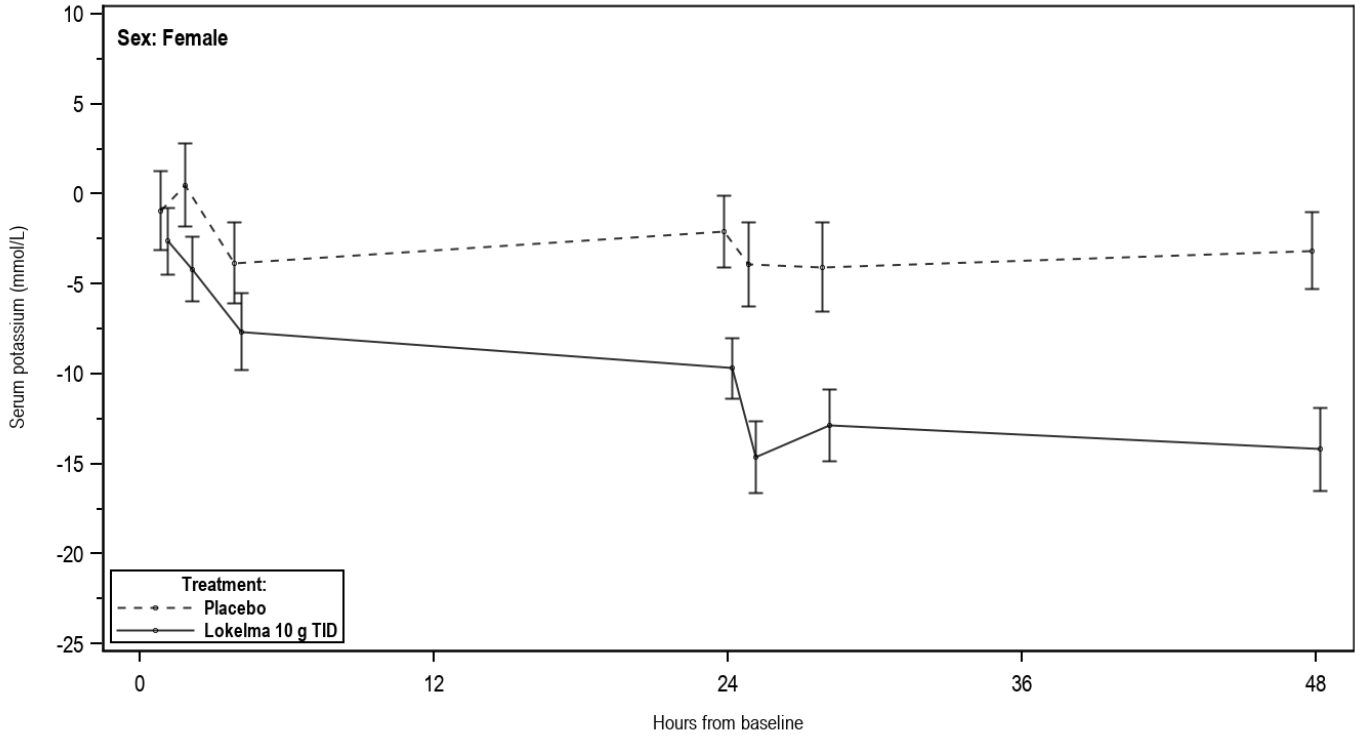
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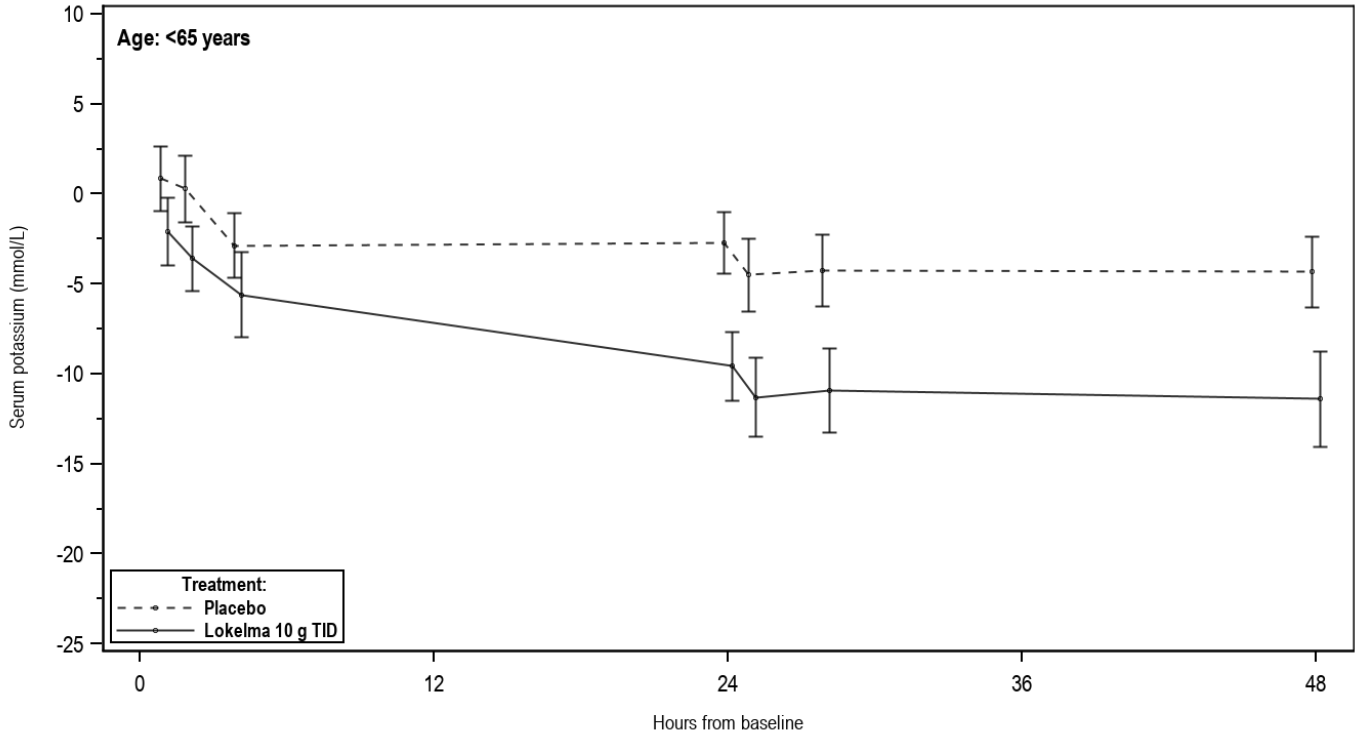
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.

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Figure 2.1.2.4 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint): % change from baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)



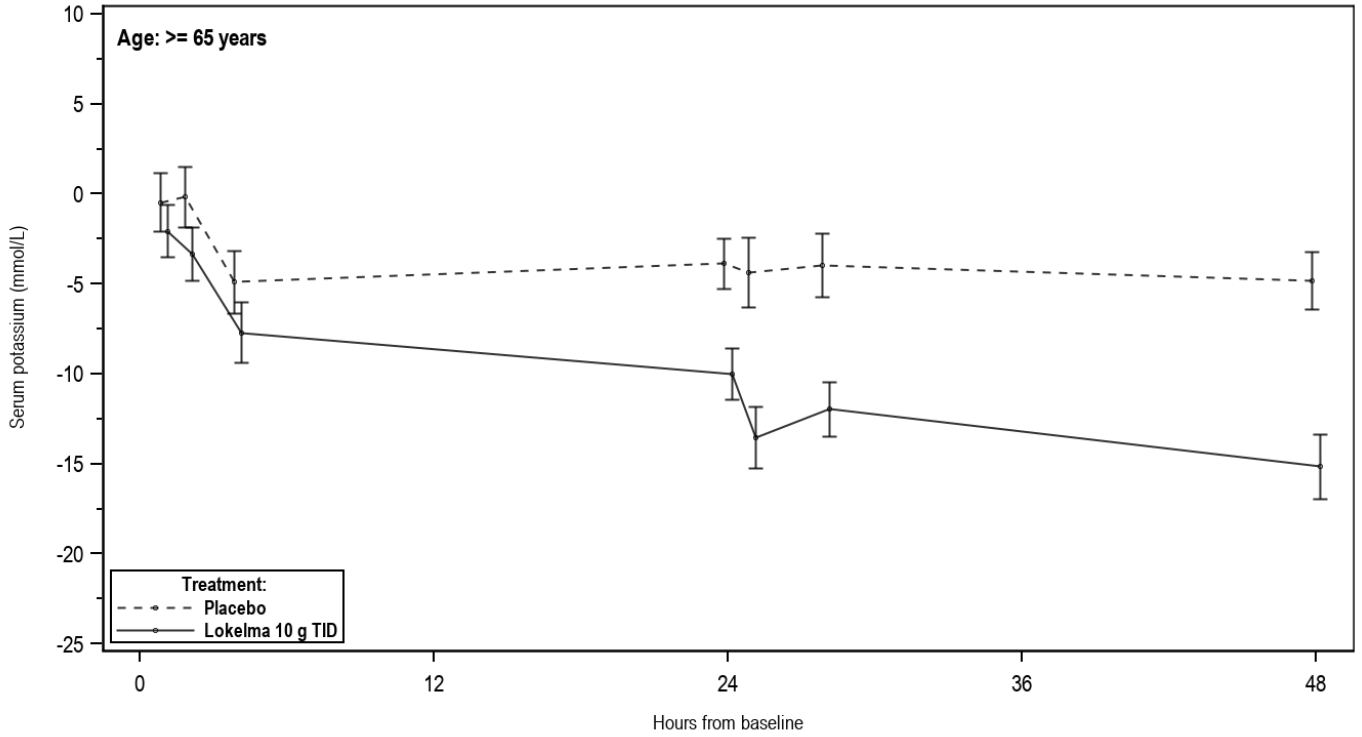
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.

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Figure 2.1.2.4 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint): % change from baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)



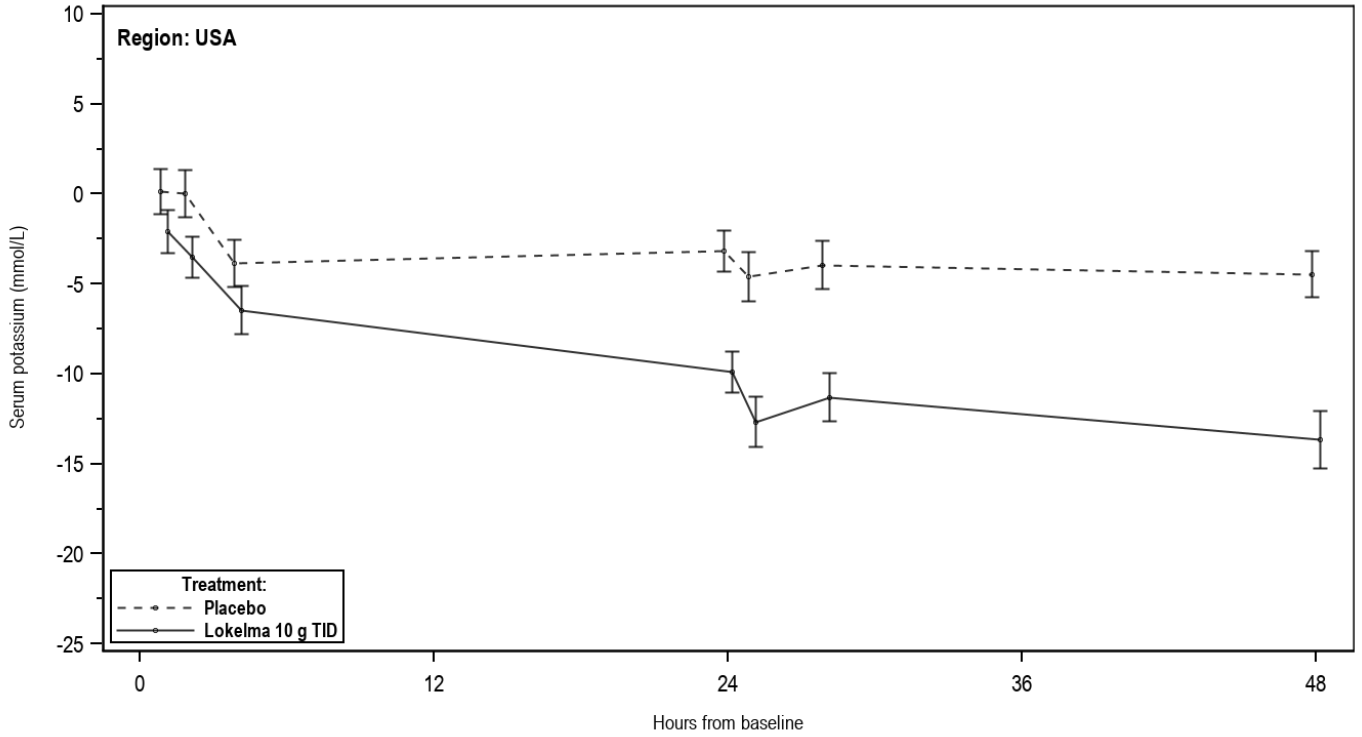
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.

f_zs003ac_sk_overtimem_c.pdf generated by zs003ac_overtime.sas at 10:31:59 on 21 January 2021

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Figure 2.1.2.4 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint): % change from baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)



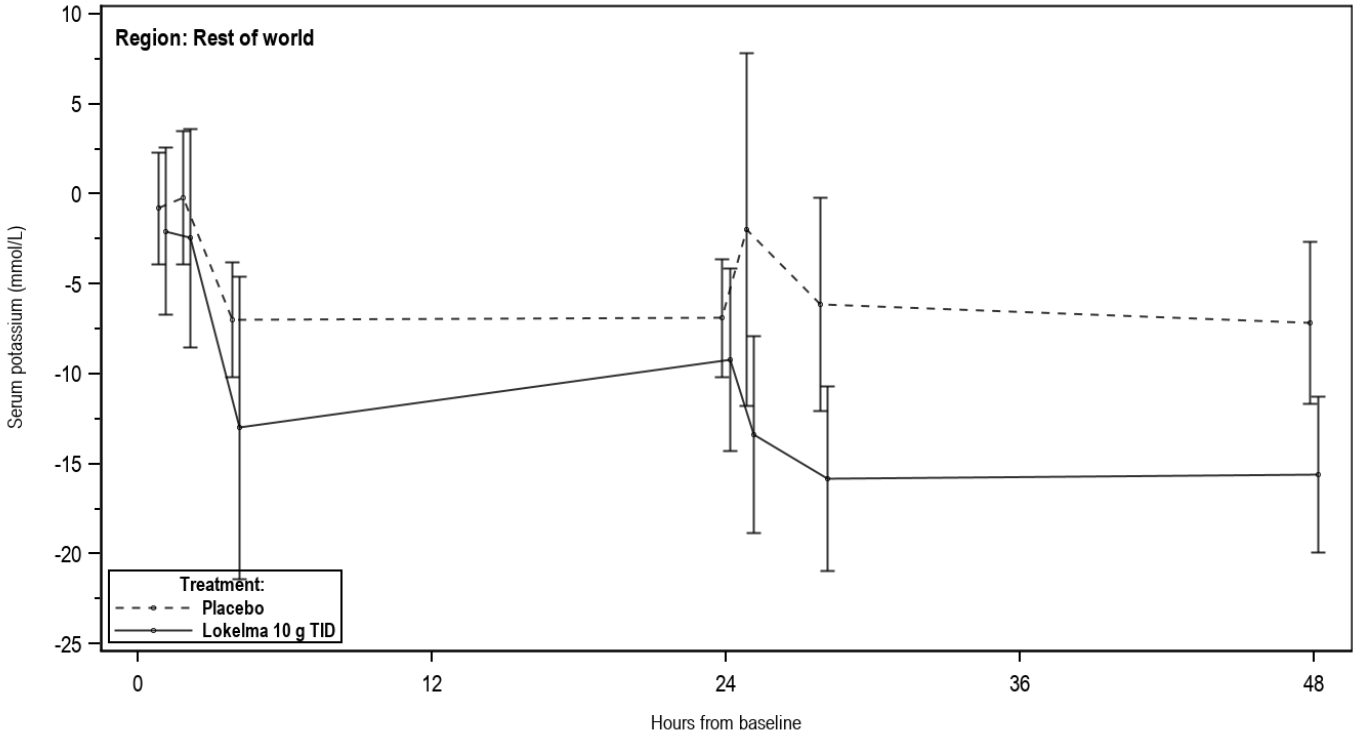
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.

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Figure 2.1.2.4 - Study ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint): % change from baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)



Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.

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Table 2.1.3.1 - Study ZS-003 acute: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)					Lokelma 10g QD (N=143)							
Subgroup / Category	N	Patients with events [n(%)]	KM % at 24 hours	KM % at 48 hours	Median time (hours)	N	Patients with events [n(%)]	KM % at 24 hours	KM % at 48 hours	Median time (hours)	Hazard ratio (95% CI)	Hazard ratio p-value	p-value for interaction
Overall	158	106 (67.1%)	54.42	32.84	24.8	143	131 (91.6%)	31.16	11.20	22.8	1.98 (1.52, 2.58)	<.0001	
Chronic kidney disease													0.0169
No	62	46 (74.2%)	48.39	26.96	23.9	60	54 (90.0%)	35.00	13.33	22.9	1.46 (0.96, 2.22)	0.0788	
Yes	96	60 (62.5%)	58.31	36.01	25.3	83	77 (92.8%)	28.33	9.58	22.7	2.78 (1.94, 3.97)	<.0001	
Congestive heart disease													0.9168
No	92	61 (66.3%)	54.31	36.29	24.8	84	74 (88.1%)	32.86	14.60	22.8	2.00 (1.40, 2.85)	0.0001	
Yes	66	45 (68.2%)	54.55	27.09	24.8	59	57 (96.6%)	28.81	6.78	21.9	1.99 (1.32, 2.99)	0.0010	
Diabetes mellitus													0.2936
No	62	45 (72.6%)	46.77	24.72	23.7	62	57 (91.9%)	22.58	11.29	4.0	1.73 (1.14, 2.64)	0.0103	
Yes	96	61 (63.5%)	59.34	38.13	25.7	81	74 (91.4%)	37.78	11.33	23.4	2.41 (1.68, 3.44)	<.0001	
RAASi medications													0.4308
No	57	42 (73.7%)	52.57	26.69	24.3	47	42 (89.4%)	25.53	14.89	22.7	1.80 (1.16, 2.80)	0.0093	
Yes	101	64 (63.4%)	55.45	36.54	25.2	96	89 (92.7%)	33.95	9.43	22.9	2.11 (1.50, 2.96)	<.0001	
Sex													0.2178
Male	98	68 (69.4%)	54.08	32.67	24.6	80	71 (88.8%)	38.25	15.19	23.4	1.75 (1.24, 2.46)	0.0014	
Female	60	38 (63.3%)	55.00	34.62	25.2	63	60 (95.2%)	22.22	6.35	4.0	2.50 (1.59, 3.93)	<.0001	
Age (years)													0.3152
<65 years	66	39 (59.1%)	59.05	38.97	25.8	54	45 (83.3%)	34.44	17.22	23.0	2.47 (1.53, 3.98)	0.0002	
>=65 years	92	67 (72.8%)	51.09	28.23	24.5	89	86 (96.6%)	29.21	7.87	21.2	1.88 (1.34, 2.64)	0.0003	
Baseline S-K													0.9449
<=5.3 mmol/L	95	57 (60.0%)	64.21	40.25	25.3	94	82 (87.2%)	38.95	14.91	23.5	1.94 (1.36, 2.76)	0.0003	
5.4-5.5 mmol/L	22	17 (77.3%)	40.91	27.27	23.6	27	27 (100.0%)	14.81	3.70	4.0	1.84 (0.87, 3.89)	0.1086	
>5.5 mmol/L	41	32 (78.0%)	39.02	19.32	22.5	22	22 (100.0%)	18.18	4.55	5.2	1.65 (0.88, 3.09)	0.1154	
Baseline eGFR													0.0229
<15 ml/min/1.73m**2	15	8 (53.3%)	66.67	40.00	47.9	10	9 (90.0%)	0.00	0.00	4.0	5.02 (1.23, 20.46)	0.0246	
15-29 ml/min/1.73m**2	44	27 (61.4%)	54.55	26.48	25.1	42	40 (95.2%)	42.86	9.52	23.5	2.42 (1.42, 4.14)	0.0012	
30-59 ml/min/1.73m**2	61	41 (67.2%)	57.33	36.48	25.3	50	46 (92.0%)	24.00	9.60	4.1	2.44 (1.56, 3.81)	<.0001	
>=60 ml/min/1.73m**2	38	30 (78.9%)	44.74	23.68	23.4	41	36 (87.8%)	34.15	17.07	23.0	1.15 (0.64, 2.05)	0.6442	
Region													0.8886
USA	148	99 (66.9%)	55.39	32.46	24.8	133	122 (91.7%)	31.58	11.13	23.0	2.01 (1.52, 2.65)	<.0001	
Rest of world	10	7 (70.0%)	40.00	40.00	23.4	10	9 (90.0%)	26.67	13.33	4.0	1.35 (0.31, 5.81)	0.6847	

Hazard ratio derived from Cox proportional hazard model with the following effects:
Acute phase treatment group, acute phase baseline eGFR, acute phase baseline S-K, age group (<65, >=65 years) and binary indicators for RAASi use, chronic kidney disease, congestive heart disease and diabetes mellitus.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
NR: median not reached

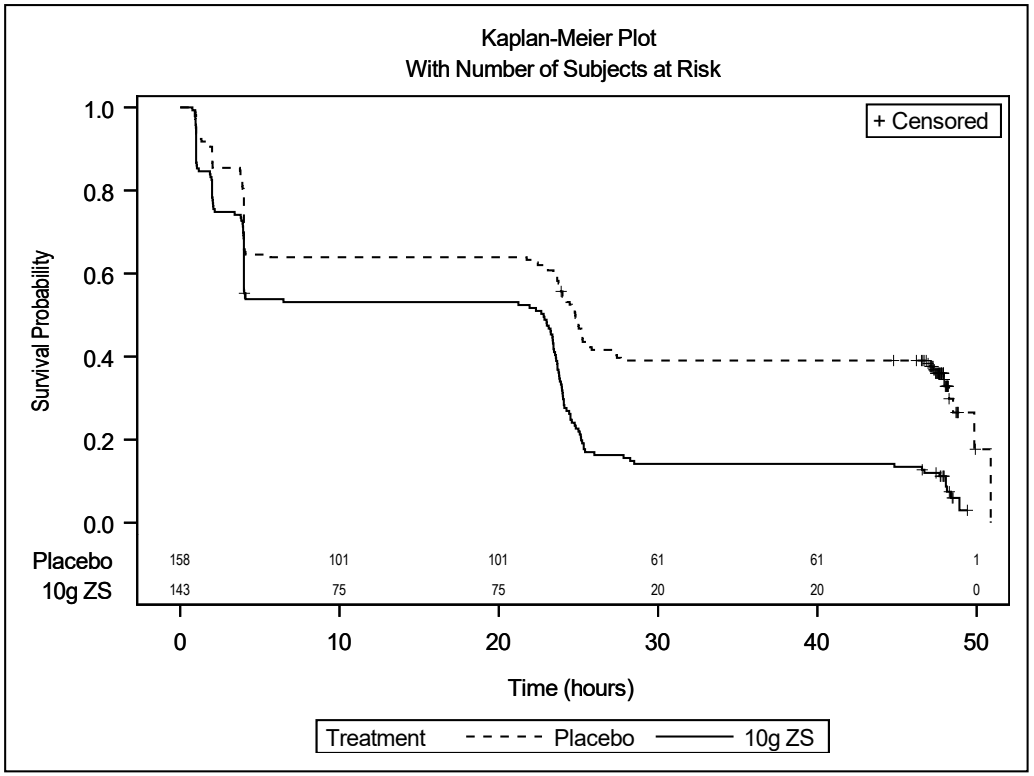
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Figure 2.1.3.2 - Study ZS-003 acute: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Overall



Plots shown for subgroups where interaction p-value is <=0.05

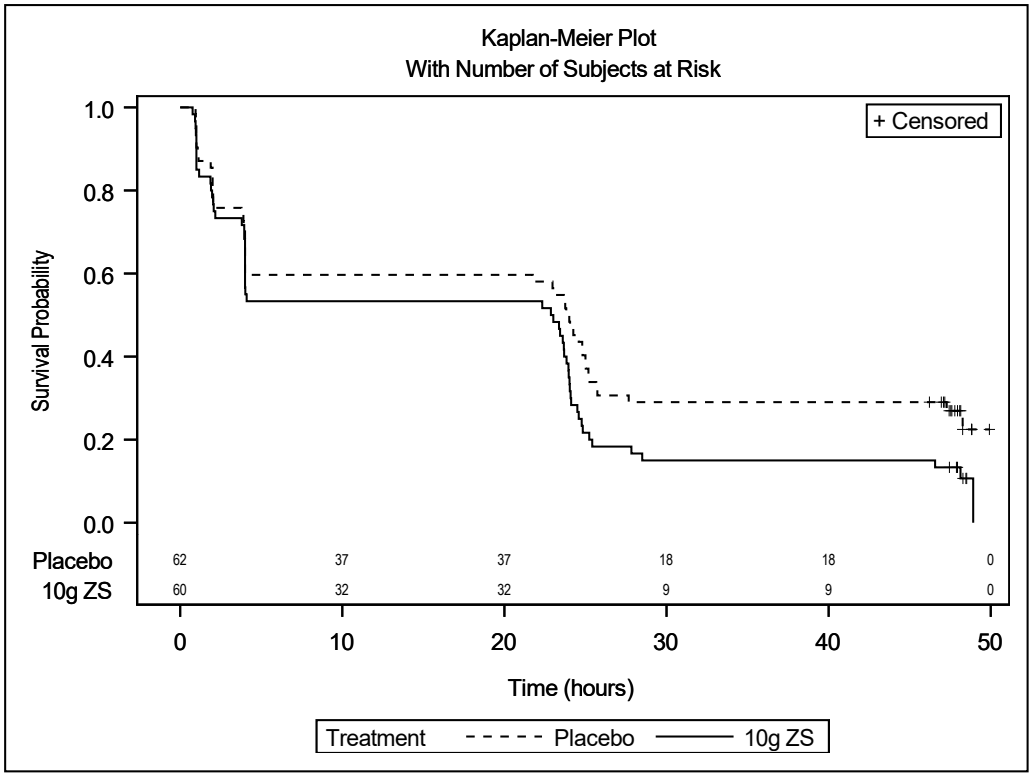
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Figure 2.1.3.2 - Study ZS-003 acute: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: No



Plots shown for subgroups where interaction p-value is <=0.05

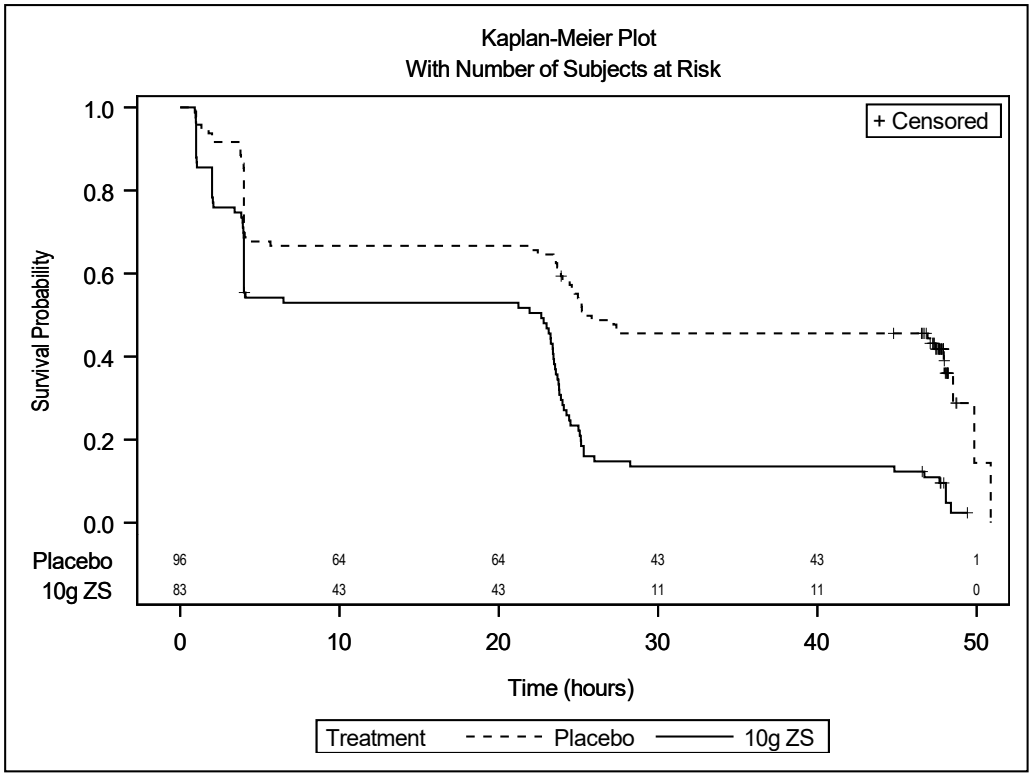
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Figure 2.1.3.2 - Study ZS-003 acute: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: Yes



Plots shown for subgroups where interaction p-value is <=0.05

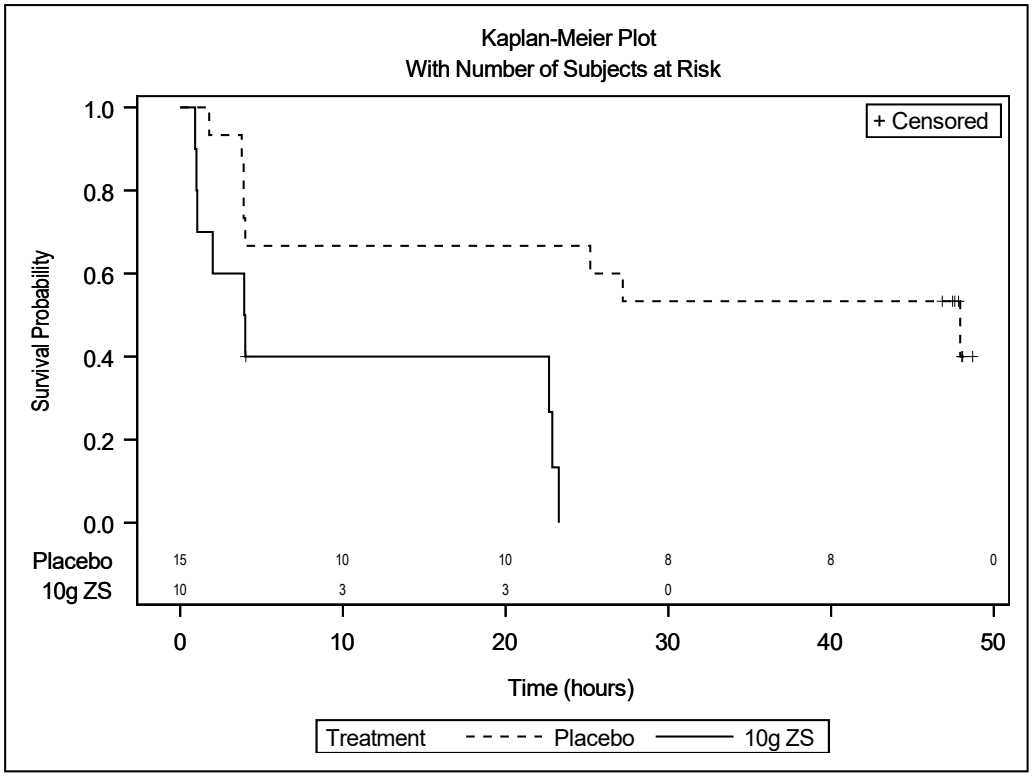
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Figure 2.1.3.2 - Study ZS-003 acute: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: <15 ml/min/1.73m2**



Plots shown for subgroups where interaction p-value is <=0.05

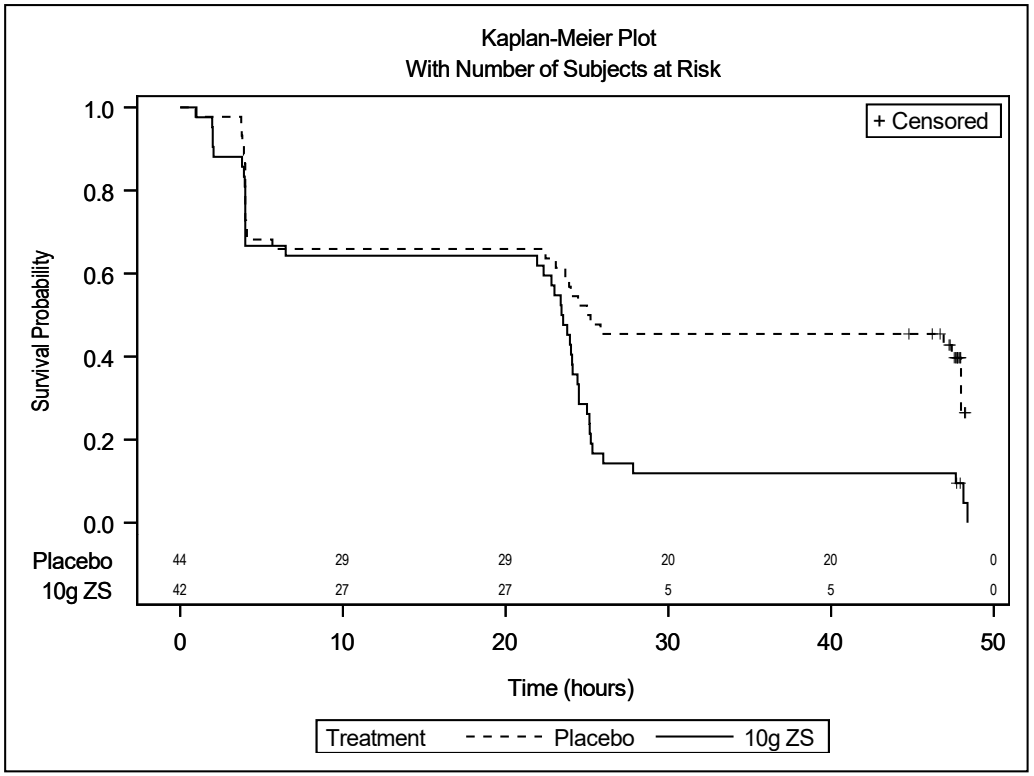
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Figure 2.1.3.2 - Study ZS-003 acute: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: 15-29 ml/min/1.73m2**



Plots shown for subgroups where interaction p-value is <=0.05

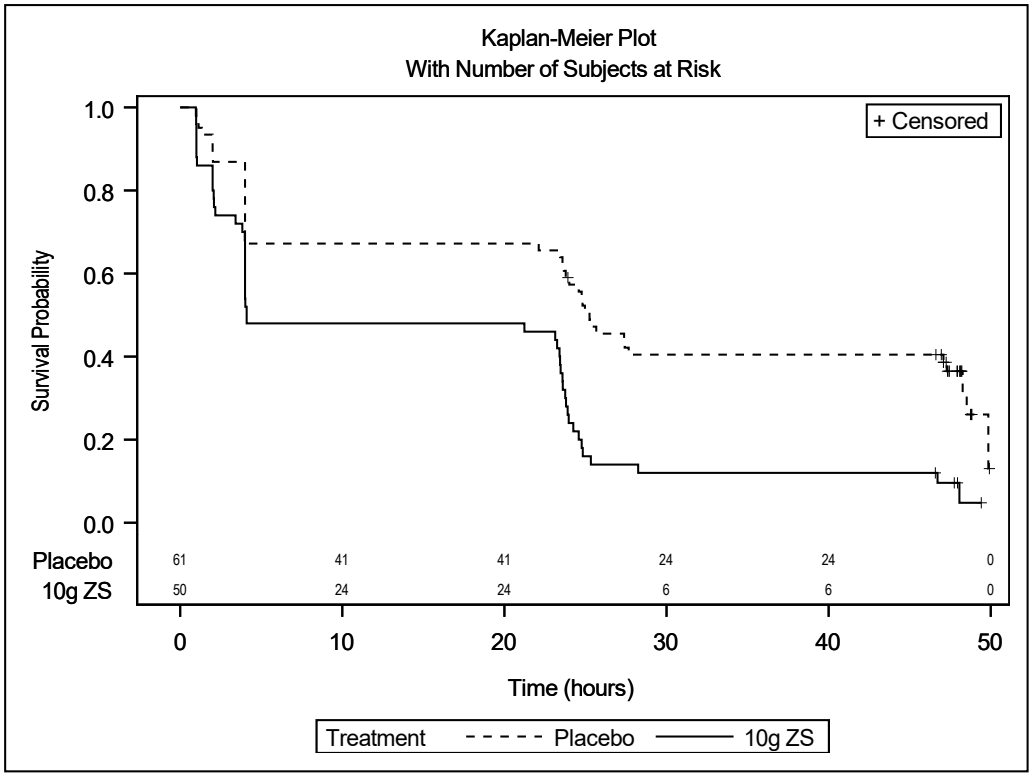
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Figure 2.1.3.2 - Study ZS-003 acute: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: 30-59 ml/min/1.73m2**



Plots shown for subgroups where interaction p-value is <=0.05

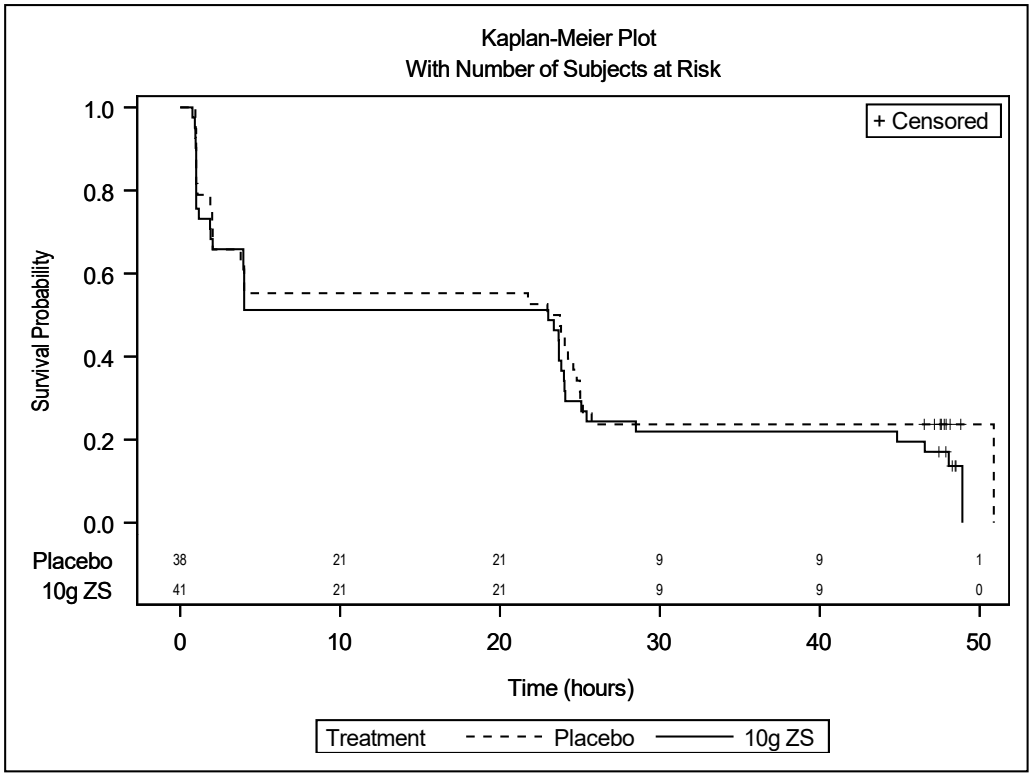
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Figure 2.1.3.2 - Study ZS-003 acute: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: >=60 ml/min/1.73m2**



Plots shown for subgroups where interaction p-value is <=0.05

f_zs003ac_tte_dec generated by zs003ac_tte.sas at 15:38:38 on 19 January 2021

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Table 2.1.4.1 - Study ZS-003 acute: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)					Lokelma 10g QD (N=143)							
Subgroup / Category	N	Patients with events [n(%)]	KM % at 24 hours	KM % at 48 hours	Median time (hours)	N	Patients with events [n(%)]	KM % at 24 hours	KM % at 48 hours	Median time (hours)	Hazard ratio (95% CI)	Hazard ratio p-value	p-value for interaction
Overall	158	125 (79.1%)	34.18	21.01	4.0	143	141 (98.6%)	11.47	1.91	1.1	1.64 (1.28, 2.12)	0.0001	
Chronic kidney disease													0.0407
No	62	55 (88.7%)	24.19	10.89	1.5	60	60 (100.0%)	11.67	1.67	1.0	1.23 (0.83, 1.83)	0.3028	
Yes	96	70 (72.9%)	40.62	27.49	4.0	83	81 (97.6%)	11.28	2.51	2.0	2.20 (1.56, 3.12)	<.0001	
Congestive heart disease													0.6605
No	92	79 (85.9%)	29.35	14.67	2.0	84	82 (97.6%)	11.20	1.87	1.0	1.63 (1.17, 2.26)	0.0035	
Yes	66	46 (69.7%)	40.91	30.30	4.0	59	59 (100.0%)	11.86	1.69	2.0	1.76 (1.16, 2.67)	0.0078	
Diabetes mellitus													0.9001
No	62	52 (83.9%)	24.19	16.13	1.5	62	61 (98.4%)	6.45	3.23	1.0	1.69 (1.12, 2.57)	0.0130	
Yes	96	73 (76.0%)	40.62	24.01	4.0	81	80 (98.8%)	15.33	1.28	2.1	1.82 (1.28, 2.57)	0.0007	
RAASi medications													0.0738
No	57	47 (82.5%)	35.09	18.47	4.0	47	47 (100.0%)	4.26	0.00	1.0	2.47 (1.55, 3.93)	0.0001	
Yes	101	78 (77.2%)	33.66	22.01	1.9	96	94 (97.9%)	15.10	2.88	2.0	1.38 (1.01, 1.88)	0.0418	
Sex													0.8570
Male	98	73 (74.5%)	39.80	24.74	4.0	80	78 (97.5%)	15.58	3.89	2.0	1.59 (1.13, 2.22)	0.0073	
Female	60	52 (86.7%)	25.00	15.00	1.5	63	63 (100.0%)	6.35	0.00	1.0	1.82 (1.21, 2.75)	0.0039	
Age (years)													0.8216
<65 years	66	50 (75.8%)	39.39	23.16	4.0	54	53 (98.1%)	11.85	0.00	1.5	1.83 (1.19, 2.83)	0.0062	
>=65 years	92	75 (81.5%)	30.43	19.57	2.0	89	88 (98.9%)	11.24	3.00	1.1	1.63 (1.18, 2.26)	0.0034	
Baseline S-K													0.1629
<=5.3 mmol/L	95	87 (91.6%)	14.74	7.11	1.0	94	93 (98.9%)	3.39	0.00	1.0	1.34 (0.98, 1.82)	0.0648	
5.4-5.5 mmol/L	22	17 (77.3%)	40.91	27.27	23.6	27	27 (100.0%)	11.11	3.70	4.0	1.76 (0.83, 3.73)	0.1423	
>5.5 mmol/L	41	21 (51.2%)	75.61	49.99	46.9	22	21 (95.5%)	45.45	6.82	24.0	3.36 (1.67, 6.79)	0.0007	
Baseline eGFR													0.0562
<15 ml/min/1.73m**2	15	9 (60.0%)	60.00	40.00	27.2	10	9 (90.0%)	13.33	0.00	4.0	4.08 (0.90, 18.50)	0.0679	
15-29 ml/min/1.73m**2	44	28 (63.6%)	47.73	.	23.7	42	41 (97.6%)	19.05	3.57	4.0	2.45 (1.45, 4.15)	0.0009	
30-59 ml/min/1.73m**2	61	50 (82.0%)	31.15	20.77	4.0	50	50 (100.0%)	10.00	2.00	1.0	1.58 (1.03, 2.42)	0.0379	
>=60 ml/min/1.73m**2	38	38 (100.0%)	13.16	0.00	1.0	41	41 (100.0%)	4.88	0.00	0.9	1.04 (0.64, 1.69)	0.8831	
Region													0.5897
USA	148	119 (80.4%)	31.76	19.11	3.8	133	132 (99.2%)	10.53	1.50	1.0	1.60 (1.23, 2.09)	0.0004	
Rest of world	10	6 (60.0%)	70.00	50.00	36.6	10	9 (90.0%)	26.67	13.33	4.0	2.73 (0.58, 12.97)	0.2060	

Hazard ratio derived from Cox proportional hazard model with the following effects:
Acute phase treatment group, acute phase baseline eGFR, acute phase baseline S-K, age group (<65, >=65 years) and binary indicators for RAASi use, chronic kidney disease, congestive heart disease and diabetes mellitus.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
'.' in KM % columns denotes number at risk has reached zero before the timepoint
NR: median not reached

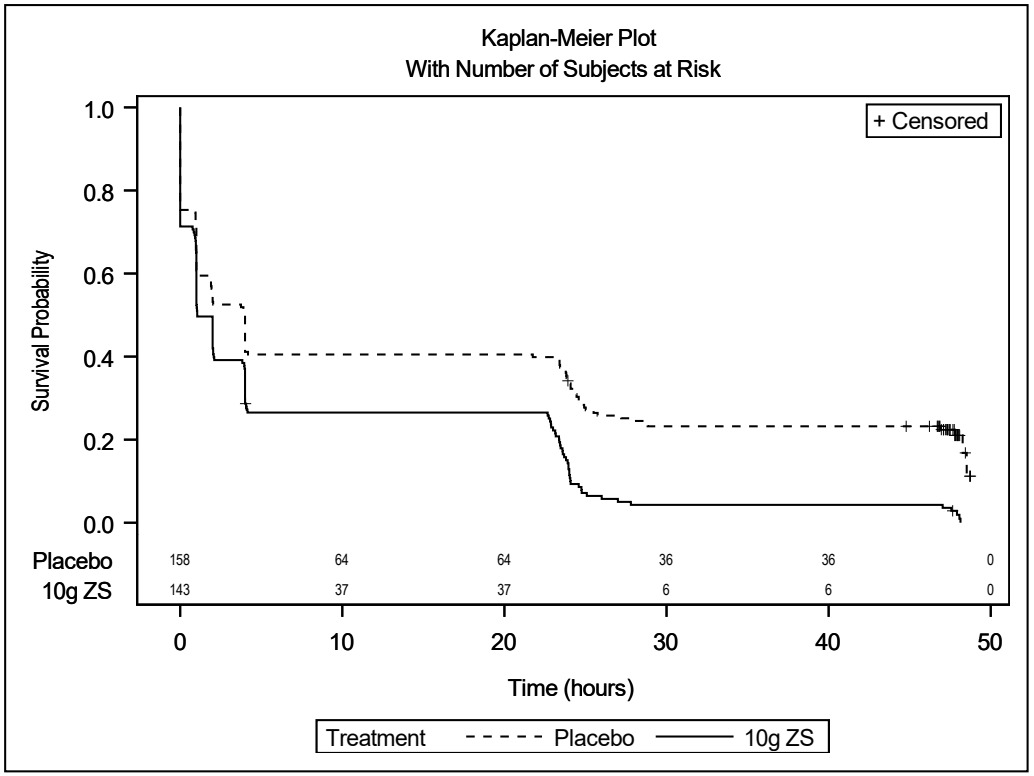
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Figure 2.1.4.2 - Study ZS-003 acute: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Overall



Plots shown for subgroups where interaction p-value is <=0.05

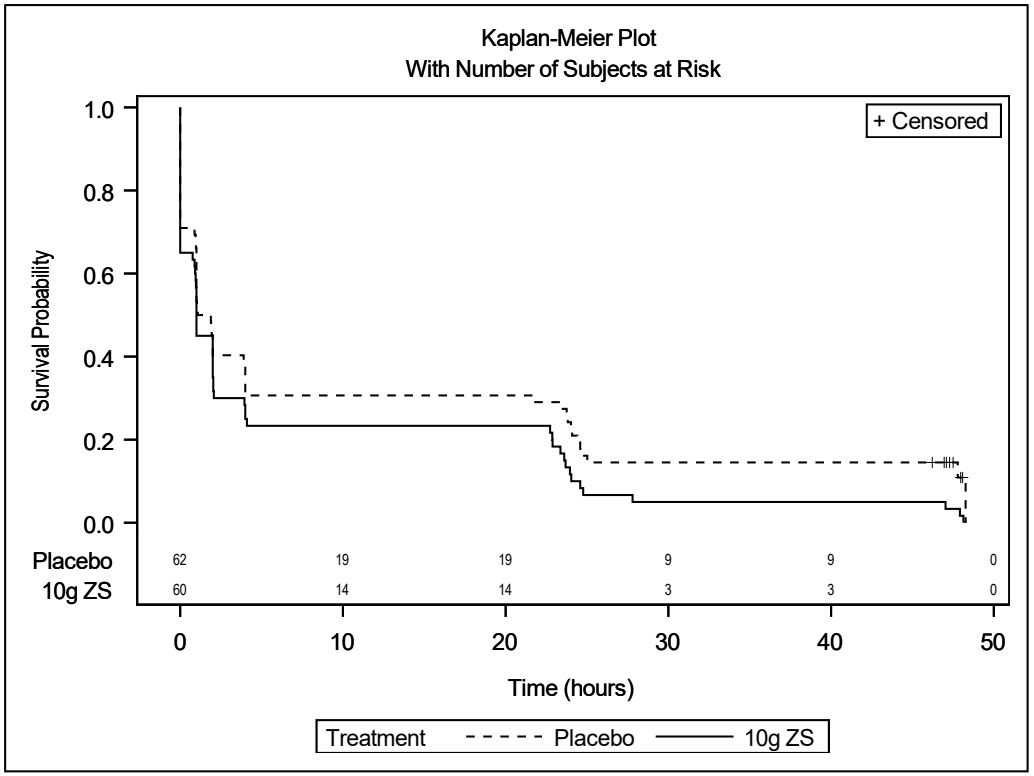
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Figure 2.1.4.2 - Study ZS-003 acute: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: No



Plots shown for subgroups where interaction p-value is <=0.05

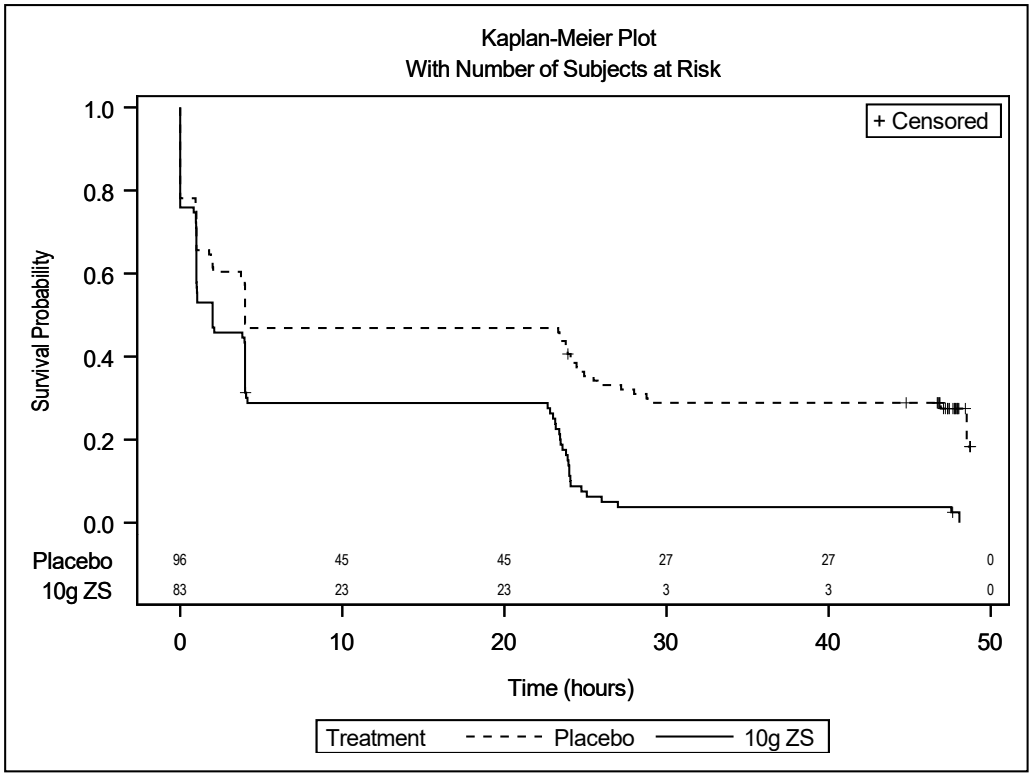
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Figure 2.1.4.2 - Study ZS-003 acute: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: Yes



Plots shown for subgroups where interaction p-value is <=0.05

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Table 2.1.5.1 - Study ZS-003 acute: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)		Lokelma 10g QD (N=143)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Overall											
Day 1 / 1-hr Post-dose 1	158	58 (36.7%)	143	65 (45.5%)	1.33 (0.73, 2.42)	0.3507	1.17 (0.82, 1.67)	0.3973	3.2 (-23.5, 29.9)	0.8153	
Day 1 / 2-hr Post-dose 1	158	54 (34.2%)	143	70 (49.0%)	1.94 (1.09, 3.42)	0.0233	1.30 (0.91, 1.87)	0.1463	8.3 (-15.8, 32.4)	0.4993	
Day 1 / 4-hr Post-dose 1	158	80 (50.6%)	143	87 (60.8%)	1.32 (0.78, 2.22)	0.3041	1.16 (0.85, 1.57)	0.3483	7.5 (-11.7, 26.8)	0.4432	
Day 2 / 0-hr Pre-dose	158	78 (49.4%)	140	108 (77.1%)	4.08 (2.25, 7.38)	<.0001	1.50 (1.12, 2.01)	0.0064	19.8 (-1.9, 41.4)	0.0736	
Day 2 / 1-hr Post-dose 1	157	85 (54.1%)	140	115 (82.1%)	4.35 (2.40, 7.91)	<.0001	1.45 (1.10, 1.93)	0.0091	31.0 (12.9, 49.2)	0.0008	
Day 2 / 4-hr Post-dose 1	157	78 (49.7%)	140	119 (85.0%)	7.00 (3.73, 13.14)	<.0001	1.66 (1.25, 2.21)	0.0005	30.4 (10.4, 50.5)	0.0029	
Day 3 / 0-hr Pre-dose	157	75 (47.8%)	140	121 (86.4%)	7.53 (4.11, 13.82)	<.0001	1.78 (1.33, 2.38)	<.0001	39.3 (20.0, 58.6)	<.0001	
Chronic kidney disease											
Day 1 / 1-hr Post-dose 1											0.1838
No	62	29 (46.8%)	60	31 (51.7%)	0.80 (0.30, 2.09)	0.6419	0.92 (0.54, 1.56)	0.7525	-1.0 (-38.1, 36.1)	0.9581	
Yes	96	29 (30.2%)	83	34 (41.0%)	1.98 (0.87, 4.52)	0.1042	1.55 (0.93, 2.59)	0.0948	6.5 (-30.2, 43.2)	0.7278	
Day 1 / 2-hr Post-dose 1											0.1084
No	62	32 (51.6%)	60	37 (61.7%)	1.30 (0.54, 3.15)	0.5606	1.05 (0.65, 1.72)	0.8340	2.0 (-32.7, 36.7)	0.9109	
Yes	96	22 (22.9%)	83	33 (39.8%)	2.98 (1.35, 6.57)	0.0068	1.96 (1.12, 3.41)	0.0178	13.1 (-16.2, 42.3)	0.3812	
Day 1 / 4-hr Post-dose 1											0.1014
No	62	38 (61.3%)	60	35 (58.3%)	0.65 (0.28, 1.53)	0.3258	0.87 (0.54, 1.40)	0.5744	-8.4 (-37.7, 20.9)	0.5728	
Yes	96	42 (43.8%)	83	52 (62.7%)	2.32 (1.13, 4.75)	0.0216	1.45 (0.96, 2.18)	0.0774	14.5 (-13.4, 42.5)	0.3078	
Day 2 / 0-hr Pre-dose											0.1201
No	62	38 (61.3%)	60	46 (76.7%)	1.91 (0.78, 4.72)	0.1586	1.16 (0.75, 1.81)	0.5023	11.2 (-18.0, 40.4)	0.4523	
Yes	96	40 (41.7%)	80	62 (77.5%)	7.31 (3.20, 16.69)	<.0001	1.89 (1.26, 2.82)	0.0020	27.5 (-1.7, 56.6)	0.0647	
Day 2 / 1-hr Post-dose 1											0.0254
No	62	43 (69.4%)	60	46 (76.7%)	1.29 (0.51, 3.25)	0.5884	1.02 (0.66, 1.56)	0.9381	2.4 (-28.8, 33.6)	0.8813	
Yes	95	42 (44.2%)	80	69 (86.3%)	11.30 (4.76, 26.84)	<.0001	1.96 (1.33, 2.89)	0.0006	45.2 (21.0, 69.4)	0.0003	
Day 2 / 4-hr Post-dose 1											0.5152
No	62	35 (56.5%)	60	53 (88.3%)	7.00 (2.43, 20.17)	0.0003	1.50 (0.97, 2.32)	0.0665	31.9 (2.1, 61.6)	0.0357	
Yes	95	43 (45.3%)	80	66 (82.5%)	7.19 (3.26, 15.87)	<.0001	1.83 (1.24, 2.70)	0.0022	34.0 (8.1, 59.9)	0.0102	
Day 3 / 0-hr Pre-dose											0.1393
No	62	36 (58.1%)	60	50 (83.3%)	3.42 (1.43, 8.17)	0.0057	1.40 (0.90, 2.16)	0.1327	28.4 (-2.1, 58.9)	0.0684	
Yes	95	39 (41.1%)	80	71 (88.8%)	14.89 (6.09, 36.38)	<.0001	2.17 (1.47, 3.22)	0.0001	49.0 (23.9, 74.0)	0.0001	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline eGFR, acute phase baseline S-K, age group (<65, >=65 years) and binary indicators for RAASi use, chronic kidney disease, congestive heart disease and diabetes mellitus.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 2.1.5.1 - Study ZS-003 acute: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)		Lokelma 10g QD (N=143)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Congestive heart disease											
Day 1 / 1-hr Post-dose 1											0.4109
No	92	40 (43.5%)	84	41 (48.8%)	1.14 (0.52, 2.47)	0.7475	1.10 (0.70, 1.72)	0.6810	2.8 (-27.7, 33.4)	0.8554	
Yes	66	18 (27.3%)	59	24 (40.7%)	1.95 (0.68, 5.59)	0.2153	1.59 (0.84, 2.99)	0.1538	5.9 (-37.7, 49.6)	0.7897	
Day 1 / 2-hr Post-dose 1											0.4759
No	92	31 (33.7%)	84	46 (54.8%)	3.26 (1.48, 7.16)	0.0033	1.49 (0.93, 2.37)	0.0937	12.6 (-17.1, 42.2)	0.4054	
Yes	66	23 (34.8%)	59	24 (40.7%)	1.15 (0.46, 2.84)	0.7668	1.16 (0.65, 2.07)	0.6176	5.2 (-32.0, 42.4)	0.7840	
Day 1 / 4-hr Post-dose 1											0.3430
No	92	52 (56.5%)	84	50 (59.5%)	0.97 (0.49, 1.93)	0.9350	1.03 (0.69, 1.52)	0.8877	-1.7 (-23.6, 20.1)	0.8773	
Yes	66	28 (42.4%)	59	37 (62.7%)	1.87 (0.80, 4.34)	0.1468	1.36 (0.83, 2.23)	0.2256	11.8 (-24.0, 47.5)	0.5183	
Day 2 / 0-hr Pre-dose											0.6627
No	92	50 (54.3%)	81	65 (80.2%)	4.24 (1.90, 9.44)	0.0004	1.43 (0.99, 2.08)	0.0581	28.1 (2.7, 53.5)	0.0302	
Yes	66	28 (42.4%)	59	43 (72.9%)	4.50 (1.76, 11.50)	0.0017	1.64 (1.02, 2.66)	0.0427	20.6 (-16.8, 58.1)	0.2806	
Day 2 / 1-hr Post-dose 1											0.8868
No	91	47 (51.6%)	81	62 (76.5%)	3.35 (1.63, 6.88)	0.0010	1.45 (0.99, 2.12)	0.0588	28.7 (5.4, 52.1)	0.0159	
Yes	66	38 (57.6%)	59	53 (89.8%)	9.21 (2.88, 29.51)	0.0002	1.50 (0.98, 2.29)	0.0591	36.0 (5.9, 66.1)	0.0193	
Day 2 / 4-hr Post-dose 1											0.9347
No	91	48 (52.7%)	81	72 (88.9%)	8.25 (3.47, 19.60)	<.0001	1.65 (1.14, 2.38)	0.0076	35.0 (9.9, 60.2)	0.0064	
Yes	66	30 (45.5%)	59	47 (79.7%)	5.78 (2.15, 15.55)	0.0005	1.64 (1.03, 2.61)	0.0355	23.1 (-13.4, 59.5)	0.2156	
Day 3 / 0-hr Pre-dose											0.4999
No	91	48 (52.7%)	81	71 (87.7%)	6.34 (2.89, 13.91)	<.0001	1.65 (1.14, 2.39)	0.0075	36.0 (10.7, 61.3)	0.0054	
Yes	66	27 (40.9%)	59	50 (84.7%)	10.32 (3.76, 28.34)	<.0001	2.00 (1.24, 3.20)	0.0042	39.8 (3.3, 76.4)	0.0327	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline eGFR, acute phase baseline S-K, age group (<65, >=65 years) and binary indicators for RAASi use, chronic kidney disease, congestive heart disease and diabetes mellitus.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 2.1.5.1 - Study ZS-003 acute: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)		Lokelma 10g QD (N=143)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Diabetes mellitus											
Day 1 / 1-hr Post-dose 1											0.4937
No	62	28 (45.2%)	62	36 (58.1%)	2.42 (0.92, 6.40)	0.0738	1.35 (0.80, 2.26)	0.2613	8.4 (-31.2, 48.0)	0.6781	
Yes	96	30 (31.3%)	81	29 (35.8%)	0.92 (0.41, 2.09)	0.8411	1.04 (0.62, 1.74)	0.8845	1.0 (-31.4, 33.5)	0.9496	
Day 1 / 2-hr Post-dose 1											0.5782
No	62	24 (38.7%)	62	38 (61.3%)	3.12 (1.31, 7.42)	0.0102	1.55 (0.91, 2.62)	0.1071	15.0 (-19.2, 49.1)	0.3902	
Yes	96	30 (31.3%)	81	32 (39.5%)	1.39 (0.62, 3.11)	0.4278	1.20 (0.72, 1.99)	0.4772	5.7 (-22.2, 33.6)	0.6883	
Day 1 / 4-hr Post-dose 1											0.9238
No	62	40 (64.5%)	62	44 (71.0%)	1.42 (0.59, 3.40)	0.4322	1.15 (0.74, 1.79)	0.5235	9.1 (-18.7, 36.8)	0.5213	
Yes	96	40 (41.7%)	81	43 (53.1%)	1.31 (0.66, 2.58)	0.4379	1.16 (0.75, 1.80)	0.5034	7.1 (-17.0, 31.2)	0.5633	
Day 2 / 0-hr Pre-dose											0.5383
No	62	36 (58.1%)	60	47 (78.3%)	3.08 (1.20, 7.90)	0.0189	1.33 (0.85, 2.08)	0.2049	16.9 (-16.8, 50.6)	0.3261	
Yes	96	42 (43.8%)	80	61 (76.3%)	4.94 (2.21, 11.04)	<.0001	1.65 (1.11, 2.45)	0.0142	24.9 (-2.1, 51.9)	0.0707	
Day 2 / 1-hr Post-dose 1											0.0684
No	62	45 (72.6%)	60	49 (81.7%)	1.74 (0.68, 4.47)	0.2518	1.14 (0.75, 1.72)	0.5327	11.6 (-19.4, 42.7)	0.4639	
Yes	95	40 (42.1%)	80	66 (82.5%)	8.26 (3.71, 18.41)	<.0001	1.90 (1.27, 2.83)	0.0017	40.1 (16.4, 63.8)	0.0009	
Day 2 / 4-hr Post-dose 1											0.6667
No	62	34 (54.8%)	60	51 (85.0%)	6.63 (2.39, 18.41)	0.0003	1.60 (1.03, 2.49)	0.0383	28.7 (-2.6, 60.0)	0.0726	
Yes	95	44 (46.3%)	80	68 (85.0%)	7.67 (3.39, 17.32)	<.0001	1.77 (1.21, 2.60)	0.0036	37.3 (13.1, 61.4)	0.0025	
Day 3 / 0-hr Pre-dose											0.9652
No	62	31 (50.0%)	60	53 (88.3%)	8.71 (3.24, 23.44)	<.0001	1.79 (1.14, 2.81)	0.0114	40.8 (10.0, 71.5)	0.0094	
Yes	95	44 (46.3%)	80	68 (85.0%)	7.07 (3.24, 15.44)	<.0001	1.80 (1.23, 2.64)	0.0027	42.0 (17.6, 66.4)	0.0007	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline eGFR, acute phase baseline S-K, age group (<65, >=65 years) and binary indicators for RAASi use, chronic kidney disease, congestive heart disease and diabetes mellitus.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 2.1.5.1 - Study ZS-003 acute: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)		Lokelma 10g QD (N=143)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
RAASi medications											
Day 1 / 1-hr Post-dose 1											0.2373
No	57	13 (22.8%)	47	23 (48.9%)	4.06 (1.29, 12.74)	0.0163	1.79 (0.87, 3.68)	0.1114	14.3 (-37.1, 65.7)	0.5853	
Yes	101	45 (44.6%)	96	42 (43.8%)	0.81 (0.38, 1.73)	0.5905	1.02 (0.67, 1.56)	0.9310	-1.3 (-33.3, 30.6)	0.9348	
Day 1 / 2-hr Post-dose 1											0.7175
No	57	17 (29.8%)	47	22 (46.8%)	2.31 (0.71, 7.58)	0.1661	1.25 (0.64, 2.47)	0.5128	7.8 (-41.5, 57.2)	0.7552	
Yes	101	37 (36.6%)	96	48 (50.0%)	1.98 (1.00, 3.89)	0.0485	1.36 (0.88, 2.10)	0.1625	11.2 (-14.7, 37.0)	0.3972	
Day 1 / 4-hr Post-dose 1											0.9905
No	57	27 (47.4%)	47	28 (59.6%)	1.62 (0.66, 4.00)	0.2957	1.20 (0.69, 2.07)	0.5201	10.2 (-23.0, 43.5)	0.5470	
Yes	101	53 (52.5%)	96	59 (61.5%)	1.25 (0.64, 2.43)	0.5171	1.17 (0.81, 1.70)	0.4022	8.2 (-17.0, 33.4)	0.5214	
Day 2 / 0-hr Pre-dose											0.5159
No	57	29 (50.9%)	47	35 (74.5%)	2.79 (1.09, 7.16)	0.0326	1.36 (0.82, 2.25)	0.2395	18.0 (-17.1, 53.2)	0.3146	
Yes	101	49 (48.5%)	93	73 (78.5%)	5.70 (2.52, 12.85)	<.0001	1.63 (1.13, 2.34)	0.0091	24.1 (-3.5, 51.7)	0.0876	
Day 2 / 1-hr Post-dose 1											0.6801
No	56	29 (51.8%)	47	40 (85.1%)	9.33 (2.85, 30.52)	0.0002	1.66 (1.02, 2.72)	0.0418	39.3 (7.0, 71.6)	0.0171	
Yes	101	56 (55.4%)	93	75 (80.6%)	3.45 (1.65, 7.22)	0.0010	1.42 (1.00, 2.01)	0.0487	27.2 (4.5, 49.9)	0.0190	
Day 2 / 4-hr Post-dose 1											0.7325
No	56	27 (48.2%)	47	43 (91.5%)	12.73 (3.67, 44.19)	<.0001	1.79 (1.10, 2.93)	0.0202	44.2 (10.9, 77.5)	0.0093	
Yes	101	51 (50.5%)	93	76 (81.7%)	5.47 (2.53, 11.85)	<.0001	1.59 (1.11, 2.28)	0.0106	29.9 (6.4, 53.4)	0.0125	
Day 3 / 0-hr Pre-dose											0.7078
No	56	25 (44.6%)	47	42 (89.4%)	10.65 (3.44, 32.99)	<.0001	1.90 (1.15, 3.15)	0.0129	43.6 (10.5, 76.7)	0.0099	
Yes	101	50 (49.5%)	93	79 (84.9%)	6.31 (3.03, 13.15)	<.0001	1.70 (1.19, 2.43)	0.0034	41.3 (17.9, 64.8)	0.0006	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline eGFR, acute phase baseline S-K, age group (<65, >=65 years) and binary indicators for RAASi use, chronic kidney disease, congestive heart disease and diabetes mellitus.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 2.1.5.1 - Study ZS-003 acute: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)		Lokelma 10g QD (N=143)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Sex											
Day 1 / 1-hr Post-dose 1											0.7916
Male	98	32 (32.7%)	80	33 (41.3%)	1.31 (0.56, 3.04)	0.5346	1.13 (0.69, 1.87)	0.6290	2.9 (-34.4, 40.1)	0.8796	
Female	60	26 (43.3%)	63	32 (50.8%)	1.32 (0.54, 3.21)	0.5412	1.14 (0.67, 1.95)	0.6276	4.8 (-32.6, 42.3)	0.8000	
Day 1 / 2-hr Post-dose 1											0.8618
Male	98	31 (31.6%)	80	38 (47.5%)	2.02 (0.92, 4.46)	0.0801	1.29 (0.80, 2.10)	0.3003	7.8 (-21.5, 37.1)	0.6019	
Female	60	23 (38.3%)	63	32 (50.8%)	1.81 (0.77, 4.23)	0.1739	1.30 (0.75, 2.26)	0.3555	8.9 (-25.1, 42.8)	0.6079	
Day 1 / 4-hr Post-dose 1											0.9653
Male	98	46 (46.9%)	80	46 (57.5%)	1.26 (0.60, 2.66)	0.5441	1.15 (0.76, 1.74)	0.5098	6.6 (-20.5, 33.7)	0.6341	
Female	60	34 (56.7%)	63	41 (65.1%)	1.38 (0.64, 3.01)	0.4125	1.15 (0.72, 1.82)	0.5552	7.1 (-20.4, 34.5)	0.6133	
Day 2 / 0-hr Pre-dose											0.4699
Male	98	49 (50.0%)	78	58 (74.4%)	3.40 (1.54, 7.52)	0.0025	1.37 (0.93, 2.01)	0.1139	16.9 (-11.4, 45.2)	0.2411	
Female	60	29 (48.3%)	62	50 (80.6%)	6.74 (2.50, 18.20)	0.0002	1.70 (1.06, 2.71)	0.0269	30.8 (-3.9, 65.6)	0.0822	
Day 2 / 1-hr Post-dose 1											0.8079
Male	97	52 (53.6%)	78	62 (79.5%)	3.68 (1.73, 7.80)	0.0007	1.42 (0.98, 2.06)	0.0663	29.9 (6.0, 53.8)	0.0141	
Female	60	33 (55.0%)	62	53 (85.5%)	6.85 (2.41, 19.45)	0.0003	1.56 (1.00, 2.42)	0.0507	33.0 (4.3, 61.7)	0.0241	
Day 2 / 4-hr Post-dose 1											0.7861
Male	97	44 (45.4%)	78	64 (82.1%)	7.79 (3.30, 18.37)	<.0001	1.70 (1.15, 2.50)	0.0077	29.3 (1.6, 57.1)	0.0384	
Female	60	34 (56.7%)	62	55 (88.7%)	6.66 (2.46, 18.00)	0.0002	1.56 (1.01, 2.42)	0.0442	33.6 (2.8, 64.3)	0.0324	
Day 3 / 0-hr Pre-dose											0.9971
Male	97	44 (45.4%)	78	65 (83.3%)	6.64 (3.05, 14.45)	<.0001	1.77 (1.20, 2.61)	0.0037	36.5 (11.1, 61.9)	0.0049	
Female	60	31 (51.7%)	62	56 (90.3%)	10.65 (3.74, 30.32)	<.0001	1.78 (1.14, 2.79)	0.0110	42.4 (12.5, 72.3)	0.0055	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline eGFR, acute phase baseline S-K, age group (<65, >=65 years) and binary indicators for RAASi use, chronic kidney disease, congestive heart disease and diabetes mellitus.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 2.1.5.1 - Study ZS-003 acute: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)		Lokelma 10g QD (N=143)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Age (years)											
Day 1 / 1-hr Post-dose 1											0.8704
<65 years	66	18 (27.3%)	54	25 (46.3%)	1.80 (0.66, 4.93)	0.2528	1.30 (0.69, 2.47)	0.4136	7.3 (-32.6, 47.2)	0.7193	
>=65 years	92	40 (43.5%)	89	40 (44.9%)	1.16 (0.52, 2.57)	0.7114	1.15 (0.73, 1.80)	0.5581	1.5 (-30.5, 33.5)	0.9257	
Day 1 / 2-hr Post-dose 1											0.9664
<65 years	66	20 (30.3%)	54	29 (53.7%)	2.60 (0.94, 7.14)	0.0643	1.38 (0.76, 2.52)	0.2907	9.9 (-29.4, 49.2)	0.6202	
>=65 years	92	34 (37.0%)	89	41 (46.1%)	1.75 (0.85, 3.61)	0.1307	1.33 (0.83, 2.13)	0.2311	10.2 (-18.2, 38.6)	0.4822	
Day 1 / 4-hr Post-dose 1											0.9894
<65 years	66	26 (39.4%)	54	30 (55.6%)	1.27 (0.55, 2.92)	0.5741	1.12 (0.65, 1.93)	0.6794	4.0 (-27.6, 35.5)	0.8047	
>=65 years	92	54 (58.7%)	89	57 (64.0%)	1.33 (0.66, 2.66)	0.4245	1.16 (0.79, 1.70)	0.4444	11.7 (-15.0, 38.5)	0.3896	
Day 2 / 0-hr Pre-dose											0.8276
<65 years	66	28 (42.4%)	52	41 (78.8%)	4.59 (1.75, 12.00)	0.0019	1.58 (0.96, 2.60)	0.0727	22.7 (-13.5, 58.8)	0.2193	
>=65 years	92	50 (54.3%)	88	67 (76.1%)	3.60 (1.67, 7.74)	0.0010	1.46 (1.00, 2.12)	0.0472	20.6 (-6.6, 47.7)	0.1376	
Day 2 / 1-hr Post-dose 1											0.7726
<65 years	65	29 (44.6%)	52	40 (76.9%)	4.94 (1.87, 13.03)	0.0013	1.58 (0.96, 2.61)	0.0722	32.8 (2.8, 62.8)	0.0324	
>=65 years	92	56 (60.9%)	88	75 (85.2%)	4.67 (2.11, 10.35)	0.0001	1.43 (1.01, 2.04)	0.0442	28.7 (4.0, 53.5)	0.0227	
Day 2 / 4-hr Post-dose 1											0.6755
<65 years	65	31 (47.7%)	52	43 (82.7%)	5.03 (1.96, 12.95)	0.0008	1.58 (0.98, 2.56)	0.0623	34.7 (4.0, 65.4)	0.0269	
>=65 years	92	47 (51.1%)	88	76 (86.4%)	11.38 (4.45, 29.08)	<.0001	1.75 (1.21, 2.54)	0.0030	32.7 (5.7, 59.6)	0.0174	
Day 3 / 0-hr Pre-dose											0.8352
<65 years	65	31 (47.7%)	52	46 (88.5%)	8.13 (2.89, 22.83)	<.0001	1.76 (1.10, 2.82)	0.0194	40.9 (9.0, 72.7)	0.0120	
>=65 years	92	44 (47.8%)	88	75 (85.2%)	8.26 (3.77, 18.11)	<.0001	1.85 (1.27, 2.70)	0.0013	45.4 (20.5, 70.4)	0.0004	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline eGFR, acute phase baseline S-K, age group (<65, >=65 years) and binary indicators for RAASi use, chronic kidney disease, congestive heart disease and diabetes mellitus.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 2.1.5.1 - Study ZS-003 acute: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)		Lokelma 10g QD (N=143)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Baseline S-K											
Day 1 / 1-hr Post-dose 1											<.0001
<=5.3 mmol/L	95	53 (55.8%)	94	52 (55.3%)	0.99 (0.49, 2.02)	0.9836	1.01 (0.69, 1.50)	0.9427	-0.7 (-24.1, 22.7)	0.9506	
5.4-5.5 mmol/L	22	5 (22.7%)	27	12 (44.4%)	2.12 (0.41, 11.01)	0.3726	1.76 (0.54, 5.76)	0.3521	8.7 (-77.0, 94.5)	0.8417	
>5.5 mmol/L	41	0 (0.0%)	22	1 (4.5%)	n/a	n/a	NC	NC	NC	NC	
Day 1 / 2-hr Post-dose 1											0.8961
<=5.3 mmol/L	95	47 (49.5%)	94	60 (63.8%)	2.12 (1.08, 4.18)	0.0289	1.27 (0.86, 1.87)	0.2321	15.1 (-6.0, 36.2)	0.1614	
5.4-5.5 mmol/L	22	4 (18.2%)	27	8 (29.6%)	1.43 (0.16, 12.81)	0.7490	1.76 (0.42, 7.44)	0.4400	NC	NC	
>5.5 mmol/L	41	3 (7.3%)	22	2 (9.1%)	1.66 (0.22, 12.34)	0.6210	1.54 (0.24, 9.85)	0.6499	NC	NC	
Day 1 / 4-hr Post-dose 1											0.3071
<=5.3 mmol/L	95	65 (68.4%)	94	61 (64.9%)	0.83 (0.41, 1.66)	0.5918	0.98 (0.69, 1.40)	0.9111	-2.9 (-25.1, 19.3)	0.7983	
5.4-5.5 mmol/L	22	9 (40.9%)	27	20 (74.1%)	3.33 (0.76, 14.61)	0.1109	1.61 (0.67, 3.83)	0.2837	21.0 (-41.9, 83.9)	0.5131	
>5.5 mmol/L	41	6 (14.6%)	22	6 (27.3%)	4.29 (0.84, 21.93)	0.0803	3.10 (0.78, 12.34)	0.1087	13.3 (-111.1, 137.8)	0.8339	
Day 2 / 0-hr Pre-dose											0.4900
<=5.3 mmol/L	95	62 (65.3%)	92	80 (87.0%)	4.40 (1.95, 9.93)	0.0004	1.35 (0.97, 1.90)	0.0767	27.2 (2.2, 52.3)	0.0331	
5.4-5.5 mmol/L	22	9 (40.9%)	26	19 (73.1%)	4.65 (0.99, 21.76)	0.0511	1.80 (0.75, 4.31)	0.1891	31.9 (-21.9, 85.8)	0.2453	
>5.5 mmol/L	41	7 (17.1%)	22	9 (40.9%)	4.05 (0.97, 16.96)	0.0554	2.23 (0.76, 6.55)	0.1437	19.7 (-40.0, 79.3)	0.5177	
Day 2 / 1-hr Post-dose 1											0.4965
<=5.3 mmol/L	95	62 (65.3%)	92	79 (85.9%)	3.57 (1.63, 7.81)	0.0015	1.32 (0.94, 1.85)	0.1063	24.6 (0.1, 49.2)	0.0489	
5.4-5.5 mmol/L	22	11 (50.0%)	26	23 (88.5%)	40.82 (2.65, 629.68)	0.0079	1.84 (0.83, 4.08)	0.1347	43.9 (-12.2, 99.9)	0.1249	
>5.5 mmol/L	40	12 (30.0%)	22	13 (59.1%)	15.50 (2.26, 106.32)	0.0053	2.62 (1.08, 6.34)	0.0324	30.2 (-30.4, 90.8)	0.3288	
Day 2 / 4-hr Post-dose 1											0.3934
<=5.3 mmol/L	95	59 (62.1%)	92	83 (90.2%)	6.87 (2.86, 16.48)	<.0001	1.45 (1.03, 2.03)	0.0316	31.5 (6.9, 56.2)	0.0121	
5.4-5.5 mmol/L	22	8 (36.4%)	26	23 (88.5%)	11.66 (2.21, 61.50)	0.0038	2.26 (0.96, 5.36)	0.0628	59.0 (2.0, 116.1)	0.0424	
>5.5 mmol/L	40	11 (27.5%)	22	13 (59.1%)	6.67 (1.51, 29.39)	0.0121	2.25 (0.92, 5.49)	0.0764	29.8 (-32.6, 92.2)	0.3486	
Day 3 / 0-hr Pre-dose											0.1606
<=5.3 mmol/L	95	56 (58.9%)	92	80 (87.0%)	4.96 (2.34, 10.56)	<.0001	1.49 (1.05, 2.10)	0.0245	29.8 (5.3, 54.3)	0.0170	
5.4-5.5 mmol/L	22	10 (45.5%)	26	24 (92.3%)	13.10 (2.02, 84.93)	0.0070	2.02 (0.88, 4.61)	0.0952	43.9 (-10.4, 98.2)	0.1131	
>5.5 mmol/L	40	9 (22.5%)	22	17 (77.3%)	19.63 (3.59, 107.31)	0.0006	3.15 (1.32, 7.55)	0.0099	50.5 (-29.6, 130.6)	0.2170	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline eGFR, acute phase baseline S-K, age group (<65, >=65 years) and binary indicators for RAASi use, chronic kidney disease, congestive heart disease and diabetes mellitus.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 2.1.5.1 - Study ZS-003 acute: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)		Lokelma 10g QD (N=143)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Baseline eGFR											
Day 1 / 1-hr Post-dose 1											0.8519
<15 ml/min/1.73m**2	15	3 (20.0%)	10	2 (20.0%)	0.20 (<0.01, >999.99)	0.9273	1.50 (0.61, 3.69)	0.3796	NC	NC	
15-29 ml/min/1.73m**2	44	9 (20.5%)	42	11 (26.2%)	1.89 (0.59, 6.08)	0.2859	1.35 (0.76, 2.37)	0.3034	12.8 (-38.2, 63.9)	0.6222	
30-59 ml/min/1.73m**2	61	23 (37.7%)	50	26 (52.0%)	1.89 (0.83, 4.31)	0.1291	0.96 (0.54, 1.71)	0.8878	19.2 (-14.9, 53.3)	0.2698	
>=60 ml/min/1.73m**2	38	23 (60.5%)	41	26 (63.4%)	0.85 (0.31, 2.28)	0.7402	NC	NC	-2.3 (-37.2, 32.5)	0.8949	
Day 1 / 2-hr Post-dose 1											0.6169
<15 ml/min/1.73m**2	15	3 (20.0%)	10	1 (10.0%)	0.24 (<0.01, 10.95)	0.4663	0.43 (0.02, 10.59)	0.6031	NC	NC	
15-29 ml/min/1.73m**2	44	7 (15.9%)	42	12 (28.6%)	3.01 (0.91, 9.93)	0.0707	2.16 (0.82, 5.72)	0.1199	8.5 (-44.5, 61.5)	0.7526	
30-59 ml/min/1.73m**2	61	21 (34.4%)	50	27 (54.0%)	2.49 (1.11, 5.59)	0.0265	1.60 (0.90, 2.84)	0.1077	25.9 (-0.1, 51.9)	0.0505	
>=60 ml/min/1.73m**2	38	23 (60.5%)	41	30 (73.2%)	1.73 (0.64, 4.65)	0.2810	1.19 (0.68, 2.10)	0.5409	11.6 (-25.5, 48.7)	0.5392	
Day 1 / 4-hr Post-dose 1											0.7849
<15 ml/min/1.73m**2	15	4 (26.7%)	10	6 (60.0%)	11.08 (0.42, 295.19)	0.1511	2.38 (0.39, 14.53)	0.3469	27.0 (-184.9, 238.9)	0.8028	
15-29 ml/min/1.73m**2	44	18 (40.9%)	42	21 (50.0%)	2.30 (0.84, 6.27)	0.1030	1.47 (0.76, 2.81)	0.2500	20.3 (-19.9, 60.6)	0.3219	
30-59 ml/min/1.73m**2	61	35 (57.4%)	50	34 (68.0%)	1.58 (0.67, 3.76)	0.2968	1.15 (0.71, 1.85)	0.5670	7.9 (-21.7, 37.5)	0.6020	
>=60 ml/min/1.73m**2	38	23 (60.5%)	41	26 (63.4%)	1.01 (0.38, 2.68)	0.9829	1.01 (0.56, 1.81)	0.9742	0.7 (-34.7, 36.1)	0.9703	
Day 2 / 0-hr Pre-dose											0.5916
<15 ml/min/1.73m**2	15	7 (46.7%)	9	7 (77.8%)	16.82 (1.11, 254.45)	0.0417	2.75 (0.63, 12.02)	0.1782	53.6 (-58.2, 165.4)	0.3476	
15-29 ml/min/1.73m**2	44	16 (36.4%)	42	27 (64.3%)	3.51 (1.38, 8.93)	0.0084	1.84 (0.97, 3.48)	0.0612	38.8 (6.5, 71.2)	0.0187	
30-59 ml/min/1.73m**2	61	28 (45.9%)	48	40 (83.3%)	5.91 (2.29, 15.28)	0.0002	1.74 (1.07, 2.84)	0.0259	35.9 (4.6, 67.3)	0.0247	
>=60 ml/min/1.73m**2	38	27 (71.1%)	41	34 (82.9%)	1.65 (0.52, 5.26)	0.3970	1.12 (0.66, 1.89)	0.6773	8.4 (-30.8, 47.6)	0.6752	
Day 2 / 1-hr Post-dose 1											0.0918
<15 ml/min/1.73m**2	15	1 (6.7%)	9	8 (88.9%)	>999.99 (<0.01, >999.99)	0.6704	24.65 (0.36, >999.99)	0.1370	50.7 (-577.7, 679.1)	0.8744	
15-29 ml/min/1.73m**2	44	22 (50.0%)	42	31 (73.8%)	4.26 (1.51, 11.98)	0.0061	1.64 (0.93, 2.89)	0.0846	32.1 (-2.0, 66.1)	0.0649	
30-59 ml/min/1.73m**2	60	32 (53.3%)	48	42 (87.5%)	7.97 (2.60, 24.43)	0.0003	1.60 (1.01, 2.55)	0.0465	36.8 (4.8, 68.7)	0.0241	
>=60 ml/min/1.73m**2	38	30 (78.9%)	41	34 (82.9%)	1.27 (0.36, 4.42)	0.7100	1.03 (0.61, 1.72)	0.9139	7.6 (-34.0, 49.1)	0.7212	
Day 2 / 4-hr Post-dose 1											0.6179
<15 ml/min/1.73m**2	15	5 (33.3%)	9	8 (88.9%)	21.15 (1.05, 425.02)	0.0462	2.89 (0.62, 13.57)	0.1781	45.5 (-72.7, 163.8)	0.4506	
15-29 ml/min/1.73m**2	44	18 (40.9%)	42	31 (73.8%)	5.87 (2.07, 16.66)	0.0009	1.97 (1.08, 3.61)	0.0276	46.5 (11.5, 81.6)	0.0092	
30-59 ml/min/1.73m**2	60	29 (48.3%)	48	43 (89.6%)	9.54 (3.22, 28.30)	<.0001	1.82 (1.13, 2.93)	0.0131	41.5 (9.2, 73.8)	0.0118	
>=60 ml/min/1.73m**2	38	26 (68.4%)	41	37 (90.2%)	5.66 (1.46, 21.93)	0.0121	1.38 (0.82, 2.31)	0.2305	24.8 (-15.9, 65.6)	0.2324	
Day 3 / 0-hr Pre-dose											0.0578
<15 ml/min/1.73m**2	15	4 (26.7%)	9	9 (100.0%)	n/a	n/a	4.97 (0.95, 26.05)	0.0579	65.1 (-70.8, 201.1)	0.3479	
15-29 ml/min/1.73m**2	44	15 (34.1%)	42	40 (95.2%)	53.27 (9.78, 290.19)	<.0001	2.85 (1.55, 5.24)	0.0008	67.7 (33.7, 101.7)	<.0001	
30-59 ml/min/1.73m**2	60	29 (48.3%)	48	41 (85.4%)	6.69 (2.42, 18.47)	0.0002	1.71 (1.06, 2.76)	0.0284	34.2 (2.9, 65.6)	0.0323	
>=60 ml/min/1.73m**2	38	27 (71.1%)	41	31 (75.6%)	1.24 (0.43, 3.59)	0.6899	1.06 (0.62, 1.80)	0.8432	3.2 (-35.7, 42.1)	0.8717	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline eGFR, acute phase baseline S-K, age group (<65, >=65 years) and binary indicators for RAASi use, chronic kidney disease, congestive heart disease and diabetes mellitus.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

t_zs003ac_prop_norm48.pdf generated by zs003ac_prop.sas at 15:35:55 on 19 January 2021

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Table 2.1.5.1 - Study ZS-003 acute: Proportion of subjects with normalised serum potassium at 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=158)		Lokelma 10g QD (N=143)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Region											
Day 1 / 1-hr Post-dose 1											0.8652
USA	148	56 (37.8%)	133	62 (46.6%)	1.29 (0.69, 2.40)	0.4216	1.15 (0.80, 1.66)	0.4542	3.0 (-24.8, 30.7)	0.8349	
Rest of world	10	2 (20.0%)	10	3 (30.0%)	0.04 (<0.01, >999.99)	0.9321	NC	NC	NC	NC	
Day 1 / 2-hr Post-dose 1											0.7659
USA	148	53 (35.8%)	133	68 (51.1%)	1.93 (1.08, 3.45)	0.0260	1.30 (0.90, 1.87)	0.1586	8.3 (-14.4, 31.1)	0.4724	
Rest of world	10	1 (10.0%)	10	2 (20.0%)	0.04 (<0.01, >999.99)	0.9400	NC	NC	NC	NC	
Day 1 / 4-hr Post-dose 1											0.1375
USA	148	79 (53.4%)	133	81 (60.9%)	1.14 (0.66, 1.96)	0.6463	1.10 (0.81, 1.50)	0.5475	3.9 (-16.6, 24.4)	0.7088	
Rest of world	10	1 (10.0%)	10	6 (60.0%)	>999.99 (<0.01, >999.99)	0.0961	4.44 (0.42, 46.84)	0.2148	NC	NC	
Day 2 / 0-hr Pre-dose											0.7624
USA	148	75 (50.7%)	131	103 (78.6%)	4.01 (2.17, 7.42)	<.0001	1.48 (1.10, 2.00)	0.0103	19.4 (-3.0, 41.7)	0.0892	
Rest of world	10	3 (30.0%)	9	5 (55.6%)	>999.99 (<0.01, >999.99)	0.9764	0.72 (<0.01, 70.89)	0.8901	NC	NC	
Day 2 / 1-hr Post-dose 1											0.7732
USA	147	82 (55.8%)	131	110 (84.0%)	4.67 (2.48, 8.82)	<.0001	1.45 (1.08, 1.93)	0.0120	31.1 (12.0, 50.3)	0.0014	
Rest of world	10	3 (30.0%)	9	5 (55.6%)	0.99 (0.04, 23.87)	0.9936	1.13 (0.17, 7.67)	0.9016	NC	NC	
Day 2 / 4-hr Post-dose 1											0.4820
USA	147	75 (51.0%)	131	112 (85.5%)	6.66 (3.47, 12.79)	<.0001	1.62 (1.21, 2.18)	0.0013	29.0 (8.1, 49.9)	0.0066	
Rest of world	10	3 (30.0%)	9	7 (77.8%)	>999.99 (<0.01, >999.99)	0.3123	1.88 (0.36, 9.73)	0.4498	37.0 (-130.2, 204.3)	0.6643	
Day 3 / 0-hr Pre-dose											0.7248
USA	147	71 (48.3%)	131	113 (86.3%)	7.27 (3.89, 13.58)	<.0001	1.76 (1.31, 2.37)	0.0002	39.7 (19.9, 59.5)	<.0001	
Rest of world	10	4 (40.0%)	9	8 (88.9%)	27.67 (<0.01, >999.99)	0.9837	1.41 (0.31, 6.39)	0.6563	12.0 (-142.2, 166.2)	0.8786	

OR, RR and ARR derived from model with the following effects:
Acute phase treatment group, acute phase baseline eGFR, acute phase baseline S-K, age group (<65, >=65 years) and binary indicators for RAASi use, chronic kidney disease, congestive heart disease and diabetes mellitus.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

t_zs003ac_prop_norm48.pdf generated by zs003ac_prop.sas at 15:35:55 on 19 January 2021

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Table 2.2.1.1 - Study ZS-003 acute: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	158	17 (10.8%)	143	17 (11.9%)	1.12 (0.55 , 2.29)	0.7575	1.10 (0.59 , 2.08)	0.7575	1.13 (-6.05 , 8.30)	0.7579	
Chronic kidney disease											0.3411
No	62	5 (8.1%)	60	8 (13.3%)	1.75 (0.54 , 5.70)	0.3503	1.65 (0.57 , 4.77)	0.3523	5.27 (-5.68 , 16.22)	0.3457	
Yes	96	12 (12.5%)	83	9 (10.8%)	0.85 (0.34 , 2.13)	0.7314	0.87 (0.38 , 1.96)	0.7317	-1.66 (-11.06 , 7.75)	0.7300	
Congestive heart disease											0.1555
No	92	6 (6.5%)	84	10 (11.9%)	1.94 (0.67 , 5.58)	0.2210	1.83 (0.69 , 4.81)	0.2230	5.38 (-3.19 , 13.95)	0.2182	
Yes	66	11 (16.7%)	59	7 (11.9%)	0.67 (0.24 , 1.87)	0.4471	0.71 (0.30 , 1.72)	0.4492	-4.80 (-17.01 , 7.40)	0.4405	
Diabetes mellitus											0.2215
No	62	5 (8.1%)	62	9 (14.5%)	1.94 (0.61 , 6.15)	0.2625	1.80 (0.64 , 5.07)	0.2657	6.45 (-4.63 , 17.53)	0.2539	
Yes	96	12 (12.5%)	81	8 (9.9%)	0.77 (0.30 , 1.98)	0.5836	0.79 (0.34 , 1.84)	0.5845	-2.62 (-11.90 , 6.65)	0.5792	
RAASi medications											0.2161
No	57	10 (17.5%)	47	6 (12.8%)	0.69 (0.23 , 2.06)	0.5031	0.73 (0.29 , 1.85)	0.5054	-4.78 (-18.51 , 8.95)	0.4952	
Yes	101	7 (6.9%)	96	11 (11.5%)	1.74 (0.64 , 4.69)	0.2749	1.65 (0.67 , 4.09)	0.2765	4.53 (-3.54 , 12.60)	0.2715	
Sex											0.7065
Male	98	11 (11.2%)	80	11 (13.8%)	1.26 (0.52 , 3.08)	0.6111	1.23 (0.56 , 2.68)	0.6109	2.53 (-7.27 , 12.32)	0.6134	
Female	60	6 (10.0%)	63	6 (9.5%)	0.95 (0.29 , 3.12)	0.9291	0.95 (0.33 , 2.79)	0.9291	-0.48 (-10.97 , 10.02)	0.9291	
Age (years)											0.1721
<65 years	66	6 (9.1%)	54	9 (16.7%)	2.00 (0.66 , 6.03)	0.2180	1.83 (0.70 , 4.83)	0.2199	7.58 (-4.54 , 19.70)	0.2206	
>=65 years	92	11 (12.0%)	89	8 (9.0%)	0.73 (0.28 , 1.90)	0.5162	0.75 (0.32 , 1.78)	0.5169	-2.97 (-11.87 , 5.94)	0.5135	
Baseline S-K											0.9152
<=5.3 mmol/L	95	9 (9.5%)	94	11 (11.7%)	1.27 (0.50 , 3.21)	0.6191	1.24 (0.54 , 2.84)	0.6194	2.23 (-6.54 , 11.00)	0.6184	
5.4-5.5 mmol/L	22	2 (9.1%)	27	2 (7.4%)	0.80 (0.10 , 6.19)	0.8308	0.81 (0.12 , 5.33)	0.8307	-1.68 (-17.24 , 13.87)	0.8320	
>5.5 mmol/L	41	6 (14.6%)	22	4 (18.2%)	1.30 (0.32 , 5.19)	0.7138	1.24 (0.39 , 3.94)	0.7124	3.55 (-15.86 , 22.96)	0.7202	
Baseline eGFR											0.2842
<15 ml/min/1.73m**2	15	1 (6.7%)	10	1 (10.0%)	1.56 (0.09 , 28.15)	0.7649	1.50 (0.11 , 21.31)	0.7646	3.33 (-19.14 , 25.81)	0.7713	
15-29 ml/min/1.73m**2	44	9 (20.5%)	42	7 (16.7%)	0.78 (0.26 , 2.32)	0.6523	0.81 (0.33 , 1.99)	0.6530	-3.79 (-20.19 , 12.62)	0.6508	
30-59 ml/min/1.73m**2	61	5 (8.2%)	50	2 (4.0%)	0.47 (0.09 , 2.52)	0.3752	0.49 (0.10 , 2.41)	0.3785	-4.20 (-12.97 , 4.57)	0.3482	
>=60 ml/min/1.73m**2	38	2 (5.3%)	41	7 (17.1%)	3.71 (0.72 , 19.10)	0.1174	3.24 (0.72 , 14.66)	0.1262	11.81 (-1.72 , 25.34)	0.0871	
Region											0.9103
USA	148	14 (9.5%)	133	14 (10.5%)	1.13 (0.52 , 2.46)	0.7657	1.11 (0.55 , 2.25)	0.7657	1.07 (-5.96 , 8.10)	0.7662	
Rest of world	10	3 (30.0%)	10	3 (30.0%)	1.00 (0.15 , 6.77)	1.0000	1.00 (0.26 , 3.81)	1.0000	0.00 (-40.17 , 40.17)	1.0000	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_zs003ac_ae_any.pdf generated by zs003ac_ae_soc_pt.sas at 13:52:17 on 25 February 2021

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Table 2.2.1.2 - Study ZS-003 acute: Subjects experiencing any serious adverse event (SAE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	158	1 (0.6%)	143	0 (0.0%)	0.37 (0.01 , 9.05)	0.5391	0.37 (0.02 , 8.96)	0.5395	-0.63 (-1.87 , 0.60)	0.3158	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_zs003ac_ae_sae.pdf generated by zs003ac_ae_soc_pt.sas at 13:52:20 on 25 February 2021

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Table 2.2.1.3 - Study ZS-003 acute: Subjects experiencing any AE leading to discontinuation of study medication (DAE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	158	1 (0.6%)	143	1 (0.7%)	1.11 (0.07 , 17.84)	0.9436	1.10 (0.07 , 17.50)	0.9436	0.07 (-1.78 , 1.91)	0.9437	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_zs003ac_ae_dae.pdf generated by zs003ac_ae_soc_pt.sas at 13:52:25 on 25 February 2021

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Table 2.2.1.4 - Study ZS-003 acute: Subjects experiencing any AE graded as severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	158	0 (0.0%)	143	1 (0.7%)	3.34 (0.13 , 82.57)	0.4617	3.31 (0.14 , 80.67)	0.4622	0.70 (-0.67 , 2.07)	0.3156	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_zs003ac_ae_sev.pdf generated by zs003ac_ae_soc_pt.sas at 13:52:28 on 25 February 2021

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Table 2.2.1.5 - Study ZS-003 acute: Subjects experiencing any AE graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	158	17 (10.8%)	143	16 (11.2%)	1.04 (0.51 , 2.15)	0.9052	1.04 (0.55 , 1.98)	0.9052	0.43 (-6.64 , 7.50)	0.9053	
Chronic kidney disease											0.2654
No	62	5 (8.1%)	60	8 (13.3%)	1.75 (0.54 , 5.70)	0.3503	1.65 (0.57 , 4.77)	0.3523	5.27 (-5.68 , 16.22)	0.3457	
Yes	96	12 (12.5%)	83	8 (9.6%)	0.75 (0.29 , 1.93)	0.5455	0.77 (0.33 , 1.80)	0.5465	-2.86 (-12.03 , 6.31)	0.5408	
Congestive heart disease											0.2125
No	92	6 (6.5%)	84	9 (10.7%)	1.72 (0.59 , 5.06)	0.3243	1.64 (0.61 , 4.42)	0.3256	4.19 (-4.13 , 12.51)	0.3233	
Yes	66	11 (16.7%)	59	7 (11.9%)	0.67 (0.24 , 1.87)	0.4471	0.71 (0.30 , 1.72)	0.4492	-4.80 (-17.01 , 7.40)	0.4405	
Diabetes mellitus											0.1619
No	62	5 (8.1%)	62	9 (14.5%)	1.94 (0.61 , 6.15)	0.2625	1.80 (0.64 , 5.07)	0.2657	6.45 (-4.63 , 17.53)	0.2539	
Yes	96	12 (12.5%)	81	7 (8.6%)	0.66 (0.25 , 1.77)	0.4112	0.69 (0.29 , 1.67)	0.4132	-3.86 (-12.87 , 5.15)	0.4014	
RAASi medications											0.2783
No	57	10 (17.5%)	47	6 (12.8%)	0.69 (0.23 , 2.06)	0.5031	0.73 (0.29 , 1.85)	0.5054	-4.78 (-18.51 , 8.95)	0.4952	
Yes	101	7 (6.9%)	96	10 (10.4%)	1.56 (0.57 , 4.28)	0.3868	1.50 (0.60 , 3.79)	0.3877	3.49 (-4.38 , 11.35)	0.3851	
Sex											0.8179
Male	98	11 (11.2%)	80	10 (12.5%)	1.13 (0.45 , 2.81)	0.7931	1.11 (0.50 , 2.49)	0.7930	1.28 (-8.29 , 10.85)	0.7939	
Female	60	6 (10.0%)	63	6 (9.5%)	0.95 (0.29 , 3.12)	0.9291	0.95 (0.33 , 2.79)	0.9291	-0.48 (-10.97 , 10.02)	0.9291	
Age (years)											0.2457
<65 years	66	6 (9.1%)	54	8 (14.8%)	1.74 (0.56 , 5.36)	0.3354	1.63 (0.60 , 4.41)	0.3363	5.72 (-6.02 , 17.47)	0.3394	
>=65 years	92	11 (12.0%)	89	8 (9.0%)	0.73 (0.28 , 1.90)	0.5162	0.75 (0.32 , 1.78)	0.5169	-2.97 (-11.87 , 5.94)	0.5135	
Baseline S-K											0.9286
<=5.3 mmol/L	95	9 (9.5%)	94	10 (10.6%)	1.14 (0.44 , 2.94)	0.7902	1.12 (0.48 , 2.64)	0.7902	1.16 (-7.41 , 9.74)	0.7901	
5.4-5.5 mmol/L	22	2 (9.1%)	27	2 (7.4%)	0.80 (0.10 , 6.19)	0.8308	0.81 (0.12 , 5.33)	0.8307	-1.68 (-17.24 , 13.87)	0.8320	
>5.5 mmol/L	41	6 (14.6%)	22	4 (18.2%)	1.30 (0.32 , 5.19)	0.7138	1.24 (0.39 , 3.94)	0.7124	3.55 (-15.86 , 22.96)	0.7202	
Baseline eGFR											0.2175
<15 ml/min/1.73m**2	15	1 (6.7%)	10	0 (0.0%)	0.46 (0.02 , 12.45)	0.6447	0.48 (0.02 , 10.84)	0.6479	-6.67 (-19.29 , 5.96)	0.3006	
15-29 ml/min/1.73m**2	44	9 (20.5%)	42	7 (16.7%)	0.78 (0.26 , 2.32)	0.6523	0.81 (0.33 , 1.99)	0.6530	-3.79 (-20.19 , 12.62)	0.6508	
30-59 ml/min/1.73m**2	61	5 (8.2%)	50	2 (4.0%)	0.47 (0.09 , 2.52)	0.3752	0.49 (0.10 , 2.41)	0.3785	-4.20 (-12.97 , 4.57)	0.3482	
>=60 ml/min/1.73m**2	38	2 (5.3%)	41	7 (17.1%)	3.71 (0.72 , 19.10)	0.1174	3.24 (0.72 , 14.66)	0.1262	11.81 (-1.72 , 25.34)	0.0871	
Region											0.5558
USA	148	14 (9.5%)	133	14 (10.5%)	1.13 (0.52 , 2.46)	0.7657	1.11 (0.55 , 2.25)	0.7657	1.07 (-5.96 , 8.10)	0.7662	
Rest of world	10	3 (30.0%)	10	2 (20.0%)	0.58 (0.07 , 4.56)	0.6075	0.67 (0.14 , 3.17)	0.6104	-10.00 (-47.70 , 27.70)	0.6032	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_zs003ac_ae_nsev.pdf generated by zs003ac_ae_soc_pt.sas at 13:52:32 on 25 February 2021

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Table 2.2.1.6 - Study ZS-003 acute: Subjects experiencing any AE resulting in death, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	158	0 (0.0%)	143	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_zs003ac_ae_death.pdf generated by zs003ac_ae_soc_pt.sas at 13:52:36 on 25 February 2021

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Table 2.2.1.7 - Study ZS-003 acute: Adverse events leading to discontinuation (DAE) by SOC and PT, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)	
Subgroup / Category / SOC / PT	N	n (%)	N	n (%)
Overall				
Any AE	158	1 (0.6%)	143	1 (0.7%)
Gastrointestinal disorders	158	0 (0.0%)	143	1 (0.7%)
Diarrhoea	158	0 (0.0%)	143	1 (0.7%)
Vomiting	158	0 (0.0%)	143	1 (0.7%)
Investigations	158	1 (0.6%)	143	0 (0.0%)
Blood potassium increased	158	1 (0.6%)	143	0 (0.0%)
Chronic kidney disease				
No				
Any AE	62	0 (0.0%)	60	0 (0.0%)
Yes				
Any AE	96	1 (1.0%)	83	1 (1.2%)
Gastrointestinal disorders	96	0 (0.0%)	83	1 (1.2%)
Diarrhoea	96	0 (0.0%)	83	1 (1.2%)
Vomiting	96	0 (0.0%)	83	1 (1.2%)
Investigations	96	1 (1.0%)	83	0 (0.0%)
Blood potassium increased	96	1 (1.0%)	83	0 (0.0%)
Congestive heart disease				
No				
Any AE	92	0 (0.0%)	84	1 (1.2%)
Gastrointestinal disorders	92	0 (0.0%)	84	1 (1.2%)
Diarrhoea	92	0 (0.0%)	84	1 (1.2%)
Vomiting	92	0 (0.0%)	84	1 (1.2%)
Yes				
Any AE	66	1 (1.5%)	59	0 (0.0%)
Investigations	66	1 (1.5%)	59	0 (0.0%)
Blood potassium increased	66	1 (1.5%)	59	0 (0.0%)
Diabetes mellitus				
No				
Any AE	62	0 (0.0%)	62	0 (0.0%)
Yes				
Any AE	96	1 (1.0%)	81	1 (1.2%)
Gastrointestinal disorders	96	0 (0.0%)	81	1 (1.2%)
Diarrhoea	96	0 (0.0%)	81	1 (1.2%)
Vomiting	96	0 (0.0%)	81	1 (1.2%)
Investigations	96	1 (1.0%)	81	0 (0.0%)
Blood potassium increased	96	1 (1.0%)	81	0 (0.0%)
RAASi medications				
No				
Any AE	57	1 (1.8%)	47	0 (0.0%)
Investigations	57	1 (1.8%)	47	0 (0.0%)
Blood potassium increased	57	1 (1.8%)	47	0 (0.0%)

t_zs003ac_ae_dae_socpt.pdf generated by zs003ac_ae_soc_pt.sas at 13:53:09 on 25 February 2021

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Table 2.2.1.7 - Study ZS-003 acute: Adverse events leading to discontinuation (DAE) by SOC and PT, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)	
Subgroup / Category / SOC / PT	**N**	**n (%)**	**N**	**n (%)**
RAASi medications *(contd.)*				
Yes				
Any AE	101	0 (0.0%)	96	1 (1.0%)
Gastrointestinal disorders	101	0 (0.0%)	96	1 (1.0%)
Diarrhoea	101	0 (0.0%)	96	1 (1.0%)
Vomiting	101	0 (0.0%)	96	1 (1.0%)
Sex				
Male				
Any AE	98	0 (0.0%)	80	1 (1.3%)
Gastrointestinal disorders	98	0 (0.0%)	80	1 (1.3%)
Diarrhoea	98	0 (0.0%)	80	1 (1.3%)
Vomiting	98	0 (0.0%)	80	1 (1.3%)
Female				
Any AE	60	1 (1.7%)	63	0 (0.0%)
Investigations	60	1 (1.7%)	63	0 (0.0%)
Blood potassium increased	60	1 (1.7%)	63	0 (0.0%)
Age (years)				
<65 years				
Any AE	66	1 (1.5%)	54	1 (1.9%)
Gastrointestinal disorders	66	0 (0.0%)	54	1 (1.9%)
Diarrhoea	66	0 (0.0%)	54	1 (1.9%)
Vomiting	66	0 (0.0%)	54	1 (1.9%)
Investigations	66	1 (1.5%)	54	0 (0.0%)
Blood potassium increased	66	1 (1.5%)	54	0 (0.0%)
>=65 years				
Any AE	92	0 (0.0%)	89	0 (0.0%)
Baseline S-K				
<=5.3 mmol/L				
Any AE	95	0 (0.0%)	94	1 (1.1%)
Gastrointestinal disorders	95	0 (0.0%)	94	1 (1.1%)
Diarrhoea	95	0 (0.0%)	94	1 (1.1%)
Vomiting	95	0 (0.0%)	94	1 (1.1%)
5.4-5.5 mmol/L				
Any AE	22	0 (0.0%)	27	0 (0.0%)
>5.5 mmol/L				
Any AE	41	1 (2.4%)	22	0 (0.0%)
Investigations	41	1 (2.4%)	22	0 (0.0%)
Blood potassium increased	41	1 (2.4%)	22	0 (0.0%)
Baseline eGFR				
<15 ml/min/1.73m**2				
Any AE	15	0 (0.0%)	10	1 (10.0%)
Gastrointestinal disorders	15	0 (0.0%)	10	1 (10.0%)
Diarrhoea	15	0 (0.0%)	10	1 (10.0%)
Vomiting	15	0 (0.0%)	10	1 (10.0%)

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Table 2.2.1.7 - Study ZS-003 acute: Adverse events leading to discontinuation (DAE) by SOC and PT, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)	
Subgroup / Category / SOC / PT	**N**	**n (%)**	**N**	**n (%)**
Baseline eGFR *(contd.)*				
15-29 ml/min/1.73m**2				
Any AE	44	1 (2.3%)	42	0 (0.0%)
Investigations	44	1 (2.3%)	42	0 (0.0%)
Blood potassium increased	44	1 (2.3%)	42	0 (0.0%)
30-59 ml/min/1.73m**2				
Any AE	61	0 (0.0%)	50	0 (0.0%)
>=60 ml/min/1.73m**2				
Any AE	38	0 (0.0%)	41	0 (0.0%)
Region				
USA				
Any AE	148	1 (0.7%)	133	0 (0.0%)
Investigations	148	1 (0.7%)	133	0 (0.0%)
Blood potassium increased	148	1 (0.7%)	133	0 (0.0%)
Rest of world				
Any AE	10	0 (0.0%)	10	1 (10.0%)
Gastrointestinal disorders	10	0 (0.0%)	10	1 (10.0%)
Diarrhoea	10	0 (0.0%)	10	1 (10.0%)
Vomiting	10	0 (0.0%)	10	1 (10.0%)

t_zs003ac_ae_dae_socpt.pdf generated by zs003ac_ae_soc_pt.sas at 13:53:09 on 25 February 2021

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Table 2.2.1.8 - Study ZS-003 acute: Adverse events (AE) by SOC and PT occurring in at least 10% of subjects in any treatment group, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	158	17 (10.8%)	143	17 (11.9%)	1.12 (0.55 , 2.29)	0.7575	1.10 (0.59 , 2.08)	0.7575	1.13 (-6.05 , 8.30)	0.7579	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 2.2.1.9 - Study ZS-003 acute: Serious adverse events (SAE) by SOC and PT occurring in at least 5% of subjects in any treatment group, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	158	1 (0.6%)	143	0 (0.0%)	0.37 (0.01 , 9.05)	0.5391	0.37 (0.02 , 8.96)	0.5395	-0.63 (-1.87 , 0.60)	0.3158	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 2.2.1.10 - Study ZS-003 acute: AEs graded as severe by SOC and PT occurring in at least 5% of subjects in any treatment group, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	158	0 (0.0%)	143	1 (0.7%)	3.34 (0.13 , 82.57)	0.4617	3.31 (0.14 , 80.67)	0.4622	0.70 (-0.67 , 2.07)	0.3156	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 2.2.1.11 - Study ZS-003 acute: AEs graded as non-severe by SOC and PT occurring in at least 10% of subjects in any treatment group, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	158	17 (10.8%)	143	16 (11.2%)	1.04 (0.51 , 2.15)	0.9052	1.04 (0.55 , 1.98)	0.9052	0.43 (-6.64 , 7.50)	0.9053	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 2.2.2.1 - Study ZS-003 acute: AEs of special interest: urinary tract infection—subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	158	0 (0.0%)	143	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_zs003ac_aesi_uti_ae.pdf generated by zs003ac_ae_soc_pt.sas at 13:52:40 on 25 February 2021

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Table 2.2.2.2 - Study ZS-003 acute: AEs of special interest: urinary tract infection—subjects experiencing any serious adverse event (SAE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	158	0 (0.0%)	143	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 2.2.2.3 - Study ZS-003 acute: AEs of special interest: urinary tract infection—subjects experiencing any AE graded as severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	158	0 (0.0%)	143	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Table 2.2.2.4 - Study ZS-003 acute: AEs of special interest: urinary tract infection—subjects experiencing any AE graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=158)		10g ZS (N=143)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	158	0 (0.0%)	143	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
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Anhang 4-G5: Metaanalysen zu den Studien ZS002, ZS002J und ZS003

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Table 3.1.1.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value	Study interaction p-value
Overall	221	203						<.0001
Through 24 hours								
Time			-0.00117	0.000213	-5.50	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00261	0.000298	-8.74	<.0001		
Through 48 hours								
Time			-0.00078	0.000126	-6.15	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00278	0.000175	-15.86	<.0001		
Acute Baseline S-K value							<.0001	
<=5.3 mmol/L	127	125						
Through 24 hours								
Time			-0.00092	0.000274	-3.36	0.0009		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00225	0.000381	-5.90	<.0001		
Through 48 hours								
Time			-0.00057	0.000167	-3.43	0.0007		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00232	0.000235	-9.89	<.0001		
5.4-5.5 mmol/L	37	43						
Through 24 hours								
Time			-0.00160	0.000534	-3.00	0.0036		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00298	0.000698	-4.27	<.0001		
Through 48 hours								
Time			-0.00068	0.000266	-2.57	0.0120		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00369	0.000346	-10.68	<.0001		
>5.5 mmol/L	57	35						
Through 24 hours								
Time			-0.00158	0.000427	-3.69	0.0004		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00323	0.000670	-4.82	<.0001		
Through 48 hours								
Time			-0.00149	0.000238	-6.27	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00318	0.000367	-8.68	<.0001		
Chronic kidney disease							0.0047	
Yes	128	116						
Through 24 hours								
Time			-0.00078	0.000261	-3.00	0.0029		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00316	0.000364	-8.67	<.0001		
Through 48 hours								
Time			-0.00075	0.000159	-4.74	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00316	0.000222	-14.24	<.0001		

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time, time*treatment and study, random effects for intercept and time with an unstructured covariance matrix.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.
Study interaction p-value estimated from the above mixed effects longitudinal model with study*time*treatment as additional fixed effects.
Interaction p-values are based on analysis through 48 hours.

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Table 3.1.1.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value	Study interaction p-value
Chronic kidney disease *(contd.)*								
No	93	87						
Through 24 hours								
Time			-0.00168	0.000355	-4.72	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00189	0.000496	-3.81	0.0002		
Through 48 hours								
Time			-0.00083	0.000203	-4.08	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00226	0.000279	-8.09	<.0001		
Congestive Heart Disease							0.7550	
Yes	81	75						
Through 24 hours								
Time			-0.00141	0.000366	-3.87	0.0002		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00241	0.000505	-4.78	<.0001		
Through 48 hours								
Time			-0.00089	0.000199	-4.44	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00258	0.000276	-9.35	<.0001		
No	140	128						
Through 24 hours								
Time			-0.00104	0.000261	-3.99	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00269	0.000368	-7.31	<.0001		
Through 48 hours								
Time			-0.00071	0.000164	-4.34	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00291	0.000227	-12.84	<.0001		
Diabetes mellitus							0.4871	
Yes	131	116						
Through 24 hours								
Time			-0.00113	0.000261	-4.33	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00258	0.000371	-6.97	<.0001		
Through 48 hours								
Time			-0.00076	0.000157	-4.87	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00294	0.000216	-13.62	<.0001		
No	90	87						
Through 24 hours								
Time			-0.00125	0.000359	-3.49	0.0006		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00259	0.000493	-5.26	<.0001		
Through 48 hours								
Time			-0.00081	0.000211	-3.85	0.0002		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00254	0.000293	-8.66	<.0001		

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time, time*treatment and study, random effects for intercept and time with an unstructured covariance matrix.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.
Study interaction p-value estimated from the above mixed effects longitudinal model with study*time*treatment as additional fixed effects.
Interaction p-values are based on analysis through 48 hours.

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Table 3.1.1.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value	Study interaction p-value
RAASi Medications							0.4085	
Yes	147	142						
Through 24 hours								
Time			-0.00104	0.000263	-3.95	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00277	0.000365	-7.61	<.0001		
Through 48 hours								
Time			-0.00080	0.000154	-5.22	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00286	0.000212	-13.50	<.0001		
No	74	61						
Through 24 hours								
Time			-0.00142	0.000366	-3.88	0.0002		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00230	0.000522	-4.41	<.0001		
Through 48 hours								
Time			-0.00072	0.000222	-3.26	0.0014		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00260	0.000311	-8.36	<.0001		
Acute Baseline eGFR							<.0001	
<15	26	19						
Through 24 hours								
Time			-0.00100	0.000543	-1.84	0.0724		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00268	0.000816	-3.28	0.0013		
Through 48 hours								
Time			-0.00052	0.000311	-1.67	0.1017		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00391	0.000468	-8.34	<.0001		
15-29+	56	56						
Through 24 hours								
Time			-0.00150	0.000387	-3.88	0.0002		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00289	0.000528	-5.47	<.0001		
Through 48 hours								
Time			-0.00112	0.000238	-4.68	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00323	0.000322	-10.05	<.0001		
30-59+	100	83						
Through 24 hours								
Time			-0.00104	0.000333	-3.11	0.0022		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00281	0.000485	-5.79	<.0001		
Through 48 hours								
Time			-0.00067	0.000183	-3.66	0.0003		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00287	0.000266	-10.80	<.0001		

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time, time*treatment and study, random effects for intercept and time with an unstructured covariance matrix.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.
Study interaction p-value estimated from the above mixed effects longitudinal model with study*time*treatment as additional fixed effects.
Interaction p-values are based on analysis through 48 hours.

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Table 3.1.1.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 24 and 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Subgroup / Category / Timepoint / Statistic	n (Placebo)	n (Lokelma 10 g)	Estimate	Standard error	t value	p-value	Subgroup interaction p-value	Study interaction p-value
Acute Baseline eGFR *(contd.)*								
>=60	39	45						
Through 24 hours								
Time			-0.00127	0.000531	-2.38	0.0195		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00158	0.000692	-2.29	0.0231		
Through 48 hours								
Time			-0.00091	0.000306	-2.99	0.0037		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00121	0.000392	-3.09	0.0021		
Sex							0.1054	
Male	144	117						
Through 24 hours								
Time			-0.00164	0.000263	-6.23	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00224	0.000381	-5.88	<.0001		
Through 48 hours								
Time			-0.00097	0.000154	-6.27	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00253	0.000218	-11.58	<.0001		
Female	77	86						
Through 24 hours								
Time			-0.00036	0.000358	-1.01	0.3131		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00323	0.000482	-6.70	<.0001		
Through 48 hours								
Time			-0.00046	0.000218	-2.11	0.0367		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00316	0.000294	-10.76	<.0001		
Age							0.0078	
<65 years	76	66						
Through 24 hours								
Time			-0.00117	0.000348	-3.35	0.0010		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00245	0.000504	-4.86	<.0001		
Through 48 hours								
Time			-0.00089	0.000207	-4.33	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00207	0.000292	-7.09	<.0001		
>=65 years	145	137						
Through 24 hours								
Time			-0.00119	0.000269	-4.44	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00265	0.000371	-7.14	<.0001		
Through 48 hours								
Time			-0.00073	0.000157	-4.63	<.0001		
10g ZS time-treatment interaction (Ref: Placebo*Time)			-0.00310	0.000216	-14.36	<.0001		

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
Model includes: fixed effects for time, time*treatment and study, random effects for intercept and time with an unstructured covariance matrix.
Subgroup interaction p-values are estimated from the above mixed effects longitudinal model with subgroup and subgroup*time*treatment as additional fixed effects.
Study interaction p-value estimated from the above mixed effects longitudinal model with study*time*treatment as additional fixed effects.
Interaction p-values are based on analysis through 48 hours.

t_zsiss_sk_exp.pdf generated by zs002_zs002j_zs003ac_zsiss_sk_exp.sas at 12:51:09 on 17 February 2021

Lokelma

Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Overall																	0.0145
Baseline																	
Absolute value	221	5.33 (0.399)	5.3 (5.1, 5.6)	4.5, 6.6			203	5.27 (0.360)	5.2 (5.0, 5.5)	4.5, 6.8							
1 hour																	
Absolute value	221	5.33 (0.577)	5.3 (5.0, 5.8)	3.8, 7.1			203	5.11 (0.479)	5.1 (4.8, 5.4)	3.9, 6.7							
Change from baseline	221	0.00 (0.391)	0.0 (-0.2, 0.3)	-1.7, 1.2	-0.01 (0.028)	(-0.07, 0.04)	203	-0.16 (0.383)	-0.1 (-0.4, 0.1)	-1.3, 1.5	-0.18 (0.029)	(-0.24, -0.12)	-0.17 (-0.24, -0.09)	<.0001	-0.41 (-0.60, -0.22)		
Percent change from baseline	221	0.03 (7.312)	0.0 (-4.0, 5.0)	-30.9, 21.8			203	-2.89 (7.269)	-2.2 (-7.5, 1.8)	-24.1, 32.2							
2 hours																	
Absolute value	220	5.28 (0.549)	5.2 (4.9, 5.6)	3.8, 6.7			202	5.04 (0.452)	5.0 (4.7, 5.3)	4.0, 6.7							
Change from baseline	220	-0.05 (0.412)	-0.0 (-0.3, 0.2)	-1.6, 1.0	-0.07 (0.028)	(-0.12, -0.01)	202	-0.23 (0.385)	-0.2 (-0.5, 0.0)	-1.4, 0.9	-0.26 (0.029)	(-0.31, -0.20)	-0.19 (-0.26, -0.12)	<.0001	-0.46 (-0.65, -0.27)		
Percent change from baseline	220	-0.91 (7.652)	-0.7 (-5.8, 4.0)	-27.3, 22.2			202	-4.34 (7.135)	-3.9 (-8.7, 0.0)	-23.4, 17.3							
4 hours																	
Absolute value	220	5.08 (0.519)	5.0 (4.8, 5.4)	3.7, 6.3			203	4.88 (0.471)	4.9 (4.5, 5.2)	3.8, 6.5							
Change from baseline	220	-0.24 (0.437)	-0.2 (-0.5, 0.0)	-1.8, 1.1	-0.26 (0.030)	(-0.32, -0.20)	203	-0.38 (0.432)	-0.4 (-0.7, -0.1)	-2.2, 0.7	-0.41 (0.031)	(-0.47, -0.35)	-0.15 (-0.23, -0.07)	0.0003	-0.33 (-0.52, -0.13)		
Percent change from baseline	220	-4.45 (8.184)	-4.2 (-9.5, 0.0)	-32.7, 21.2			203	-7.16 (8.033)	-7.4 (-12.5, -1.8)	-36.7, 14.3							
24 hours																	
Absolute value	219	5.13 (0.482)	5.1 (4.8, 5.4)	4.0, 6.7			200	4.74 (0.402)	4.7 (4.5, 5.0)	3.9, 6.2							
Change from baseline	219	-0.19 (0.369)	-0.2 (-0.4, 0.0)	-1.4, 0.9	-0.21 (0.027)	(-0.26, -0.15)	200	-0.53 (0.394)	-0.5 (-0.8, -0.3)	-1.9, 0.6	-0.55 (0.028)	(-0.61, -0.50)	-0.35 (-0.42, -0.28)	<.0001	-0.90 (-1.10, -0.70)		
Percent change from baseline	219	-3.44 (6.850)	-3.8 (-7.7, 0.0)	-25.5, 17.0			200	-9.88 (7.170)	-10.3 (-14.8, -5.7)	-30.4, 12.2							
28 hours																	
Absolute value	217	5.09 (0.499)	5.1 (4.7, 5.4)	3.8, 6.4			200	4.57 (0.433)	4.6 (4.3, 4.8)	3.7, 6.7							
Change from baseline	217	-0.23 (0.439)	-0.2 (-0.5, 0.1)	-1.4, 1.0	-0.25 (0.031)	(-0.31, -0.19)	200	-0.70 (0.468)	-0.7 (-1.0, -0.4)	-2.0, 0.8	-0.72 (0.032)	(-0.78, -0.66)	-0.47 (-0.55, -0.39)	<.0001	-1.02 (-1.23, -0.82)		
Percent change from baseline	217	-4.23 (8.193)	-4.0 (-9.8, 1.7)	-22.6, 21.3			200	-12.99 (8.395)	-13.2 (-19.6, -7.3)	-33.9, 16.2							
48 hours																	
Absolute value	218	5.08 (0.487)	5.1 (4.7, 5.4)	3.9, 6.4			200	4.44 (0.480)	4.4 (4.1, 4.8)	2.9, 6.2							
Change from baseline	218	-0.24 (0.405)	-0.2 (-0.6, 0.0)	-1.4, 0.8	-0.26 (0.032)	(-0.32, -0.20)	200	-0.83 (0.538)	-0.8 (-1.2, -0.5)	-2.5, 1.0	-0.85 (0.033)	(-0.92, -0.79)	-0.59 (-0.68, -0.51)	<.0001	-1.24 (-1.45, -1.03)		
Percent change from baseline	218	-4.44 (7.580)	-4.7 (-10.2, 1.0)	-24.1, 15.6			200	-15.48 (9.724)	-15.7 (-22.2, -9.4)	-44.0, 19.2							

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

t_zsiss_sk_overtime.pdf generated by zsiss_overtime.sas at 15:17:00 on 19 February 2021

04/03/2021

Lokelma

Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Acute Baseline S-K value																0.0050	
<=5.3 mmol/L																	
Baseline																	
Absolute value	127	5.06 (0.203)	5.1 (4.9, 5.2)	4.5, 5.3			125	5.05 (0.186)	5.1 (4.9, 5.2)	4.5, 5.3							
1 hour																	
Absolute value	127	5.05 (0.420)	5.0 (4.8, 5.3)	3.8, 6.3			125	4.95 (0.403)	4.9 (4.7, 5.2)	3.9, 6.3							
Change from baseline	127	-0.00 (0.359)	0.0 (-0.2, 0.2)	-1.3, 1.0	-0.05 (0.037)	(-0.13, 0.02)	125	-0.10 (0.372)	-0.1 (-0.3, 0.1)	-1.0, 1.5	-0.14 (0.037)	(-0.21, -0.07)	-0.09 (-0.18, 0.00)	0.0566	-0.26 (-0.51, -0.02)		
Percent change from baseline	127	-0.09 (7.043)	0.0 (-4.0, 3.9)	-25.5, 19.2			125	-1.98 (7.406)	-2.0 (-6.0, 2.0)	-20.0, 32.2							
2 hours																	
Absolute value	127	5.04 (0.411)	5.0 (4.8, 5.3)	3.8, 6.3			124	4.88 (0.380)	4.9 (4.6, 5.2)	4.0, 6.1							
Change from baseline	127	-0.02 (0.362)	-0.0 (-0.3, 0.2)	-0.9, 1.0	-0.07 (0.036)	(-0.14, 0.00)	124	-0.17 (0.358)	-0.2 (-0.3, 0.1)	-1.0, 0.9	-0.21 (0.036)	(-0.29, -0.14)	-0.14 (-0.23, -0.06)	0.0013	-0.43 (-0.68, -0.18)		
Percent change from baseline	127	-0.40 (7.154)	-0.4 (-5.7, 4.2)	-19.1, 22.2			124	-3.41 (7.036)	-3.8 (-6.6, 1.9)	-19.2, 17.3							
4 hours																	
Absolute value	127	4.88 (0.420)	4.9 (4.6, 5.1)	3.9, 6.1			125	4.77 (0.426)	4.8 (4.5, 5.1)	3.8, 5.9							
Change from baseline	127	-0.17 (0.401)	-0.2 (-0.4, 0.0)	-0.9, 1.1	-0.22 (0.040)	(-0.30, -0.15)	125	-0.28 (0.404)	-0.2 (-0.5, 0.0)	-1.2, 0.7	-0.32 (0.039)	(-0.40, -0.24)	-0.10 (-0.20, -0.00)	0.0491	-0.27 (-0.51, -0.02)		
Percent change from baseline	127	-3.38 (8.010)	-3.9 (-8.0, 0.0)	-17.6, 21.2			125	-5.53 (7.962)	-4.1 (-10.7, 0.0)	-24.0, 14.3							
24 hours																	
Absolute value	127	4.93 (0.375)	4.9 (4.7, 5.1)	4.0, 6.0			123	4.63 (0.362)	4.6 (4.4, 4.9)	3.9, 5.5							
Change from baseline	127	-0.12 (0.326)	-0.1 (-0.3, 0.1)	-0.9, 0.8	-0.17 (0.036)	(-0.24, -0.10)	123	-0.41 (0.361)	-0.4 (-0.6, -0.2)	-1.3, 0.6	-0.46 (0.035)	(-0.53, -0.39)	-0.28 (-0.37, -0.20)	<.0001	-0.85 (-1.11, -0.59)		
Percent change from baseline	127	-2.42 (6.470)	-2.5 (-6.1, 1.3)	-18.4, 17.0			123	-8.16 (7.090)	-7.8 (-12.9, -3.8)	-25.0, 12.2							
28 hours																	
Absolute value	126	4.92 (0.467)	4.9 (4.6, 5.2)	3.8, 6.1			123	4.50 (0.375)	4.5 (4.2, 4.7)	3.7, 5.5							
Change from baseline	126	-0.13 (0.424)	-0.1 (-0.4, 0.1)	-1.1, 1.0	-0.18 (0.040)	(-0.26, -0.10)	123	-0.54 (0.397)	-0.5 (-0.8, -0.3)	-1.6, 0.8	-0.58 (0.040)	(-0.66, -0.51)	-0.40 (-0.50, -0.30)	<.0001	-1.00 (-1.26, -0.73)		
Percent change from baseline	126	-2.60 (8.389)	-2.0 (-9.2, 2.0)	-21.6, 21.3			123	-10.64 (7.751)	-10.4 (-15.7, -6.0)	-29.5, 16.2							
48 hours																	
Absolute value	127	4.91 (0.456)	4.9 (4.6, 5.2)	3.9, 6.1			123	4.41 (0.509)	4.3 (4.1, 4.8)	2.9, 6.2							
Change from baseline	127	-0.15 (0.403)	-0.2 (-0.5, 0.1)	-1.0, 0.8	-0.20 (0.044)	(-0.29, -0.11)	123	-0.63 (0.502)	-0.7 (-1.0, -0.3)	-2.3, 1.0	-0.67 (0.044)	(-0.76, -0.59)	-0.47 (-0.59, -0.36)	<.0001	-1.06 (-1.33, -0.80)		
Percent change from baseline	127	-2.98 (7.946)	-3.8 (-9.6, 2.0)	-19.5, 15.6			123	-12.49 (9.823)	-12.6 (-18.9, -6.0)	-44.0, 19.2							
5.4-5.5 mmol/L																	
Baseline																	
Absolute value	37	5.46 (0.051)	5.5 (5.4, 5.5)	5.4, 5.5			43	5.43 (0.050)	5.4 (5.4, 5.5)	5.4, 5.5							
1 hour																	
Absolute value	37	5.36 (0.508)	5.3 (5.1, 5.6)	3.8, 6.7			43	5.17 (0.393)	5.2 (4.8, 5.4)	4.1, 6.3							
Change from baseline	37	-0.10 (0.504)	-0.1 (-0.4, 0.1)	-1.7, 1.2	-0.08 (0.083)	(-0.24, 0.09)	43	-0.26 (0.380)	-0.3 (-0.6, 0.0)	-1.3, 0.9	-0.25 (0.077)	(-0.41, -0.10)	-0.17 (-0.38, 0.03)	0.0911	-0.37 (-0.81, 0.07)		
Percent change from baseline	37	-1.82 (9.185)	-1.9 (-7.3, 2.3)	-30.9, 21.8			43	-4.86 (7.000)	-5.5 (-10.7, 0.0)	-24.1, 16.7							
2 hours																	
Absolute value	37	5.31 (0.441)	5.3 (5.0, 5.6)	4.0, 6.3			43	5.16 (0.388)	5.2 (4.9, 5.4)	4.3, 6.0							
Change from baseline	37	-0.16 (0.448)	-0.2 (-0.4, 0.1)	-1.5, 0.8	-0.14 (0.078)	(-0.29, 0.02)	43	-0.27 (0.371)	-0.2 (-0.5, -0.1)	-1.1, 0.6	-0.26 (0.072)	(-0.40, -0.12)	-0.13 (-0.31, 0.06)	0.1805	-0.29 (-0.73, 0.16)		
Percent change from baseline	37	-2.84 (8.173)	-3.6 (-7.4, 1.9)	-27.3, 14.5			43	-5.04 (6.848)	-3.7 (-8.8, -1.8)	-20.4, 11.1							

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

t_zsiss_sk_overtime.pdf generated by zsiss_overtime.sas at 15:17:00 on 19 February 2021

04/03/2021

Lokelma

Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Acute Baseline S-K value *(contd.)*																	
5.4-5.5 mmol/L *(contd.)*																	
4 hours																	
Absolute value	37	5.10 (0.484)	5.2 (4.9, 5.4)	3.7, 6.2			43	4.89 (0.411)	4.9 (4.6, 5.3)	4.0, 5.7							
Change from baseline	37	-0.36 (0.492)	-0.3 (-0.6, -0.1)	-1.8, 0.7	-0.34 (0.084)	(-0.51, -0.17)	43	-0.54 (0.397)	-0.6 (-0.8, -0.2)	-1.5, 0.2	-0.53 (0.078)	(-0.69, -0.38)	-0.19 (-0.40, 0.01)	0.0645	-0.41 (-0.86, 0.03)		
Percent change from baseline	37	-6.55 (8.970)	-6.2 (-10.9, -1.5)	-32.7, 12.7			43	-10.00 (7.317)	-10.9 (-14.8, -3.2)	-27.3, 3.7							
24 hours																	
Absolute value	37	5.13 (0.360)	5.1 (4.9, 5.3)	4.1, 5.9			42	4.77 (0.318)	4.7 (4.6, 5.0)	4.2, 5.5							
Change from baseline	37	-0.33 (0.371)	-0.3 (-0.6, -0.1)	-1.4, 0.4	-0.31 (0.070)	(-0.45, -0.18)	42	-0.66 (0.312)	-0.7 (-0.9, -0.4)	-1.3, 0.1	-0.65 (0.065)	(-0.78, -0.53)	-0.34 (-0.50, -0.18)	<.0001	-0.97 (-1.44, -0.50)		
Percent change from baseline	37	-6.11 (6.764)	-6.2 (-10.5, -1.9)	-25.5, 7.6			42	-12.24 (5.749)	-13.0 (-16.7, -7.4)	-23.6, 1.9							
28 hours																	
Absolute value	37	5.17 (0.399)	5.1 (4.9, 5.5)	4.4, 5.9			42	4.53 (0.392)	4.5 (4.3, 4.7)	3.7, 5.5							
Change from baseline	37	-0.29 (0.409)	-0.3 (-0.6, 0.1)	-1.1, 0.5	-0.27 (0.077)	(-0.42, -0.12)	42	-0.90 (0.386)	-0.9 (-1.2, -0.7)	-1.8, 0.0	-0.89 (0.071)	(-1.03, -0.75)	-0.62 (-0.80, -0.44)	<.0001	-1.54 (-2.04, -1.03)		
Percent change from baseline	37	-5.32 (7.484)	-6.2 (-10.9, 1.8)	-20.0, 9.8			42	-16.59 (7.083)	-17.1 (-21.8, -12.6)	-32.7, 0.0							
48 hours																	
Absolute value	37	5.14 (0.327)	5.2 (4.9, 5.4)	4.5, 5.7			42	4.36 (0.410)	4.3 (4.1, 4.8)	3.5, 5.1							
Change from baseline	37	-0.32 (0.330)	-0.2 (-0.5, -0.1)	-1.0, 0.3	-0.30 (0.073)	(-0.45, -0.16)	42	-1.07 (0.398)	-1.2 (-1.3, -0.7)	-1.9, -0.3	-1.06 (0.068)	(-1.20, -0.93)	-0.76 (-0.94, -0.59)	<.0001	-2.05 (-2.59, -1.50)		
Percent change from baseline	37	-5.87 (6.037)	-3.7 (-9.3, -1.8)	-18.2, 5.6			42	-19.80 (7.362)	-21.8 (-24.1, -11.9)	-34.6, -5.6							
>5.5 mmol/L																	
Baseline																	
Absolute value	57	5.86 (0.260)	5.8 (5.7, 5.9)	5.6, 6.6			35	5.86 (0.264)	5.8 (5.6, 6.0)	5.6, 6.8							
1 hour																	
Absolute value	57	5.94 (0.432)	5.9 (5.7, 6.2)	5.0, 7.1			35	5.64 (0.436)	5.6 (5.3, 5.8)	5.0, 6.7							
Change from baseline	57	0.09 (0.368)	0.1 (-0.2, 0.3)	-0.7, 1.1	0.06 (0.063)	(-0.06, 0.19)	35	-0.22 (0.398)	-0.2 (-0.5, -0.1)	-1.0, 0.9	-0.23 (0.072)	(-0.37, -0.09)	-0.29 (-0.45, -0.14)	0.0004	-0.81 (-1.24, -0.37)		
Percent change from baseline	57	1.51 (6.300)	1.7 (-3.4, 5.2)	-12.3, 17.4			35	-3.70 (6.682)	-3.4 (-8.5, -1.5)	-15.0, 15.5							
2 hours																	
Absolute value	56	5.79 (0.530)	5.9 (5.4, 6.2)	4.3, 6.7			35	5.46 (0.450)	5.4 (5.2, 5.7)	4.5, 6.7							
Change from baseline	56	-0.05 (0.485)	0.0 (-0.3, 0.3)	-1.6, 0.8	-0.08 (0.072)	(-0.22, 0.06)	35	-0.40 (0.446)	-0.4 (-0.7, -0.1)	-1.4, 0.6	-0.41 (0.085)	(-0.58, -0.24)	-0.33 (-0.52, -0.14)	0.0010	-0.75 (-1.18, -0.31)		
Percent change from baseline	56	-0.82 (8.310)	0.0 (-6.1, 5.3)	-27.1, 14.3			35	-6.74 (7.365)	-6.9 (-11.9, -1.7)	-23.4, 9.8							
4 hours																	
Absolute value	56	5.52 (0.477)	5.5 (5.2, 6.0)	4.6, 6.3			35	5.30 (0.469)	5.3 (5.0, 5.5)	3.8, 6.5							
Change from baseline	56	-0.32 (0.453)	-0.3 (-0.6, 0.0)	-1.3, 0.7	-0.35 (0.072)	(-0.50, -0.21)	35	-0.56 (0.468)	-0.5 (-0.8, -0.3)	-2.2, 0.2	-0.57 (0.085)	(-0.74, -0.40)	-0.22 (-0.41, -0.03)	0.0266	-0.52 (-0.95, -0.09)		
Percent change from baseline	56	-5.50 (7.764)	-5.6 (-10.4, 0.0)	-22.0, 12.5			35	-9.52 (7.767)	-8.9 (-13.8, -5.1)	-36.7, 3.6							
24 hours																	
Absolute value	55	5.60 (0.458)	5.7 (5.3, 5.9)	4.6, 6.7			35	5.09 (0.431)	5.1 (4.8, 5.3)	3.9, 6.2							
Change from baseline	55	-0.24 (0.428)	-0.3 (-0.5, 0.1)	-1.3, 0.9	-0.27 (0.070)	(-0.41, -0.13)	35	-0.77 (0.437)	-0.8 (-1.0, -0.5)	-1.9, 0.4	-0.78 (0.081)	(-0.94, -0.62)	-0.51 (-0.70, -0.33)	<.0001	-1.24 (-1.70, -0.78)		
Percent change from baseline	55	-4.00 (7.322)	-5.3 (-8.6, 1.7)	-21.6, 15.5			35	-13.08 (7.242)	-12.9 (-17.2, -8.9)	-30.4, 7.1							
28 hours																	
Absolute value	54	5.41 (0.469)	5.4 (5.1, 5.7)	4.6, 6.4			35	4.86 (0.547)	4.8 (4.6, 5.1)	3.9, 6.7							
Change from baseline	54	-0.43 (0.427)	-0.5 (-0.7, -0.1)	-1.4, 0.5	-0.45 (0.074)	(-0.60, -0.30)	35	-1.00 (0.550)	-1.0 (-1.2, -0.7)	-2.0, 0.5	-1.01 (0.087)	(-1.18, -0.83)	-0.56 (-0.76, -0.36)	<.0001	-1.19 (-1.65, -0.73)		

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Lokelma

Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Acute Baseline S-K value *(contd.)*																	
>5.5 mmol/L *(contd.)*																	
28 hours *(contd.)*																	
Percent change from baseline	54	-7.30 (7.267)	-7.7 (-12.3, -1.8)	-22.6, 8.5			35	-16.94 (9.187)	-18.2 (-21.4, -12.1)	-33.9, 8.1							
48 hours																	
Absolute value	54	5.43 (0.451)	5.4 (5.1, 5.8)	4.4, 6.4			35	4.63 (0.408)	4.6 (4.3, 4.9)	3.7, 5.5							
Change from baseline	54	-0.40 (0.403)	-0.5 (-0.7, -0.1)	-1.4, 0.6	-0.43 (0.070)	(-0.57, -0.29)	35	-1.22 (0.475)	-1.3 (-1.6, -1.0)	-2.5, -0.3	-1.24 (0.080)	(-1.39, -1.08)	-0.81 (-0.99, -0.63)	<.0001	-1.90 (-2.41, -1.39)		
Percent change from baseline	54	-6.89 (6.908)	-8.6 (-11.1, -1.8)	-24.1, 10.3			35	-20.78 (7.587)	-21.3 (-26.3, -17.2)	-37.0, -5.4							

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Chronic kidney disease																0.0006	
Yes																	
Baseline																	
Absolute value	128	5.39 (0.412)	5.4 (5.1, 5.6)	4.5, 6.6			116	5.32 (0.345)	5.3 (5.1, 5.5)	4.6, 6.5							
1 hour																	
Absolute value	128	5.40 (0.559)	5.3 (5.0, 5.9)	3.8, 6.6			116	5.15 (0.459)	5.2 (4.8, 5.4)	4.1, 6.7							
Change from baseline	128	0.01 (0.352)	0.0 (-0.2, 0.3)	-1.3, 0.9	0.00 (0.038)	(-0.07, 0.08)	116	-0.17 (0.371)	-0.1 (-0.4, 0.1)	-1.3, 0.9	-0.19 (0.039)	(-0.26, -0.11)	-0.19 (-0.28, -0.10)	<.0001	-0.50 (-0.76, -0.25)		
Percent change from baseline	128	0.21 (6.582)	0.0 (-3.8, 5.1)	-25.5, 17.3			116	-3.09 (6.925)	-2.3 (-7.8, 1.1)	-24.1, 16.7							
2 hours																	
Absolute value	127	5.39 (0.542)	5.3 (5.0, 5.7)	3.8, 6.7			115	5.06 (0.436)	5.1 (4.8, 5.3)	4.2, 6.4							
Change from baseline	127	0.01 (0.380)	0.0 (-0.3, 0.3)	-0.9, 1.0	-0.00 (0.039)	(-0.08, 0.07)	115	-0.26 (0.391)	-0.2 (-0.5, 0.0)	-1.4, 0.9	-0.28 (0.040)	(-0.36, -0.20)	-0.28 (-0.37, -0.18)	<.0001	-0.70 (-0.96, -0.44)		
Percent change from baseline	127	0.18 (7.094)	0.0 (-4.3, 5.4)	-19.1, 22.2			115	-4.81 (7.226)	-4.2 (-8.9, 0.0)	-23.4, 17.3							
4 hours																	
Absolute value	127	5.17 (0.537)	5.1 (4.8, 5.5)	3.9, 6.3			116	4.89 (0.457)	4.9 (4.6, 5.2)	3.8, 6.5							
Change from baseline	127	-0.21 (0.425)	-0.2 (-0.5, 0.0)	-1.2, 0.9	-0.22 (0.043)	(-0.31, -0.14)	116	-0.43 (0.437)	-0.4 (-0.7, -0.1)	-2.2, 0.3	-0.45 (0.044)	(-0.54, -0.37)	-0.23 (-0.34, -0.12)	<.0001	-0.52 (-0.78, -0.26)		
Percent change from baseline	127	-3.82 (7.992)	-4.2 (-9.4, 0.0)	-20.7, 20.0			116	-8.00 (7.920)	-7.5 (-12.6, -1.9)	-36.7, 5.9							
24 hours																	
Absolute value	127	5.25 (0.495)	5.2 (4.9, 5.6)	4.1, 6.7			113	4.75 (0.348)	4.8 (4.5, 5.0)	3.9, 5.7							
Change from baseline	127	-0.13 (0.356)	-0.2 (-0.4, 0.1)	-0.9, 0.9	-0.15 (0.037)	(-0.22, -0.07)	113	-0.57 (0.353)	-0.5 (-0.8, -0.3)	-1.7, 0.4	-0.59 (0.038)	(-0.66, -0.52)	-0.44 (-0.53, -0.36)	<.0001	-1.24 (-1.51, -0.96)		
Percent change from baseline	127	-2.43 (6.587)	-3.5 (-7.1, 1.7)	-15.9, 17.0			113	-10.58 (6.367)	-10.2 (-14.8, -6.2)	-30.4, 7.9							
28 hours																	
Absolute value	126	5.12 (0.504)	5.1 (4.7, 5.5)	4.0, 6.3			113	4.56 (0.456)	4.5 (4.3, 4.8)	3.7, 6.7							
Change from baseline	126	-0.25 (0.428)	-0.2 (-0.5, 0.1)	-1.2, 0.9	-0.26 (0.043)	(-0.35, -0.18)	113	-0.76 (0.485)	-0.7 (-1.1, -0.4)	-2.0, 0.5	-0.78 (0.045)	(-0.87, -0.69)	-0.52 (-0.62, -0.41)	<.0001	-1.12 (-1.39, -0.84)		
Percent change from baseline	126	-4.59 (7.862)	-4.0 (-10.1, 1.7)	-21.6, 17.6			113	-14.11 (8.635)	-13.8 (-20.4, -7.4)	-33.9, 8.1							
48 hours																	
Absolute value	126	5.15 (0.473)	5.2 (4.8, 5.4)	4.1, 6.4			113	4.39 (0.475)	4.3 (4.1, 4.7)	2.9, 6.2							
Change from baseline	126	-0.22 (0.372)	-0.2 (-0.5, 0.0)	-1.0, 0.7	-0.23 (0.043)	(-0.32, -0.15)	113	-0.93 (0.526)	-1.0 (-1.3, -0.6)	-2.3, 1.0	-0.95 (0.045)	(-1.04, -0.86)	-0.72 (-0.82, -0.61)	<.0001	-1.57 (-1.86, -1.28)		
Percent change from baseline	126	-4.01 (6.914)	-3.9 (-9.3, 0.9)	-18.2, 15.6			113	-17.26 (9.518)	-18.2 (-23.7, -11.1)	-44.0, 19.2							
No																	
Baseline																	
Absolute value	93	5.25 (0.366)	5.2 (5.0, 5.5)	4.6, 6.3			87	5.20 (0.370)	5.1 (5.0, 5.4)	4.5, 6.8							
1 hour																	
Absolute value	93	5.24 (0.591)	5.2 (4.8, 5.5)	3.8, 7.1			87	5.06 (0.502)	5.0 (4.7, 5.4)	3.9, 6.6							
Change from baseline	93	-0.01 (0.441)	-0.1 (-0.2, 0.2)	-1.7, 1.2	-0.03 (0.049)	(-0.13, 0.07)	87	-0.14 (0.401)	-0.1 (-0.4, 0.1)	-1.0, 1.5	-0.16 (0.050)	(-0.26, -0.07)	-0.13 (-0.26, -0.01)	0.0377	-0.31 (-0.60, -0.01)		
Percent change from baseline	93	-0.22 (8.243)	-1.8 (-4.1, 4.0)	-30.9, 21.8			87	-2.61 (7.735)	-2.0 (-7.4, 1.9)	-20.0, 32.2							
2 hours																	
Absolute value	93	5.12 (0.524)	5.0 (4.7, 5.4)	4.0, 6.7			87	5.00 (0.473)	5.0 (4.7, 5.4)	4.0, 6.7							
Change from baseline	93	-0.13 (0.442)	-0.1 (-0.4, 0.2)	-1.6, 1.0	-0.15 (0.047)	(-0.25, -0.06)	87	-0.20 (0.375)	-0.2 (-0.4, 0.0)	-1.4, 0.7	-0.22 (0.047)	(-0.32, -0.13)	-0.07 (-0.19, 0.05)	0.2476	-0.16 (-0.45, 0.13)		
Percent change from baseline	93	-2.41 (8.158)	-1.9 (-7.3, 3.2)	-27.3, 18.9			87	-3.71 (7.006)	-3.0 (-7.8, 1.0)	-20.9, 14.3							

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
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Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Chronic kidney disease *(contd.)*																	
No *(contd.)*																	
4 hours																	
Absolute value	93	4.96 (0.469)	4.9 (4.7, 5.2)	3.7, 6.2			87	4.88 (0.490)	4.8 (4.5, 5.2)	3.8, 6.1							
Change from baseline	93	-0.29 (0.451)	-0.2 (-0.6, 0.0)	-1.8, 1.1	-0.31 (0.048)	(-0.40, -0.21)	87	-0.32 (0.419)	-0.4 (-0.6, 0.0)	-1.2, 0.7	-0.35 (0.049)	(-0.44, -0.25)	-0.04 (-0.16, 0.09)	0.5655	-0.07 (-0.36, 0.22)		
Percent change from baseline	93	-5.31 (8.406)	-4.1 (-10.9, 0.0)	-32.7, 21.2			87	-6.05 (8.091)	-6.4 (-12.1, 0.0)	-24.0, 14.3							
24 hours																	
Absolute value	92	4.98 (0.420)	4.9 (4.7, 5.2)	4.0, 6.0			87	4.72 (0.465)	4.7 (4.4, 5.0)	3.9, 6.2							
Change from baseline	92	-0.26 (0.376)	-0.2 (-0.5, -0.0)	-1.4, 0.5	-0.28 (0.046)	(-0.37, -0.19)	87	-0.47 (0.436)	-0.5 (-0.8, -0.2)	-1.9, 0.6	-0.50 (0.046)	(-0.59, -0.41)	-0.22 (-0.33, -0.10)	0.0003	-0.52 (-0.82, -0.23)		
Percent change from baseline	92	-4.83 (6.998)	-4.3 (-9.3, -0.3)	-25.5, 9.6			87	-8.97 (8.042)	-10.4 (-14.5, -2.9)	-28.2, 12.2							
28 hours																	
Absolute value	91	5.04 (0.489)	5.0 (4.7, 5.4)	3.8, 6.4			87	4.59 (0.402)	4.6 (4.3, 4.8)	3.8, 6.0							
Change from baseline	91	-0.20 (0.455)	-0.2 (-0.5, 0.1)	-1.4, 1.0	-0.22 (0.048)	(-0.32, -0.13)	87	-0.61 (0.432)	-0.6 (-0.9, -0.3)	-1.8, 0.8	-0.64 (0.048)	(-0.73, -0.54)	-0.41 (-0.53, -0.29)	<.0001	-0.92 (-1.23, -0.61)		
Percent change from baseline	91	-3.74 (8.652)	-3.9 (-9.6, 1.8)	-22.6, 21.3			87	-11.54 (7.888)	-11.8 (-16.4, -6.5)	-26.7, 16.2							
48 hours																	
Absolute value	92	4.97 (0.488)	5.0 (4.6, 5.3)	3.9, 6.2			87	4.50 (0.482)	4.4 (4.2, 4.9)	3.3, 5.9							
Change from baseline	92	-0.27 (0.447)	-0.3 (-0.6, 0.1)	-1.4, 0.8	-0.29 (0.053)	(-0.40, -0.19)	87	-0.70 (0.527)	-0.7 (-1.1, -0.4)	-2.5, 0.6	-0.72 (0.053)	(-0.83, -0.62)	-0.43 (-0.57, -0.29)	<.0001	-0.87 (-1.18, -0.57)		
Percent change from baseline	92	-5.03 (8.411)	-5.6 (-11.3, 1.6)	-24.1, 15.1			87	-13.16 (9.551)	-14.0 (-20.0, -7.1)	-37.0, 11.3							

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	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Congestive Heart Disease																0.3165	
Yes																	
Baseline																	
Absolute value	81	5.30 (0.409)	5.2 (5.0, 5.5)	4.6, 6.4			75	5.27 (0.372)	5.2 (5.0, 5.5)	4.6, 6.5							
1 hour																	
Absolute value	81	5.36 (0.586)	5.3 (4.9, 5.8)	4.1, 6.7			75	5.18 (0.520)	5.2 (4.8, 5.5)	4.1, 6.7							
Change from baseline	81	0.05 (0.393)	0.0 (-0.2, 0.3)	-0.7, 1.2	0.01 (0.055)	(-0.10, 0.12)	75	-0.09 (0.394)	-0.1 (-0.3, 0.1)	-1.3, 1.5	-0.14 (0.057)	(-0.25, -0.02)	-0.15 (-0.28, -0.02)	0.0226	-0.36 (-0.68, -0.05)		
Percent change from baseline	81	0.97 (7.472)	0.0 (-3.8, 6.0)	-13.7, 21.8			75	-1.67 (7.548)	-2.0 (-5.5, 1.9)	-24.1, 32.2							
2 hours																	
Absolute value	81	5.26 (0.582)	5.2 (4.8, 5.6)	3.8, 6.7			74	5.12 (0.448)	5.2 (4.8, 5.4)	4.2, 6.4							
Change from baseline	81	-0.04 (0.389)	0.0 (-0.2, 0.2)	-1.6, 0.8	-0.09 (0.053)	(-0.19, 0.02)	74	-0.16 (0.358)	-0.1 (-0.3, 0.0)	-1.1, 0.9	-0.20 (0.054)	(-0.31, -0.10)	-0.12 (-0.24, 0.00)	0.0521	-0.30 (-0.62, 0.02)		
Percent change from baseline	81	-0.88 (7.175)	0.0 (-4.2, 4.0)	-27.1, 14.5			74	-2.86 (6.701)	-2.7 (-6.5, 0.0)	-20.4, 17.3							
4 hours																	
Absolute value	81	5.09 (0.569)	5.1 (4.8, 5.4)	3.7, 6.3			75	4.93 (0.493)	4.9 (4.6, 5.3)	3.8, 6.5							
Change from baseline	81	-0.21 (0.484)	-0.2 (-0.6, 0.1)	-1.8, 1.1	-0.26 (0.061)	(-0.38, -0.14)	75	-0.34 (0.462)	-0.4 (-0.6, 0.0)	-2.2, 0.6	-0.39 (0.063)	(-0.51, -0.26)	-0.13 (-0.28, 0.01)	0.0763	-0.27 (-0.58, 0.05)		
Percent change from baseline	81	-3.94 (9.129)	-3.9 (-10.2, 1.7)	-32.7, 21.2			75	-6.33 (8.408)	-6.3 (-12.0, 0.0)	-36.7, 11.3							
24 hours																	
Absolute value	81	5.11 (0.472)	5.1 (4.8, 5.4)	4.0, 6.2			75	4.77 (0.433)	4.7 (4.5, 5.1)	3.9, 6.0							
Change from baseline	81	-0.19 (0.373)	-0.2 (-0.4, 0.0)	-1.3, 0.8	-0.23 (0.052)	(-0.33, -0.13)	75	-0.50 (0.374)	-0.4 (-0.8, -0.3)	-1.7, 0.4	-0.55 (0.053)	(-0.65, -0.44)	-0.32 (-0.43, -0.20)	<.0001	-0.83 (-1.16, -0.50)		
Percent change from baseline	81	-3.44 (6.933)	-3.6 (-7.4, 0.0)	-21.6, 17.0			75	-9.36 (6.850)	-8.3 (-14.8, -5.7)	-30.4, 7.1							
28 hours																	
Absolute value	81	5.11 (0.520)	5.1 (4.8, 5.5)	3.8, 6.4			75	4.67 (0.477)	4.6 (4.3, 5.0)	3.9, 6.7							
Change from baseline	81	-0.19 (0.363)	-0.1 (-0.5, 0.0)	-1.1, 0.6	-0.23 (0.056)	(-0.34, -0.12)	75	-0.60 (0.471)	-0.6 (-1.0, -0.2)	-1.6, 0.5	-0.65 (0.057)	(-0.76, -0.54)	-0.42 (-0.55, -0.29)	<.0001	-0.98 (-1.31, -0.65)		
Percent change from baseline	81	-3.58 (6.870)	-2.1 (-8.5, 0.0)	-21.6, 13.1			75	-11.23 (8.501)	-12.2 (-18.0, -4.1)	-28.6, 8.1							
48 hours																	
Absolute value	81	5.05 (0.508)	5.1 (4.7, 5.3)	3.9, 6.3			75	4.49 (0.451)	4.4 (4.2, 4.9)	3.4, 5.5							
Change from baseline	81	-0.26 (0.386)	-0.3 (-0.6, 0.0)	-1.0, 0.7	-0.30 (0.056)	(-0.41, -0.19)	75	-0.78 (0.460)	-0.7 (-1.1, -0.4)	-1.9, 0.2	-0.83 (0.057)	(-0.94, -0.71)	-0.53 (-0.66, -0.40)	<.0001	-1.24 (-1.58, -0.89)		
Percent change from baseline	81	-4.77 (7.301)	-5.4 (-10.2, 0.0)	-19.5, 14.0			75	-14.60 (8.263)	-14.9 (-21.0, -7.7)	-33.9, 3.9							
No																	
Baseline																	
Absolute value	140	5.35 (0.393)	5.3 (5.1, 5.6)	4.5, 6.6			128	5.27 (0.354)	5.2 (5.0, 5.4)	4.5, 6.8							
1 hour																	
Absolute value	140	5.32 (0.573)	5.2 (5.0, 5.7)	3.8, 7.1			128	5.07 (0.450)	5.0 (4.8, 5.4)	3.9, 6.6							
Change from baseline	140	-0.03 (0.389)	0.0 (-0.2, 0.2)	-1.7, 1.1	-0.02 (0.035)	(-0.09, 0.05)	128	-0.19 (0.373)	-0.2 (-0.5, 0.1)	-1.0, 0.9	-0.19 (0.037)	(-0.27, -0.12)	-0.18 (-0.27, -0.08)	0.0002	-0.44 (-0.69, -0.20)		
Percent change from baseline	140	-0.51 (7.189)	0.0 (-4.2, 3.8)	-30.9, 19.2			128	-3.60 (7.032)	-3.4 (-9.1, 1.2)	-20.0, 16.7							
2 hours																	
Absolute value	139	5.28 (0.531)	5.2 (4.9, 5.6)	4.0, 6.7			128	4.99 (0.449)	5.0 (4.7, 5.3)	4.0, 6.7							
Change from baseline	139	-0.05 (0.426)	-0.1 (-0.3, 0.2)	-1.5, 1.0	-0.05 (0.036)	(-0.12, 0.02)	128	-0.28 (0.394)	-0.3 (-0.5, 0.0)	-1.4, 0.7	-0.28 (0.038)	(-0.35, -0.21)	-0.23 (-0.33, -0.14)	<.0001	-0.55 (-0.79, -0.30)		
Percent change from baseline	139	-0.93 (7.942)	-1.8 (-6.2, 4.2)	-27.3, 22.2			128	-5.19 (7.264)	-5.6 (-10.1, 0.0)	-23.4, 14.3							

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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04/03/2021

Lokelma

Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Congestive Heart Disease *(contd.)*																	
No *(contd.)*																	
4 hours																	
Absolute value	139	5.08 (0.489)	5.0 (4.8, 5.4)	4.1, 6.3			128	4.86 (0.457)	4.8 (4.5, 5.2)	3.8, 6.1							
Change from baseline	139	-0.26 (0.408)	-0.2 (-0.5, 0.0)	-1.4, 0.9	-0.25 (0.036)	(-0.32, -0.18)	128	-0.41 (0.414)	-0.4 (-0.7, -0.1)	-1.5, 0.7	-0.41 (0.038)	(-0.48, -0.34)	-0.16 (-0.25, -0.06)	0.0015	-0.37 (-0.61, -0.12)		
Percent change from baseline	139	-4.75 (7.598)	-4.2 (-9.4, 0.0)	-25.5, 20.0			128	-7.65 (7.797)	-7.5 (-12.9, -1.9)	-27.3, 14.3							
24 hours																	
Absolute value	138	5.15 (0.489)	5.1 (4.8, 5.4)	4.0, 6.7			125	4.72 (0.383)	4.7 (4.4, 5.0)	3.9, 6.2							
Change from baseline	138	-0.19 (0.369)	-0.2 (-0.4, 0.1)	-1.4, 0.9	-0.18 (0.034)	(-0.25, -0.12)	125	-0.55 (0.406)	-0.6 (-0.8, -0.3)	-1.9, 0.6	-0.55 (0.036)	(-0.62, -0.48)	-0.37 (-0.46, -0.27)	<.0001	-0.94 (-1.19, -0.68)		
Percent change from baseline	138	-3.44 (6.827)	-3.9 (-7.7, 1.4)	-25.5, 15.5			125	-10.19 (7.365)	-11.1 (-14.8, -5.9)	-28.2, 12.2							
28 hours																	
Absolute value	136	5.07 (0.487)	5.1 (4.7, 5.4)	4.0, 6.3			125	4.51 (0.394)	4.5 (4.2, 4.8)	3.7, 5.5							
Change from baseline	136	-0.26 (0.478)	-0.3 (-0.5, 0.1)	-1.4, 1.0	-0.25 (0.039)	(-0.33, -0.17)	125	-0.75 (0.458)	-0.7 (-1.1, -0.5)	-2.0, 0.8	-0.75 (0.041)	(-0.83, -0.67)	-0.50 (-0.61, -0.40)	<.0001	-1.06 (-1.32, -0.80)		
Percent change from baseline	136	-4.62 (8.890)	-5.7 (-10.8, 1.9)	-22.6, 21.3			125	-14.04 (8.186)	-13.7 (-20.3, -9.3)	-33.9, 16.2							
48 hours																	
Absolute value	137	5.09 (0.475)	5.1 (4.7, 5.4)	4.1, 6.4			125	4.41 (0.495)	4.3 (4.1, 4.8)	2.9, 6.2							
Change from baseline	137	-0.23 (0.418)	-0.2 (-0.6, 0.1)	-1.4, 0.8	-0.23 (0.042)	(-0.31, -0.14)	125	-0.86 (0.580)	-0.9 (-1.2, -0.5)	-2.5, 1.0	-0.86 (0.044)	(-0.95, -0.77)	-0.63 (-0.75, -0.52)	<.0001	-1.25 (-1.51, -0.98)		
Percent change from baseline	137	-4.25 (7.760)	-4.5 (-10.2, 1.3)	-24.1, 15.6			125	-16.00 (10.500)	-16.3 (-23.1, -9.6)	-44.0, 19.2							

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Lokelma

Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Diabetes mellitus																0.5945	
Yes																	
Baseline																	
Absolute value	131	5.34 (0.349)	5.3 (5.1, 5.6)	4.6, 6.3			116	5.30 (0.357)	5.3 (5.1, 5.5)	4.8, 6.8							
1 hour																	
Absolute value	131	5.37 (0.539)	5.3 (5.0, 5.8)	4.4, 7.1			116	5.17 (0.462)	5.2 (4.8, 5.4)	4.1, 6.7							
Change from baseline	131	0.03 (0.356)	0.0 (-0.2, 0.3)	-0.8, 1.1	0.00 (0.035)	(-0.07, 0.07)	116	-0.13 (0.376)	-0.1 (-0.3, 0.1)	-1.3, 0.9	-0.15 (0.037)	(-0.22, -0.07)	-0.15 (-0.24, -0.06)	0.0019	-0.44 (-0.69, -0.19)		
Percent change from baseline	131	0.50 (6.614)	0.0 (-3.7, 5.1)	-13.8, 20.0			116	-2.39 (6.950)	-2.0 (-6.4, 1.9)	-24.1, 16.7							
2 hours																	
Absolute value	131	5.33 (0.527)	5.3 (4.9, 5.7)	4.3, 6.7			116	5.11 (0.447)	5.1 (4.8, 5.4)	4.2, 6.7							
Change from baseline	131	-0.01 (0.375)	0.0 (-0.2, 0.2)	-1.6, 1.0	-0.04 (0.036)	(-0.11, 0.03)	116	-0.19 (0.421)	-0.1 (-0.4, 0.1)	-1.4, 0.9	-0.21 (0.038)	(-0.28, -0.13)	-0.17 (-0.26, -0.07)	0.0006	-0.46 (-0.71, -0.21)		
Percent change from baseline	131	-0.23 (6.841)	0.0 (-4.3, 4.0)	-27.1, 18.9			116	-3.50 (7.648)	-2.9 (-7.5, 1.8)	-23.4, 17.3							
4 hours																	
Absolute value	131	5.17 (0.500)	5.1 (4.9, 5.4)	4.0, 6.3			116	4.93 (0.473)	5.0 (4.6, 5.3)	3.8, 6.1							
Change from baseline	131	-0.17 (0.421)	-0.2 (-0.5, 0.1)	-1.3, 1.1	-0.20 (0.040)	(-0.27, -0.12)	116	-0.37 (0.462)	-0.3 (-0.7, -0.1)	-2.2, 0.7	-0.38 (0.042)	(-0.47, -0.30)	-0.19 (-0.29, -0.08)	0.0006	-0.46 (-0.71, -0.21)		
Percent change from baseline	131	-3.06 (7.835)	-2.8 (-8.8, 1.7)	-22.0, 21.2			116	-6.79 (8.491)	-6.1 (-12.2, -1.4)	-36.7, 14.3							
24 hours																	
Absolute value	130	5.17 (0.470)	5.1 (4.8, 5.4)	4.0, 6.7			115	4.78 (0.384)	4.8 (4.5, 5.0)	4.0, 6.2							
Change from baseline	130	-0.16 (0.348)	-0.2 (-0.4, 0.1)	-1.1, 0.9	-0.19 (0.035)	(-0.26, -0.12)	115	-0.52 (0.390)	-0.5 (-0.8, -0.3)	-1.9, 0.6	-0.53 (0.036)	(-0.61, -0.46)	-0.35 (-0.44, -0.26)	<.0001	-0.98 (-1.25, -0.72)		
Percent change from baseline	130	-2.95 (6.422)	-3.7 (-7.4, 1.7)	-18.6, 15.5			115	-9.64 (6.952)	-9.7 (-14.8, -5.7)	-28.2, 12.2							
28 hours																	
Absolute value	129	5.12 (0.481)	5.1 (4.8, 5.5)	3.8, 6.4			115	4.57 (0.399)	4.6 (4.3, 4.8)	3.7, 6.0							
Change from baseline	129	-0.20 (0.423)	-0.1 (-0.5, 0.1)	-1.2, 1.0	-0.23 (0.039)	(-0.31, -0.15)	115	-0.73 (0.470)	-0.7 (-1.0, -0.4)	-2.0, 0.4	-0.75 (0.041)	(-0.83, -0.67)	-0.51 (-0.62, -0.41)	<.0001	-1.19 (-1.46, -0.91)		
Percent change from baseline	129	-3.73 (7.976)	-2.6 (-9.3, 1.8)	-20.7, 21.3			115	-13.56 (8.240)	-13.7 (-18.9, -7.4)	-33.9, 7.1							
48 hours																	
Absolute value	129	5.11 (0.468)	5.1 (4.8, 5.4)	4.1, 6.3			115	4.45 (0.473)	4.4 (4.1, 4.8)	2.9, 6.2							
Change from baseline	129	-0.22 (0.405)	-0.2 (-0.6, 0.0)	-1.0, 0.8	-0.25 (0.042)	(-0.33, -0.17)	115	-0.85 (0.549)	-0.8 (-1.2, -0.5)	-2.5, 1.0	-0.86 (0.044)	(-0.95, -0.78)	-0.62 (-0.73, -0.50)	<.0001	-1.32 (-1.59, -1.04)		
Percent change from baseline	129	-4.06 (7.595)	-3.8 (-10.2, 1.0)	-18.2, 15.1			115	-15.76 (9.751)	-15.7 (-22.2, -9.6)	-44.0, 19.2							
No																	
Baseline																	
Absolute value	90	5.32 (0.463)	5.2 (5.0, 5.6)	4.5, 6.6			87	5.22 (0.361)	5.2 (5.0, 5.4)	4.5, 6.5							
1 hour																	
Absolute value	90	5.29 (0.627)	5.2 (4.9, 5.8)	3.8, 6.7			87	5.03 (0.493)	5.0 (4.8, 5.3)	3.9, 6.5							
Change from baseline	90	-0.03 (0.437)	0.0 (-0.3, 0.3)	-1.7, 1.2	-0.03 (0.047)	(-0.13, 0.06)	87	-0.19 (0.392)	-0.2 (-0.4, 0.1)	-1.0, 1.5	-0.21 (0.048)	(-0.31, -0.12)	-0.18 (-0.31, -0.06)	0.0048	-0.37 (-0.67, -0.07)		
Percent change from baseline	90	-0.64 (8.215)	0.0 (-5.9, 5.0)	-30.9, 21.8			87	-3.54 (7.664)	-3.7 (-8.3, 1.4)	-20.0, 32.2							
2 hours																	
Absolute value	89	5.20 (0.576)	5.1 (4.8, 5.5)	3.8, 6.7			86	4.94 (0.443)	4.9 (4.6, 5.2)	4.0, 6.4							
Change from baseline	89	-0.11 (0.458)	-0.1 (-0.4, 0.2)	-1.5, 1.0	-0.11 (0.045)	(-0.20, -0.02)	86	-0.29 (0.324)	-0.3 (-0.5, -0.1)	-1.0, 0.6	-0.31 (0.045)	(-0.40, -0.22)	-0.20 (-0.32, -0.09)	0.0007	-0.45 (-0.75, -0.15)		
Percent change from baseline	89	-1.92 (8.654)	-2.0 (-8.3, 4.2)	-27.3, 22.2			86	-5.46 (6.247)	-5.6 (-9.4, -1.9)	-19.2, 12.0							

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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04/03/2021

Lokelma

Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Diabetes mellitus *(contd.)*																	
No *(contd.)*																	
4 hours																	
Absolute value	89	4.95 (0.521)	4.9 (4.6, 5.3)	3.7, 6.1			87	4.82 (0.462)	4.8 (4.5, 5.1)	3.8, 6.5							
Change from baseline	89	-0.35 (0.439)	-0.3 (-0.7, -0.1)	-1.8, 0.9	-0.35 (0.046)	(-0.45, -0.26)	87	-0.41 (0.391)	-0.4 (-0.6, -0.1)	-1.3, 0.5	-0.43 (0.047)	(-0.52, -0.34)	-0.07 (-0.19, 0.04)	0.2186	-0.12 (-0.42, 0.17)		
Percent change from baseline	89	-6.50 (8.297)	-6.2 (-12.2, -1.6)	-32.7, 20.0			87	-7.67 (7.397)	-8.2 (-13.0, -1.9)	-24.0, 9.4							
24 hours																	
Absolute value	89	5.08 (0.497)	5.0 (4.7, 5.4)	4.0, 6.2			85	4.68 (0.421)	4.7 (4.4, 5.0)	3.9, 5.7							
Change from baseline	89	-0.23 (0.397)	-0.2 (-0.4, 0.0)	-1.4, 0.8	-0.23 (0.044)	(-0.32, -0.14)	85	-0.54 (0.400)	-0.6 (-0.8, -0.3)	-1.7, 0.4	-0.57 (0.045)	(-0.66, -0.48)	-0.34 (-0.45, -0.22)	<.0001	-0.78 (-1.09, -0.48)		
Percent change from baseline	89	-4.14 (7.413)	-3.9 (-7.8, 0.0)	-25.5, 17.0			85	-10.19 (7.485)	-10.7 (-14.8, -5.8)	-30.4, 7.9							
28 hours																	
Absolute value	88	5.03 (0.523)	5.0 (4.6, 5.4)	4.0, 6.3			85	4.58 (0.477)	4.5 (4.3, 4.8)	3.7, 6.7							
Change from baseline	88	-0.27 (0.461)	-0.4 (-0.5, 0.0)	-1.4, 0.9	-0.27 (0.049)	(-0.37, -0.18)	85	-0.65 (0.463)	-0.6 (-1.1, -0.3)	-1.6, 0.8	-0.67 (0.050)	(-0.77, -0.58)	-0.40 (-0.53, -0.27)	<.0001	-0.81 (-1.12, -0.50)		
Percent change from baseline	88	-4.97 (8.494)	-6.3 (-10.7, 0.7)	-22.6, 17.6			85	-12.21 (8.588)	-12.2 (-20.0, -6.7)	-29.5, 16.2							
48 hours																	
Absolute value	89	5.03 (0.513)	5.1 (4.6, 5.3)	3.9, 6.4			85	4.42 (0.491)	4.3 (4.2, 4.8)	3.1, 5.9							
Change from baseline	89	-0.27 (0.407)	-0.3 (-0.6, 0.0)	-1.4, 0.7	-0.27 (0.050)	(-0.37, -0.17)	85	-0.80 (0.525)	-0.8 (-1.2, -0.4)	-2.0, 0.6	-0.83 (0.051)	(-0.93, -0.73)	-0.55 (-0.69, -0.42)	<.0001	-1.13 (-1.45, -0.81)		
Percent change from baseline	89	-4.99 (7.566)	-5.8 (-10.2, 0.9)	-24.1, 15.6			85	-15.09 (9.731)	-15.7 (-22.2, -8.7)	-39.5, 11.3							

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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04/03/2021

Lokelma

Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
RAASi Medications																0.4337	
Yes																	
Baseline																	
Absolute value	147	5.34 (0.409)	5.3 (5.0, 5.6)	4.5, 6.6			142	5.29 (0.358)	5.3 (5.0, 5.5)	4.5, 6.8							
1 hour																	
Absolute value	147	5.32 (0.569)	5.3 (4.9, 5.7)	4.1, 7.1			142	5.13 (0.482)	5.1 (4.8, 5.4)	4.0, 6.7							
Change from baseline	147	-0.02 (0.340)	0.0 (-0.2, 0.2)	-0.8, 1.1	-0.03 (0.034)	(-0.10, 0.03)	142	-0.16 (0.413)	-0.1 (-0.4, 0.1)	-1.3, 1.5	-0.18 (0.034)	(-0.24, -0.11)	-0.14 (-0.23, -0.06)	0.0015	-0.36 (-0.59, -0.12)		
Percent change from baseline	147	-0.49 (6.318)	0.0 (-4.3, 3.8)	-13.8, 17.4			142	-2.87 (7.787)	-2.4 (-7.5, 1.8)	-24.1, 32.2							
2 hours																	
Absolute value	146	5.29 (0.562)	5.2 (4.9, 5.6)	3.8, 6.7			141	5.05 (0.447)	5.0 (4.8, 5.3)	4.2, 6.7							
Change from baseline	146	-0.05 (0.399)	-0.1 (-0.3, 0.2)	-1.0, 1.0	-0.06 (0.034)	(-0.13, 0.01)	141	-0.24 (0.408)	-0.2 (-0.5, 0.0)	-1.4, 0.9	-0.26 (0.035)	(-0.33, -0.19)	-0.20 (-0.29, -0.11)	<.0001	-0.48 (-0.72, -0.25)		
Percent change from baseline	146	-0.86 (7.452)	-1.6 (-6.0, 4.1)	-19.1, 22.2			141	-4.42 (7.451)	-3.6 (-8.8, 0.0)	-23.4, 17.3							
4 hours																	
Absolute value	146	5.11 (0.541)	5.1 (4.8, 5.4)	3.7, 6.3			142	4.89 (0.482)	4.9 (4.5, 5.2)	3.8, 6.5							
Change from baseline	146	-0.23 (0.427)	-0.2 (-0.5, 0.0)	-1.8, 0.9	-0.24 (0.037)	(-0.31, -0.17)	142	-0.41 (0.438)	-0.4 (-0.7, -0.1)	-2.2, 0.7	-0.43 (0.037)	(-0.50, -0.35)	-0.19 (-0.28, -0.09)	0.0002	-0.42 (-0.65, -0.18)		
Percent change from baseline	146	-4.16 (8.043)	-3.9 (-9.1, 0.0)	-32.7, 20.0			142	-7.55 (8.088)	-7.5 (-12.7, -1.9)	-36.7, 13.7							
24 hours																	
Absolute value	145	5.15 (0.496)	5.1 (4.8, 5.4)	4.0, 6.7			139	4.75 (0.413)	4.8 (4.5, 5.0)	3.9, 6.2							
Change from baseline	145	-0.17 (0.361)	-0.2 (-0.4, 0.0)	-1.4, 0.9	-0.19 (0.033)	(-0.25, -0.12)	139	-0.54 (0.391)	-0.5 (-0.8, -0.3)	-1.9, 0.4	-0.56 (0.033)	(-0.62, -0.49)	-0.37 (-0.46, -0.28)	<.0001	-0.97 (-1.22, -0.72)		
Percent change from baseline	145	-3.21 (6.684)	-3.8 (-7.3, 0.5)	-25.5, 17.0			139	-10.03 (7.070)	-10.2 (-15.1, -5.7)	-28.2, 7.8							
28 hours																	
Absolute value	144	5.09 (0.514)	5.1 (4.7, 5.4)	3.8, 6.4			139	4.55 (0.416)	4.5 (4.2, 4.8)	3.7, 6.0							
Change from baseline	144	-0.24 (0.397)	-0.2 (-0.5, 0.0)	-1.2, 0.8	-0.25 (0.036)	(-0.32, -0.18)	139	-0.74 (0.456)	-0.8 (-1.1, -0.4)	-2.0, 0.4	-0.76 (0.036)	(-0.83, -0.69)	-0.51 (-0.60, -0.41)	<.0001	-1.17 (-1.42, -0.92)		
Percent change from baseline	144	-4.45 (7.431)	-4.0 (-9.4, 0.0)	-20.7, 16.3			139	-13.75 (8.089)	-14.3 (-20.4, -7.8)	-33.9, 7.1							
48 hours																	
Absolute value	145	5.08 (0.508)	5.1 (4.7, 5.4)	3.9, 6.4			139	4.44 (0.487)	4.3 (4.1, 4.8)	3.1, 6.2							
Change from baseline	145	-0.25 (0.416)	-0.2 (-0.6, 0.0)	-1.4, 0.7	-0.26 (0.040)	(-0.34, -0.18)	139	-0.85 (0.530)	-0.8 (-1.2, -0.5)	-2.5, 1.0	-0.87 (0.040)	(-0.95, -0.79)	-0.61 (-0.71, -0.50)	<.0001	-1.27 (-1.52, -1.01)		
Percent change from baseline	145	-4.54 (7.767)	-4.3 (-10.2, 0.9)	-24.1, 15.6			139	-15.83 (9.475)	-15.7 (-22.3, -10.0)	-39.5, 19.2							
No																	
Baseline																	
Absolute value	74	5.31 (0.379)	5.2 (5.1, 5.5)	4.7, 6.5			61	5.21 (0.362)	5.2 (5.0, 5.4)	4.5, 6.2							
1 hour																	
Absolute value	74	5.37 (0.595)	5.3 (5.0, 5.8)	3.8, 6.7			61	5.06 (0.473)	5.0 (4.7, 5.4)	3.9, 6.5							
Change from baseline	74	0.06 (0.476)	0.1 (-0.2, 0.3)	-1.7, 1.2	0.02 (0.055)	(-0.08, 0.13)	61	-0.15 (0.307)	-0.1 (-0.4, 0.1)	-1.0, 0.6	-0.19 (0.060)	(-0.31, -0.07)	-0.21 (-0.36, -0.07)	0.0041	-0.51 (-0.85, -0.17)		
Percent change from baseline	74	1.08 (8.923)	1.8 (-3.8, 6.1)	-30.9, 21.8			61	-2.93 (5.947)	-2.0 (-7.4, 1.4)	-18.1, 12.0							
2 hours																	
Absolute value	74	5.25 (0.527)	5.2 (4.9, 5.6)	4.0, 6.7			61	5.00 (0.466)	5.0 (4.7, 5.3)	4.0, 6.1							
Change from baseline	74	-0.06 (0.441)	0.0 (-0.3, 0.2)	-1.6, 1.0	-0.09 (0.052)	(-0.19, 0.01)	61	-0.22 (0.327)	-0.3 (-0.4, 0.0)	-0.9, 0.7	-0.25 (0.056)	(-0.37, -0.14)	-0.16 (-0.30, -0.03)	0.0181	-0.40 (-0.74, -0.06)		
Percent change from baseline	74	-1.02 (8.084)	0.0 (-5.7, 3.7)	-27.3, 18.9			61	-4.13 (6.398)	-5.4 (-8.0, 0.0)	-16.9, 14.3							

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
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Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
RAASi Medications *(contd.)*																	
No *(contd.)*																	
4 hours																	
Absolute value	74	5.04 (0.471)	5.0 (4.7, 5.3)	4.1, 6.1			61	4.88 (0.448)	4.8 (4.6, 5.2)	3.9, 5.9							
Change from baseline	74	-0.28 (0.456)	-0.3 (-0.6, 0.0)	-1.4, 1.1	-0.31 (0.054)	(-0.41, -0.20)	61	-0.33 (0.418)	-0.4 (-0.6, 0.0)	-1.3, 0.7	-0.37 (0.059)	(-0.49, -0.26)	-0.06 (-0.21, 0.08)	0.3759	-0.13 (-0.47, 0.21)		
Percent change from baseline	74	-5.02 (8.482)	-5.9 (-10.9, 0.0)	-25.5, 21.2			61	-6.26 (7.895)	-6.8 (-12.2, 0.0)	-23.5, 14.3							
24 hours																	
Absolute value	74	5.10 (0.454)	5.0 (4.8, 5.4)	4.0, 6.3			61	4.71 (0.377)	4.7 (4.4, 5.0)	3.9, 5.5							
Change from baseline	74	-0.21 (0.386)	-0.2 (-0.5, 0.0)	-1.1, 0.7	-0.24 (0.049)	(-0.34, -0.15)	61	-0.51 (0.401)	-0.5 (-0.8, -0.3)	-1.7, 0.6	-0.55 (0.054)	(-0.65, -0.44)	-0.30 (-0.43, -0.17)	<.0001	-0.75 (-1.10, -0.40)		
Percent change from baseline	74	-3.89 (7.191)	-4.0 (-8.8, 0.0)	-18.6, 13.7			61	-9.53 (7.441)	-10.6 (-13.2, -5.6)	-30.4, 12.2							
28 hours																	
Absolute value	73	5.09 (0.472)	5.0 (4.8, 5.4)	4.0, 6.1			61	4.62 (0.469)	4.6 (4.3, 4.9)	3.7, 6.7							
Change from baseline	73	-0.22 (0.514)	-0.2 (-0.6, 0.1)	-1.4, 1.0	-0.25 (0.058)	(-0.36, -0.13)	61	-0.60 (0.483)	-0.5 (-0.9, -0.3)	-1.6, 0.8	-0.64 (0.063)	(-0.76, -0.51)	-0.39 (-0.55, -0.23)	<.0001	-0.76 (-1.11, -0.41)		
Percent change from baseline	73	-3.81 (9.563)	-3.4 (-10.7, 2.0)	-22.6, 21.3			61	-11.26 (8.881)	-10.2 (-16.4, -6.2)	-29.5, 16.2							
48 hours																	
Absolute value	73	5.07 (0.445)	5.1 (4.7, 5.3)	4.2, 6.3			61	4.43 (0.468)	4.4 (4.2, 4.8)	2.9, 5.3							
Change from baseline	73	-0.23 (0.386)	-0.3 (-0.5, 0.0)	-1.0, 0.8	-0.26 (0.056)	(-0.37, -0.15)	61	-0.78 (0.558)	-0.8 (-1.1, -0.4)	-2.3, 0.3	-0.82 (0.061)	(-0.94, -0.70)	-0.56 (-0.71, -0.41)	<.0001	-1.16 (-1.53, -0.80)		
Percent change from baseline	73	-4.25 (7.242)	-5.5 (-10.1, 1.1)	-17.5, 15.1			61	-14.66 (10.302)	-16.3 (-20.4, -8.6)	-44.0, 5.6							

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Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
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	Placebo (N=221)						Lokelma 10g QD (N=203)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Acute Baseline eGFR																<.0001	
<15																	
Baseline																	
Absolute value	26	5.50 (0.354)	5.5 (5.3, 5.7)	4.7, 6.3			19	5.48 (0.243)	5.4 (5.3, 5.6)	5.1, 5.9							
1 hour																	
Absolute value	26	5.49 (0.488)	5.3 (5.1, 5.8)	4.9, 6.6			19	5.20 (0.330)	5.3 (5.0, 5.4)	4.5, 5.8							
Change from baseline	26	-0.02 (0.356)	-0.1 (-0.2, 0.1)	-0.5, 1.1	-0.02 (0.063)	(-0.15, 0.10)	19	-0.28 (0.308)	-0.2 (-0.5, 0.0)	-0.9, 0.1	-0.28 (0.074)	(-0.43, -0.13)	-0.26 (-0.46, -0.06)	0.0111	-0.78 (-1.39, -0.17)		
Percent change from baseline	26	-0.26 (6.369)	-1.8 (-3.8, 1.7)	-8.4, 20.0			19	-5.01 (5.572)	-3.8 (-10.3, 0.0)	-14.9, 2.0							
2 hours																	
Absolute value	26	5.46 (0.474)	5.4 (5.1, 5.8)	4.8, 6.5			19	5.08 (0.429)	5.2 (4.7, 5.3)	4.3, 5.8							
Change from baseline	26	-0.05 (0.378)	0.0 (-0.3, 0.2)	-0.7, 0.8	-0.05 (0.072)	(-0.20, 0.09)	19	-0.40 (0.422)	-0.3 (-0.7, -0.1)	-1.4, 0.2	-0.40 (0.084)	(-0.57, -0.23)	-0.35 (-0.57, -0.12)	0.0033	-0.89 (-1.51, -0.27)		
Percent change from baseline	26	-0.78 (6.723)	0.0 (-5.8, 4.3)	-11.3, 14.3			19	-7.21 (7.506)	-5.6 (-11.9, -1.7)	-23.4, 3.8							
4 hours																	
Absolute value	26	5.23 (0.452)	5.2 (4.9, 5.4)	4.4, 6.2			19	4.91 (0.394)	4.9 (4.7, 5.3)	4.2, 5.5							
Change from baseline	26	-0.27 (0.366)	-0.2 (-0.5, -0.1)	-0.8, 0.7	-0.28 (0.069)	(-0.42, -0.14)	19	-0.57 (0.353)	-0.6 (-0.9, -0.4)	-1.1, 0.0	-0.58 (0.080)	(-0.74, -0.42)	-0.30 (-0.51, -0.08)	0.0074	-0.83 (-1.45, -0.21)		
Percent change from baseline	26	-4.90 (6.568)	-4.0 (-9.6, -1.9)	-15.4, 12.7			19	-10.43 (6.441)	-10.7 (-14.9, -6.8)	-21.5, 0.0							
24 hours																	
Absolute value	26	5.30 (0.480)	5.3 (5.0, 5.6)	4.6, 6.6			18	4.84 (0.243)	4.9 (4.6, 5.0)	4.4, 5.3							
Change from baseline	26	-0.20 (0.320)	-0.2 (-0.4, 0.0)	-0.8, 0.5	-0.21 (0.063)	(-0.34, -0.08)	18	-0.65 (0.291)	-0.6 (-0.9, -0.4)	-1.1, -0.2	-0.64 (0.075)	(-0.80, -0.49)	-0.44 (-0.64, -0.24)	<.0001	-1.46 (-2.13, -0.78)		
Percent change from baseline	26	-3.64 (5.788)	-3.7 (-7.8, 0.0)	-14.3, 9.1			18	-11.71 (4.951)	-10.7 (-16.9, -7.3)	-19.3, -3.8							
28 hours																	
Absolute value	26	5.22 (0.502)	5.3 (4.8, 5.5)	4.4, 6.3			18	4.52 (0.406)	4.5 (4.1, 4.8)	3.9, 5.3							
Change from baseline	26	-0.28 (0.516)	-0.3 (-0.7, 0.0)	-1.1, 1.0	-0.29 (0.091)	(-0.48, -0.11)	18	-0.97 (0.437)	-1.1 (-1.2, -0.7)	-1.5, 0.2	-0.96 (0.109)	(-1.18, -0.74)	-0.66 (-0.95, -0.38)	<.0001	-1.41 (-2.08, -0.74)		
Percent change from baseline	26	-4.96 (9.586)	-5.6 (-13.7, 0.0)	-20.0, 21.3			18	-17.59 (7.940)	-19.5 (-22.3, -12.6)	-28.1, 3.9							
48 hours																	
Absolute value	26	5.30 (0.422)	5.4 (5.0, 5.6)	4.4, 6.1			18	4.28 (0.370)	4.3 (4.2, 4.5)	3.5, 5.0							
Change from baseline	26	-0.20 (0.327)	-0.1 (-0.5, 0.0)	-0.7, 0.4	-0.21 (0.066)	(-0.35, -0.08)	18	-1.20 (0.381)	-1.2 (-1.5, -1.0)	-1.9, -0.3	-1.20 (0.079)	(-1.36, -1.04)	-0.99 (-1.19, -0.78)	<.0001	-2.86 (-3.70, -2.01)		
Percent change from baseline	26	-3.63 (6.102)	-2.7 (-7.9, 0.8)	-13.7, 8.5			18	-21.88 (6.762)	-21.8 (-26.3, -19.2)	-34.6, -5.7							
15-29+																	
Baseline																	
Absolute value	56	5.48 (0.455)	5.5 (5.1, 5.8)	4.6, 6.6			56	5.45 (0.423)	5.4 (5.1, 5.7)	4.8, 6.8							
1 hour																	
Absolute value	56	5.59 (0.525)	5.4 (5.2, 6.0)	4.6, 6.8			56	5.33 (0.525)	5.3 (5.0, 5.6)	4.3, 6.7							
Change from baseline	56	0.11 (0.343)	0.1 (-0.2, 0.3)	-0.5, 1.0	0.07 (0.071)	(-0.07, 0.21)	56	-0.11 (0.351)	-0.1 (-0.3, 0.1)	-1.0, 0.9	-0.16 (0.071)	(-0.30, -0.02)	-0.23 (-0.36, -0.10)	0.0008	-0.65 (-1.03, -0.27)		
Percent change from baseline	56	2.14 (6.399)	1.9 (-3.3, 5.5)	-9.1, 19.2			56	-2.05 (6.264)	-2.2 (-5.5, 1.8)	-18.1, 16.7							
2 hours																	
Absolute value	55	5.52 (0.507)	5.4 (5.2, 6.0)	4.6, 6.7			56	5.29 (0.440)	5.2 (5.0, 5.5)	4.5, 6.7							
Change from baseline	55	0.07 (0.339)	0.1 (-0.2, 0.3)	-0.5, 0.8	0.02 (0.070)	(-0.12, 0.15)	56	-0.16 (0.388)	-0.1 (-0.3, 0.0)	-1.4, 0.6	-0.20 (0.069)	(-0.34, -0.07)	-0.22 (-0.34, -0.10)	0.0006	-0.62 (-1.00, -0.24)		
Percent change from baseline	55	1.28 (6.286)	2.0 (-3.6, 5.7)	-9.8, 15.4			56	-2.74 (6.640)	-2.0 (-6.2, 0.8)	-20.9, 11.1							

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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04/03/2021

Lokelma

Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Acute Baseline eGFR *(contd.)*																	
15-29+ *(contd.)*																	
4 hours																	
Absolute value	55	5.23 (0.491)	5.2 (4.9, 5.5)	4.3, 6.3			56	5.08 (0.469)	5.1 (4.8, 5.3)	3.8, 6.5							
Change from baseline	55	-0.23 (0.390)	-0.3 (-0.5, 0.0)	-1.1, 0.7	-0.28 (0.077)	(-0.43, -0.13)	56	-0.37 (0.456)	-0.3 (-0.6, -0.1)	-2.2, 0.6	-0.41 (0.076)	(-0.56, -0.26)	-0.13 (-0.28, 0.02)	0.0953	-0.32 (-0.69, 0.05)		
Percent change from baseline	55	-4.10 (7.112)	-5.8 (-8.8, 0.0)	-19.6, 12.5			56	-6.51 (7.831)	-5.4 (-10.8, -1.8)	-36.7, 11.3							
24 hours																	
Absolute value	54	5.27 (0.476)	5.3 (4.9, 5.6)	4.3, 6.2			56	4.85 (0.410)	4.8 (4.6, 5.1)	4.1, 6.2							
Change from baseline	54	-0.17 (0.341)	-0.2 (-0.4, 0.0)	-0.8, 0.8	-0.22 (0.070)	(-0.36, -0.08)	56	-0.60 (0.370)	-0.6 (-0.8, -0.4)	-1.9, 0.1	-0.64 (0.069)	(-0.78, -0.50)	-0.42 (-0.54, -0.29)	<.0001	-1.21 (-1.61, -0.80)		
Percent change from baseline	54	-2.99 (6.185)	-3.4 (-6.9, 0.0)	-13.6, 15.4			56	-10.80 (6.221)	-10.7 (-15.0, -6.9)	-28.2, 2.0							
28 hours																	
Absolute value	54	5.22 (0.452)	5.2 (4.8, 5.6)	4.5, 6.4			56	4.70 (0.500)	4.7 (4.3, 5.0)	3.7, 6.7							
Change from baseline	54	-0.22 (0.378)	-0.2 (-0.5, 0.0)	-1.0, 0.6	-0.27 (0.076)	(-0.42, -0.12)	56	-0.75 (0.487)	-0.8 (-1.1, -0.4)	-1.9, 0.5	-0.79 (0.075)	(-0.94, -0.64)	-0.52 (-0.66, -0.37)	<.0001	-1.20 (-1.60, -0.79)		
Percent change from baseline	54	-3.97 (6.736)	-3.6 (-8.9, 0.0)	-15.8, 11.5			56	-13.54 (8.346)	-13.8 (-18.6, -7.2)	-32.5, 8.1							
48 hours																	
Absolute value	54	5.18 (0.413)	5.2 (5.0, 5.5)	4.4, 6.3			56	4.43 (0.446)	4.4 (4.1, 4.8)	3.1, 5.5							
Change from baseline	54	-0.26 (0.406)	-0.3 (-0.6, 0.0)	-1.0, 0.7	-0.32 (0.076)	(-0.47, -0.17)	56	-1.02 (0.495)	-1.0 (-1.3, -0.6)	-2.5, 0.0	-1.06 (0.075)	(-1.21, -0.91)	-0.74 (-0.89, -0.60)	<.0001	-1.67 (-2.11, -1.24)		
Percent change from baseline	54	-4.52 (7.372)	-5.3 (-10.2, 0.0)	-17.5, 14.0			56	-18.46 (8.343)	-19.4 (-24.1, -11.1)	-39.5, 0.0							
30-59+																	
Baseline																	
Absolute value	100	5.27 (0.364)	5.2 (5.1, 5.5)	4.5, 6.1			83	5.20 (0.317)	5.2 (5.0, 5.4)	4.6, 6.0							
1 hour																	
Absolute value	100	5.31 (0.568)	5.3 (4.9, 5.7)	4.1, 7.1			83	5.05 (0.418)	5.0 (4.8, 5.3)	4.1, 6.3							
Change from baseline	100	0.04 (0.377)	0.0 (-0.2, 0.3)	-0.8, 1.2	0.00 (0.042)	(-0.08, 0.09)	83	-0.15 (0.410)	-0.1 (-0.4, 0.1)	-1.3, 1.5	-0.20 (0.045)	(-0.28, -0.11)	-0.20 (-0.31, -0.08)	0.0008	-0.49 (-0.78, -0.19)		
Percent change from baseline	100	0.63 (7.019)	0.0 (-3.7, 5.4)	-13.8, 21.8			83	-2.81 (7.888)	-2.4 (-7.4, 1.4)	-24.1, 32.2							
2 hours																	
Absolute value	100	5.22 (0.558)	5.1 (4.8, 5.6)	3.8, 6.7			82	4.95 (0.389)	4.9 (4.7, 5.3)	4.2, 5.7							
Change from baseline	100	-0.06 (0.421)	-0.1 (-0.3, 0.2)	-1.6, 1.0	-0.09 (0.042)	(-0.17, -0.01)	82	-0.26 (0.370)	-0.3 (-0.5, 0.0)	-1.1, 0.7	-0.30 (0.045)	(-0.39, -0.21)	-0.21 (-0.33, -0.10)	0.0003	-0.51 (-0.81, -0.22)		
Percent change from baseline	100	-1.08 (7.824)	-1.8 (-4.9, 3.4)	-27.1, 22.2			82	-4.89 (7.092)	-5.5 (-9.6, 0.0)	-20.4, 14.3							
4 hours																	
Absolute value	100	5.02 (0.536)	4.9 (4.7, 5.3)	3.7, 6.2			83	4.80 (0.455)	4.8 (4.5, 5.1)	3.9, 5.9							
Change from baseline	100	-0.26 (0.456)	-0.2 (-0.6, 0.0)	-1.8, 1.1	-0.29 (0.046)	(-0.38, -0.20)	83	-0.40 (0.407)	-0.4 (-0.7, -0.1)	-1.5, 0.7	-0.44 (0.049)	(-0.54, -0.35)	-0.15 (-0.28, -0.03)	0.0169	-0.33 (-0.63, -0.04)		
Percent change from baseline	100	-4.79 (8.654)	-4.2 (-10.3, 0.0)	-32.7, 21.2			83	-7.65 (7.766)	-7.8 (-12.7, -1.8)	-27.3, 14.3							
24 hours																	
Absolute value	100	5.12 (0.469)	5.1 (4.8, 5.4)	4.0, 6.7			81	4.69 (0.430)	4.7 (4.4, 5.0)	3.9, 6.0							
Change from baseline	100	-0.15 (0.381)	-0.2 (-0.4, 0.1)	-1.3, 0.9	-0.18 (0.043)	(-0.27, -0.10)	81	-0.51 (0.434)	-0.6 (-0.8, -0.2)	-1.7, 0.6	-0.56 (0.046)	(-0.65, -0.47)	-0.37 (-0.49, -0.26)	<.0001	-0.89 (-1.20, -0.58)		
Percent change from baseline	100	-2.77 (7.067)	-3.0 (-7.1, 1.7)	-21.6, 17.0			81	-9.69 (8.175)	-10.5 (-15.1, -3.9)	-30.4, 12.2							
28 hours																	
Absolute value	98	5.05 (0.528)	5.1 (4.6, 5.4)	3.8, 6.3			81	4.51 (0.417)	4.5 (4.2, 4.7)	3.7, 6.0							
Change from baseline	98	-0.21 (0.434)	-0.2 (-0.5, 0.1)	-1.2, 0.8	-0.24 (0.047)	(-0.33, -0.15)	81	-0.69 (0.484)	-0.7 (-1.1, -0.4)	-2.0, 0.8	-0.74 (0.050)	(-0.84, -0.64)	-0.50 (-0.62, -0.37)	<.0001	-1.05 (-1.37, -0.74)		

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Acute Baseline eGFR *(contd.)*																	
30-59+ *(contd.)*																	
28 hours *(contd.)*																	
Percent change from baseline	98	-3.98 (8.224)	-3.9 (-10.1, 1.9)	-21.6, 15.7			81	-13.09 (8.864)	-13.7 (-20.0, -7.5)	-33.9, 16.2							
48 hours																	
Absolute value	99	5.06 (0.507)	5.1 (4.7, 5.4)	3.9, 6.4			81	4.40 (0.507)	4.3 (4.1, 4.7)	2.9, 6.2							
Change from baseline	99	-0.20 (0.394)	-0.2 (-0.5, 0.1)	-1.0, 0.7	-0.23 (0.049)	(-0.33, -0.14)	81	-0.80 (0.541)	-0.8 (-1.2, -0.5)	-2.3, 1.0	-0.85 (0.053)	(-0.95, -0.74)	-0.61 (-0.75, -0.48)	<.0001	-1.28 (-1.61, -0.96)		
Percent change from baseline	99	-3.82 (7.508)	-3.9 (-9.6, 2.0)	-19.5, 15.6			81	-15.21 (10.114)	-14.9 (-22.2, -9.3)	-44.0, 19.2							
>=60																	
Baseline																	
Absolute value	39	5.16 (0.319)	5.1 (4.9, 5.3)	4.7, 6.2			45	5.08 (0.242)	5.1 (5.0, 5.2)	4.5, 5.6							
1 hour																	
Absolute value	39	4.93 (0.500)	4.9 (4.6, 5.2)	3.8, 5.9			45	4.92 (0.479)	4.9 (4.6, 5.3)	3.9, 5.9							
Change from baseline	39	-0.23 (0.434)	-0.2 (-0.4, 0.1)	-1.7, 0.6	-0.26 (0.103)	(-0.47, -0.06)	45	-0.16 (0.400)	-0.1 (-0.5, 0.1)	-1.0, 0.7	-0.21 (0.096)	(-0.40, -0.02)	0.06 (-0.13, 0.24)	0.5543	0.16 (-0.27, 0.59)		
Percent change from baseline	39	-4.33 (8.260)	-4.1 (-7.8, 1.8)	-30.9, 11.3			45	-3.16 (7.871)	-2.0 (-9.4, 2.0)	-20.0, 14.3							
2 hours																	
Absolute value	39	4.96 (0.438)	4.8 (4.6, 5.3)	4.0, 5.8			45	4.88 (0.466)	4.8 (4.5, 5.0)	4.0, 6.1							
Change from baseline	39	-0.20 (0.466)	-0.3 (-0.5, 0.1)	-1.5, 0.7	-0.24 (0.103)	(-0.44, -0.04)	45	-0.21 (0.378)	-0.2 (-0.5, 0.0)	-1.0, 0.9	-0.26 (0.095)	(-0.44, -0.07)	-0.02 (-0.20, 0.17)	0.8528	-0.01 (-0.44, 0.42)		
Percent change from baseline	39	-3.68 (8.787)	-5.5 (-9.8, 1.9)	-27.3, 13.7			45	-4.09 (7.374)	-4.0 (-9.3, 1.0)	-18.4, 17.3							
4 hours																	
Absolute value	39	4.95 (0.500)	5.0 (4.5, 5.3)	4.1, 6.1			45	4.79 (0.469)	4.8 (4.5, 5.2)	3.8, 5.8							
Change from baseline	39	-0.20 (0.501)	-0.2 (-0.6, 0.1)	-1.4, 0.9	-0.24 (0.107)	(-0.45, -0.03)	45	-0.29 (0.463)	-0.3 (-0.6, 0.0)	-1.2, 0.7	-0.34 (0.100)	(-0.54, -0.15)	-0.10 (-0.30, 0.10)	0.3072	-0.19 (-0.62, 0.24)		
Percent change from baseline	39	-3.78 (9.462)	-3.9 (-11.8, 2.0)	-25.5, 17.3			45	-5.71 (9.081)	-5.9 (-12.5, 0.0)	-24.0, 13.7							
24 hours																	
Absolute value	39	4.86 (0.409)	4.8 (4.6, 5.1)	4.0, 5.8			45	4.65 (0.362)	4.7 (4.4, 4.9)	3.9, 5.3							
Change from baseline	39	-0.30 (0.398)	-0.3 (-0.6, -0.1)	-1.4, 0.7	-0.34 (0.098)	(-0.53, -0.14)	45	-0.43 (0.363)	-0.4 (-0.6, -0.2)	-1.3, 0.2	-0.48 (0.091)	(-0.66, -0.30)	-0.14 (-0.30, 0.02)	0.0851	-0.34 (-0.78, 0.09)		
Percent change from baseline	39	-5.63 (7.567)	-5.9 (-10.7, -2.0)	-25.5, 13.7			45	-8.33 (6.941)	-8.0 (-11.8, -3.6)	-25.0, 3.9							
28 hours																	
Absolute value	39	4.90 (0.421)	4.9 (4.7, 5.1)	4.0, 6.0			45	4.55 (0.352)	4.5 (4.3, 4.8)	3.9, 5.2							
Change from baseline	39	-0.26 (0.487)	-0.3 (-0.6, 0.1)	-1.4, 0.9	-0.30 (0.099)	(-0.49, -0.10)	45	-0.53 (0.360)	-0.5 (-0.8, -0.3)	-1.2, 0.1	-0.58 (0.092)	(-0.76, -0.39)	-0.28 (-0.45, -0.11)	0.0014	-0.63 (-1.07, -0.19)		
Percent change from baseline	39	-4.77 (9.179)	-5.8 (-10.9, 1.8)	-22.6, 17.6			45	-10.29 (6.928)	-9.8 (-14.6, -6.0)	-23.1, 2.0							
48 hours																	
Absolute value	39	4.82 (0.464)	4.8 (4.5, 5.1)	4.2, 6.1			45	4.59 (0.488)	4.5 (4.2, 4.9)	3.8, 5.9							
Change from baseline	39	-0.34 (0.471)	-0.4 (-0.7, 0.0)	-1.4, 0.8	-0.38 (0.105)	(-0.59, -0.17)	45	-0.49 (0.442)	-0.5 (-0.8, -0.2)	-1.4, 0.6	-0.54 (0.098)	(-0.74, -0.35)	-0.16 (-0.36, 0.03)	0.0972	-0.33 (-0.76, 0.10)		
Percent change from baseline	39	-6.46 (8.760)	-8.2 (-14.0, 0.0)	-24.1, 15.1			45	-9.68 (8.625)	-9.6 (-15.7, -4.0)	-26.9, 11.3							

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Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
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Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Sex																0.3661	
Male																	
Baseline																	
Absolute value	144	5.37 (0.415)	5.3 (5.1, 5.6)	4.5, 6.6			117	5.30 (0.392)	5.3 (5.0, 5.5)	4.5, 6.8							
1 hour																	
Absolute value	144	5.42 (0.577)	5.3 (5.0, 5.9)	4.1, 7.1			117	5.16 (0.517)	5.2 (4.8, 5.4)	3.9, 6.7							
Change from baseline	144	0.04 (0.365)	0.0 (-0.2, 0.3)	-0.8, 1.2	0.03 (0.034)	(-0.04, 0.09)	117	-0.14 (0.389)	-0.1 (-0.4, 0.1)	-1.0, 1.5	-0.15 (0.038)	(-0.22, -0.08)	-0.18 (-0.27, -0.08)	0.0002	-0.49 (-0.74, -0.24)		
Percent change from baseline	144	0.74 (6.789)	0.0 (-3.7, 5.1)	-13.8, 21.8			117	-2.65 (7.409)	-2.0 (-7.8, 1.8)	-19.2, 32.2							
2 hours																	
Absolute value	143	5.31 (0.554)	5.2 (4.9, 5.6)	3.8, 6.7			117	5.07 (0.464)	5.1 (4.8, 5.4)	4.0, 6.4							
Change from baseline	143	-0.06 (0.383)	-0.1 (-0.3, 0.2)	-1.6, 0.8	-0.07 (0.033)	(-0.14, -0.01)	117	-0.23 (0.393)	-0.2 (-0.5, 0.0)	-1.4, 0.9	-0.23 (0.037)	(-0.31, -0.16)	-0.16 (-0.25, -0.07)	0.0008	-0.43 (-0.68, -0.19)		
Percent change from baseline	143	-1.08 (7.013)	-1.6 (-5.7, 3.4)	-27.1, 15.4			117	-4.14 (7.268)	-4.0 (-8.8, 0.0)	-20.9, 17.3							
4 hours																	
Absolute value	143	5.13 (0.541)	5.1 (4.8, 5.4)	3.7, 6.3			117	4.93 (0.485)	4.9 (4.6, 5.3)	3.8, 6.5							
Change from baseline	143	-0.24 (0.439)	-0.3 (-0.5, 0.0)	-1.8, 1.1	-0.26 (0.038)	(-0.33, -0.18)	117	-0.37 (0.439)	-0.3 (-0.6, -0.1)	-2.2, 0.7	-0.37 (0.042)	(-0.46, -0.29)	-0.12 (-0.22, -0.01)	0.0272	-0.29 (-0.54, -0.05)		
Percent change from baseline	143	-4.38 (8.167)	-4.6 (-9.3, 0.0)	-32.7, 21.2			117	-6.78 (8.045)	-6.1 (-12.3, -1.7)	-36.7, 14.3							
24 hours																	
Absolute value	142	5.13 (0.475)	5.0 (4.8, 5.4)	4.0, 6.7			115	4.76 (0.410)	4.7 (4.5, 5.0)	3.9, 6.0							
Change from baseline	142	-0.23 (0.349)	-0.3 (-0.4, 0.0)	-1.3, 0.9	-0.25 (0.033)	(-0.32, -0.19)	115	-0.54 (0.414)	-0.5 (-0.8, -0.3)	-1.9, 0.6	-0.55 (0.037)	(-0.62, -0.47)	-0.29 (-0.39, -0.20)	<.0001	-0.81 (-1.07, -0.55)		
Percent change from baseline	142	-4.31 (6.406)	-5.4 (-7.8, 0.0)	-21.6, 17.0			115	-10.01 (7.438)	-10.3 (-14.8, -5.7)	-30.4, 12.2							
28 hours																	
Absolute value	140	5.12 (0.479)	5.1 (4.8, 5.5)	3.8, 6.4			115	4.60 (0.469)	4.6 (4.3, 4.9)	3.7, 6.7							
Change from baseline	140	-0.23 (0.412)	-0.2 (-0.5, 0.0)	-1.4, 0.8	-0.25 (0.037)	(-0.32, -0.18)	115	-0.69 (0.489)	-0.7 (-1.1, -0.3)	-2.0, 0.8	-0.70 (0.041)	(-0.78, -0.62)	-0.45 (-0.55, -0.35)	<.0001	-1.03 (-1.29, -0.77)		
Percent change from baseline	140	-4.22 (7.615)	-3.4 (-9.8, 0.2)	-22.6, 16.3			115	-12.88 (8.721)	-13.0 (-20.0, -6.6)	-33.9, 16.2							
48 hours																	
Absolute value	141	5.07 (0.485)	5.1 (4.7, 5.4)	4.1, 6.3			115	4.47 (0.465)	4.3 (4.2, 4.8)	3.5, 6.2							
Change from baseline	141	-0.28 (0.407)	-0.3 (-0.6, 0.0)	-1.4, 0.8	-0.30 (0.039)	(-0.38, -0.22)	115	-0.83 (0.543)	-0.8 (-1.2, -0.5)	-2.5, 1.0	-0.83 (0.044)	(-0.92, -0.75)	-0.53 (-0.64, -0.43)	<.0001	-1.15 (-1.42, -0.89)		
Percent change from baseline	141	-5.19 (7.515)	-5.7 (-10.7, 0.0)	-24.1, 15.1			115	-15.33 (9.578)	-16.3 (-22.2, -9.4)	-37.0, 19.2							
Female																	
Baseline																	
Absolute value	77	5.25 (0.354)	5.2 (5.0, 5.5)	4.5, 6.3			86	5.23 (0.309)	5.2 (5.0, 5.4)	4.6, 6.1							
1 hour																	
Absolute value	77	5.18 (0.547)	5.1 (4.8, 5.5)	3.8, 6.5			86	5.06 (0.418)	5.0 (4.8, 5.3)	4.0, 6.6							
Change from baseline	77	-0.07 (0.429)	-0.1 (-0.3, 0.2)	-1.7, 1.0	-0.09 (0.051)	(-0.19, 0.01)	86	-0.17 (0.376)	-0.2 (-0.4, 0.1)	-1.3, 0.7	-0.20 (0.048)	(-0.30, -0.11)	-0.11 (-0.24, 0.01)	0.0711	-0.26 (-0.57, 0.05)		
Percent change from baseline	77	-1.28 (8.085)	-1.8 (-6.1, 3.9)	-30.9, 18.9			86	-3.21 (7.103)	-3.4 (-7.4, 1.8)	-24.1, 14.3							
2 hours																	
Absolute value	77	5.21 (0.539)	5.2 (4.8, 5.6)	4.0, 6.5			85	4.99 (0.435)	4.9 (4.7, 5.3)	4.2, 6.7							
Change from baseline	77	-0.04 (0.463)	0.0 (-0.3, 0.3)	-1.5, 1.0	-0.06 (0.052)	(-0.16, 0.05)	85	-0.24 (0.375)	-0.2 (-0.5, 0.0)	-1.4, 0.6	-0.27 (0.049)	(-0.37, -0.17)	-0.22 (-0.34, -0.09)	0.0010	-0.50 (-0.81, -0.18)		
Percent change from baseline	77	-0.61 (8.758)	0.0 (-5.9, 5.8)	-27.3, 22.2			85	-4.60 (6.983)	-3.8 (-8.6, 0.0)	-23.4, 9.8							

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
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Lokelma

Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Sex *(contd.)*																	
Female *(contd.)*																	
4 hours																	
Absolute value	77	5.00 (0.467)	5.0 (4.7, 5.2)	4.0, 6.2			86	4.82 (0.445)	4.8 (4.5, 5.1)	3.8, 6.1							
Change from baseline	77	-0.25 (0.436)	-0.2 (-0.5, 0.0)	-1.4, 0.9	-0.27 (0.053)	(-0.37, -0.16)	86	-0.41 (0.425)	-0.5 (-0.7, -0.1)	-1.5, 0.6	-0.44 (0.050)	(-0.53, -0.34)	-0.17 (-0.30, -0.04)	0.0101	-0.37 (-0.68, -0.06)		
Percent change from baseline	77	-4.58 (8.267)	-3.9 (-9.7, 0.0)	-25.5, 20.0			86	-7.69 (8.034)	-8.4 (-12.7, -1.9)	-27.3, 11.3							
24 hours																	
Absolute value	77	5.15 (0.498)	5.1 (4.8, 5.5)	4.1, 6.6			85	4.72 (0.392)	4.7 (4.4, 5.0)	3.9, 6.2							
Change from baseline	77	-0.10 (0.391)	-0.1 (-0.3, 0.1)	-1.4, 0.8	-0.12 (0.049)	(-0.21, -0.02)	85	-0.51 (0.366)	-0.6 (-0.8, -0.3)	-1.3, 0.4	-0.54 (0.046)	(-0.63, -0.45)	-0.42 (-0.54, -0.31)	<.0001	-1.09 (-1.42, -0.76)		
Percent change from baseline	77	-1.84 (7.380)	-1.9 (-6.0, 3.2)	-25.5, 15.4			85	-9.70 (6.830)	-10.3 (-14.6, -5.7)	-24.5, 7.8							
28 hours																	
Absolute value	77	5.02 (0.530)	5.0 (4.7, 5.3)	4.0, 6.3			85	4.53 (0.377)	4.5 (4.2, 4.8)	3.7, 5.5							
Change from baseline	77	-0.23 (0.487)	-0.3 (-0.5, 0.1)	-1.2, 1.0	-0.25 (0.055)	(-0.36, -0.14)	85	-0.70 (0.440)	-0.7 (-1.0, -0.4)	-1.9, 0.2	-0.73 (0.052)	(-0.83, -0.63)	-0.48 (-0.62, -0.34)	<.0001	-1.01 (-1.34, -0.69)		
Percent change from baseline	77	-4.27 (9.204)	-5.7 (-9.6, 1.9)	-21.6, 21.3			85	-13.14 (7.983)	-13.7 (-18.9, -8.0)	-32.7, 3.9							
48 hours																	
Absolute value	77	5.09 (0.493)	5.1 (4.8, 5.3)	3.9, 6.4			85	4.40 (0.500)	4.4 (4.1, 4.8)	2.9, 5.9							
Change from baseline	77	-0.16 (0.394)	-0.2 (-0.5, 0.1)	-1.0, 0.7	-0.18 (0.057)	(-0.30, -0.07)	85	-0.83 (0.535)	-0.8 (-1.2, -0.5)	-2.3, 0.6	-0.86 (0.054)	(-0.97, -0.75)	-0.68 (-0.82, -0.53)	<.0001	-1.41 (-1.75, -1.06)		
Percent change from baseline	77	-3.07 (7.553)	-3.8 (-9.1, 2.0)	-17.9, 15.6			85	-15.68 (9.970)	-15.7 (-22.2, -9.4)	-44.0, 11.3							

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Note: Baseline is calculated by taking the mean of Screening timepoints at 0 hour, 30 minutes, and 1 hour then averaging with Day 1 timepoints at 0 hour.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including S-K at baseline, study, treatment, time, and treatment*time as covariates.
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Table 3.1.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)						Lokelma 10g QD (N=203)										
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Age																0.6506	
<65 years																	
Baseline																	
Absolute value	76	5.31 (0.379)	5.3 (5.0, 5.6)	4.5, 6.4			66	5.24 (0.417)	5.2 (5.0, 5.4)	4.5, 6.8							
1 hour																	
Absolute value	76	5.35 (0.570)	5.3 (5.0, 5.8)	4.4, 6.6			66	5.08 (0.479)	5.1 (4.7, 5.4)	3.9, 6.3							
Change from baseline	76	0.05 (0.383)	0.0 (-0.2, 0.2)	-0.8, 1.1	-0.11 (0.060)	(-0.23, 0.01)	66	-0.16 (0.368)	-0.2 (-0.4, 0.1)	-1.0, 0.9	-0.29 (0.058)	(-0.40, -0.18)	-0.18 (-0.31, -0.06)	0.0039	-0.55 (-0.88, -0.21)		
Percent change from baseline	76	0.81 (7.204)	0.0 (-3.8, 4.5)	-13.8, 20.0			66	-2.96 (6.809)	-3.4 (-8.0, 1.9)	-18.2, 16.7							
2 hours																	
Absolute value	76	5.31 (0.554)	5.3 (4.8, 5.6)	4.4, 6.7			66	4.98 (0.466)	4.9 (4.6, 5.3)	4.0, 6.1							
Change from baseline	76	0.01 (0.398)	0.0 (-0.3, 0.3)	-0.9, 1.0	-0.15 (0.061)	(-0.27, -0.03)	66	-0.26 (0.393)	-0.2 (-0.5, 0.0)	-1.4, 0.6	-0.39 (0.058)	(-0.51, -0.28)	-0.25 (-0.37, -0.12)	0.0001	-0.68 (-1.02, -0.35)		
Percent change from baseline	76	0.14 (7.320)	0.0 (-4.9, 5.0)	-14.5, 18.9			66	-4.88 (7.075)	-3.8 (-8.6, 0.0)	-23.4, 11.1							
4 hours																	
Absolute value	76	5.16 (0.476)	5.1 (4.9, 5.4)	4.0, 6.3			66	4.91 (0.491)	5.0 (4.5, 5.3)	4.0, 5.9							
Change from baseline	76	-0.15 (0.393)	-0.1 (-0.4, 0.1)	-1.2, 0.6	-0.31 (0.064)	(-0.43, -0.18)	66	-0.34 (0.466)	-0.4 (-0.6, 0.0)	-1.5, 0.7	-0.47 (0.062)	(-0.59, -0.34)	-0.16 (-0.30, -0.02)	0.0223	-0.43 (-0.76, -0.10)		
Percent change from baseline	76	-2.75 (7.239)	-1.9 (-7.2, 2.1)	-20.7, 12.2			66	-6.19 (8.721)	-6.5 (-12.5, 1.0)	-27.3, 13.7							
24 hours																	
Absolute value	76	5.16 (0.546)	5.1 (4.8, 5.6)	4.0, 6.7			64	4.72 (0.374)	4.8 (4.5, 5.0)	3.9, 6.0							
Change from baseline	76	-0.14 (0.384)	-0.2 (-0.4, 0.1)	-1.4, 0.9	-0.30 (0.061)	(-0.42, -0.17)	64	-0.52 (0.416)	-0.6 (-0.8, -0.3)	-1.9, 0.4	-0.65 (0.059)	(-0.77, -0.54)	-0.36 (-0.49, -0.23)	<.0001	-0.96 (-1.31, -0.61)		
Percent change from baseline	76	-2.71 (7.145)	-3.5 (-7.1, 1.9)	-25.5, 15.5			64	-9.71 (7.285)	-10.6 (-14.0, -5.9)	-28.2, 7.9							
28 hours																	
Absolute value	74	5.08 (0.482)	5.1 (4.8, 5.4)	3.8, 6.2			64	4.60 (0.404)	4.6 (4.3, 4.9)	3.7, 6.0							
Change from baseline	74	-0.22 (0.436)	-0.2 (-0.5, 0.1)	-1.4, 0.8	-0.37 (0.066)	(-0.50, -0.24)	64	-0.65 (0.495)	-0.6 (-1.1, -0.3)	-1.8, 0.4	-0.78 (0.064)	(-0.91, -0.66)	-0.41 (-0.55, -0.26)	<.0001	-0.92 (-1.27, -0.57)		
Percent change from baseline	74	-4.07 (8.021)	-2.7 (-10.1, 1.9)	-22.6, 15.1			64	-12.02 (8.589)	-11.6 (-19.8, -6.1)	-32.7, 7.1							
48 hours																	
Absolute value	75	5.08 (0.533)	5.1 (4.7, 5.5)	4.1, 6.4			64	4.57 (0.460)	4.7 (4.2, 4.9)	3.5, 6.2							
Change from baseline	75	-0.22 (0.437)	-0.2 (-0.6, 0.1)	-1.4, 0.6	-0.37 (0.069)	(-0.50, -0.23)	64	-0.67 (0.579)	-0.6 (-1.0, -0.3)	-2.5, 1.0	-0.80 (0.068)	(-0.94, -0.67)	-0.43 (-0.59, -0.28)	<.0001	-0.89 (-1.24, -0.54)		
Percent change from baseline	75	-4.09 (8.068)	-3.4 (-10.5, 2.0)	-24.1, 11.5			64	-12.41 (10.097)	-11.4 (-18.6, -5.7)	-37.0, 19.2							
>= 65 years																	
Baseline																	
Absolute value	145	5.34 (0.409)	5.3 (5.1, 5.5)	4.5, 6.6			137	5.28 (0.331)	5.3 (5.0, 5.5)	4.6, 6.5							
1 hour																	
Absolute value	145	5.33 (0.582)	5.2 (5.0, 5.7)	3.8, 7.1			137	5.13 (0.480)	5.1 (4.8, 5.4)	4.0, 6.7							
Change from baseline	145	-0.02 (0.395)	0.0 (-0.2, 0.3)	-1.7, 1.2	-0.02 (0.035)	(-0.08, 0.05)	137	-0.15 (0.392)	-0.1 (-0.4, 0.1)	-1.3, 1.5	-0.16 (0.036)	(-0.23, -0.09)	-0.15 (-0.24, -0.05)	0.0023	-0.34 (-0.58, -0.11)		
Percent change from baseline	145	-0.37 (7.360)	0.0 (-4.1, 5.0)	-30.9, 21.8			137	-2.85 (7.504)	-2.0 (-7.4, 1.4)	-24.1, 32.2							
2 hours																	
Absolute value	144	5.25 (0.548)	5.2 (4.9, 5.6)	3.8, 6.7			136	5.06 (0.445)	5.1 (4.8, 5.4)	4.2, 6.7							
Change from baseline	144	-0.08 (0.418)	-0.1 (-0.3, 0.2)	-1.6, 1.0	-0.08 (0.034)	(-0.15, -0.01)	136	-0.22 (0.381)	-0.2 (-0.5, 0.0)	-1.1, 0.9	-0.23 (0.035)	(-0.30, -0.16)	-0.15 (-0.24, -0.06)	0.0016	-0.35 (-0.58, -0.11)		
Percent change from baseline	144	-1.47 (7.790)	-1.9 (-6.2, 3.9)	-27.3, 22.2			136	-4.07 (7.175)	-3.9 (-8.8, 0.0)	-20.4, 17.3							

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Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value	Study interaction p-value
Age *(contd.)*																	
>= 65 years *(contd.)*																	
4 hours																	
Absolute value	144	5.04 (0.537)	4.9 (4.7, 5.4)	3.7, 6.3			137	4.87 (0.462)	4.9 (4.6, 5.2)	3.8, 6.5							
Change from baseline	144	-0.29 (0.452)	-0.3 (-0.6, -0.1)	-1.8, 1.1	-0.29 (0.037)	(-0.36, -0.22)	137	-0.41 (0.415)	-0.4 (-0.7, -0.1)	-2.2, 0.7	-0.42 (0.038)	(-0.49, -0.34)	-0.13 (-0.23, -0.03)	0.0135	-0.27 (-0.50, -0.03)		
Percent change from baseline	144	-5.35 (8.528)	-6.1 (-10.9, -1.6)	-32.7, 21.2			137	-7.63 (7.669)	-7.4 (-12.3, -1.9)	-36.7, 14.3							
24 hours																	
Absolute value	143	5.12 (0.446)	5.1 (4.8, 5.4)	4.0, 6.6			136	4.75 (0.416)	4.7 (4.5, 5.0)	3.9, 6.2							
Change from baseline	143	-0.21 (0.360)	-0.2 (-0.4, 0.0)	-1.3, 0.8	-0.21 (0.032)	(-0.27, -0.15)	136	-0.53 (0.384)	-0.5 (-0.8, -0.3)	-1.7, 0.6	-0.54 (0.033)	(-0.60, -0.47)	-0.33 (-0.41, -0.24)	<.0001	-0.86 (-1.11, -0.62)		
Percent change from baseline	143	-3.83 (6.682)	-3.9 (-7.8, 0.0)	-21.6, 17.0			136	-9.95 (7.141)	-9.8 (-15.0, -5.7)	-30.4, 12.2							
28 hours																	
Absolute value	143	5.09 (0.509)	5.1 (4.7, 5.4)	4.0, 6.4			136	4.56 (0.446)	4.6 (4.3, 4.8)	3.7, 6.7							
Change from baseline	143	-0.24 (0.442)	-0.3 (-0.5, 0.0)	-1.1, 1.0	-0.24 (0.037)	(-0.31, -0.16)	136	-0.72 (0.454)	-0.7 (-1.0, -0.4)	-2.0, 0.8	-0.73 (0.038)	(-0.80, -0.65)	-0.49 (-0.59, -0.39)	<.0001	-1.07 (-1.32, -0.82)		
Percent change from baseline	143	-4.32 (8.308)	-5.2 (-9.8, 0.0)	-21.6, 21.3			136	-13.44 (8.296)	-13.8 (-19.3, -7.7)	-33.9, 16.2							
48 hours																	
Absolute value	143	5.08 (0.463)	5.1 (4.7, 5.3)	3.9, 6.2			136	4.38 (0.479)	4.3 (4.1, 4.7)	2.9, 5.9							
Change from baseline	143	-0.25 (0.389)	-0.3 (-0.6, 0.0)	-1.0, 0.8	-0.25 (0.037)	(-0.33, -0.18)	136	-0.90 (0.504)	-0.9 (-1.2, -0.6)	-2.3, 0.6	-0.91 (0.038)	(-0.99, -0.83)	-0.66 (-0.76, -0.56)	<.0001	-1.45 (-1.71, -1.18)		
Percent change from baseline	143	-4.63 (7.333)	-5.7 (-10.2, 0.0)	-19.5, 15.6			136	-16.92 (9.234)	-17.9 (-22.9, -11.0)	-44.0, 11.3							

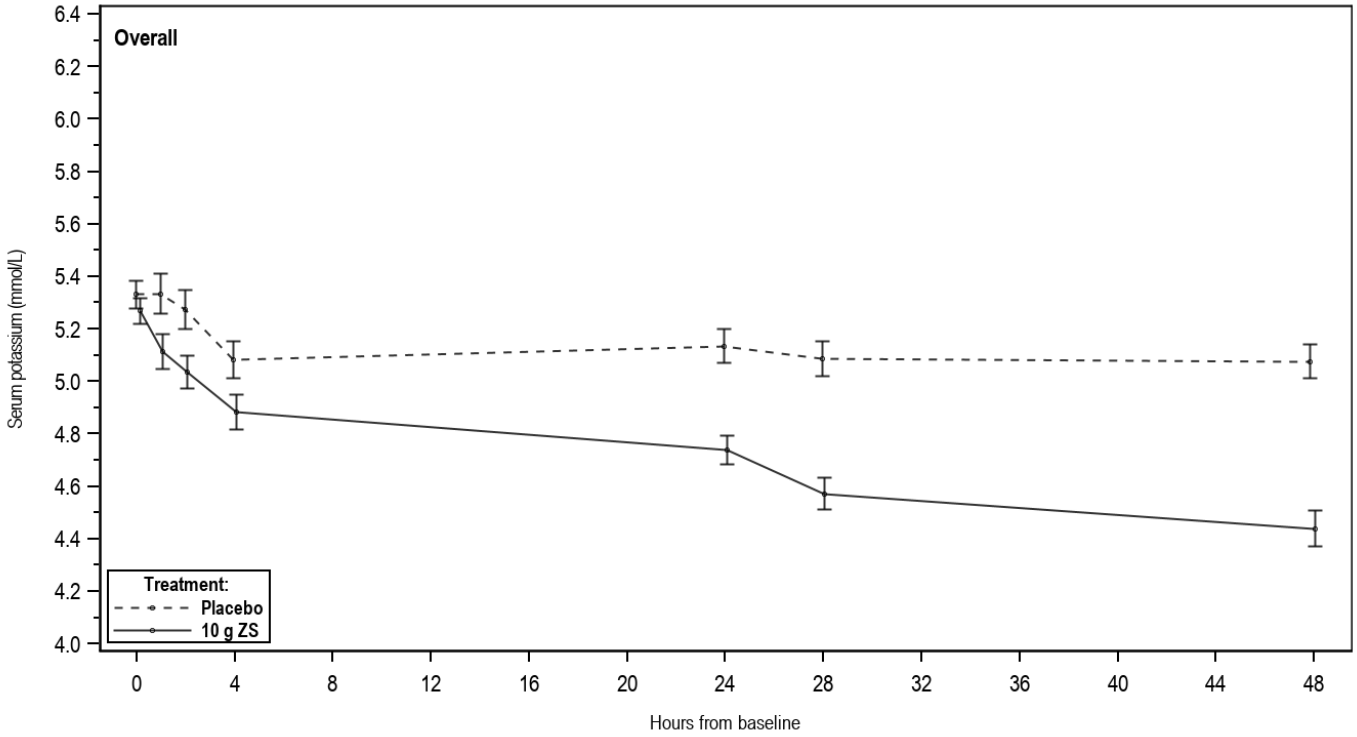
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Figure 3.1.2.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint)(95% Confidence Interval): absolute values, ZS 10g TID vs. combined placebo (Intent-to-treat population)

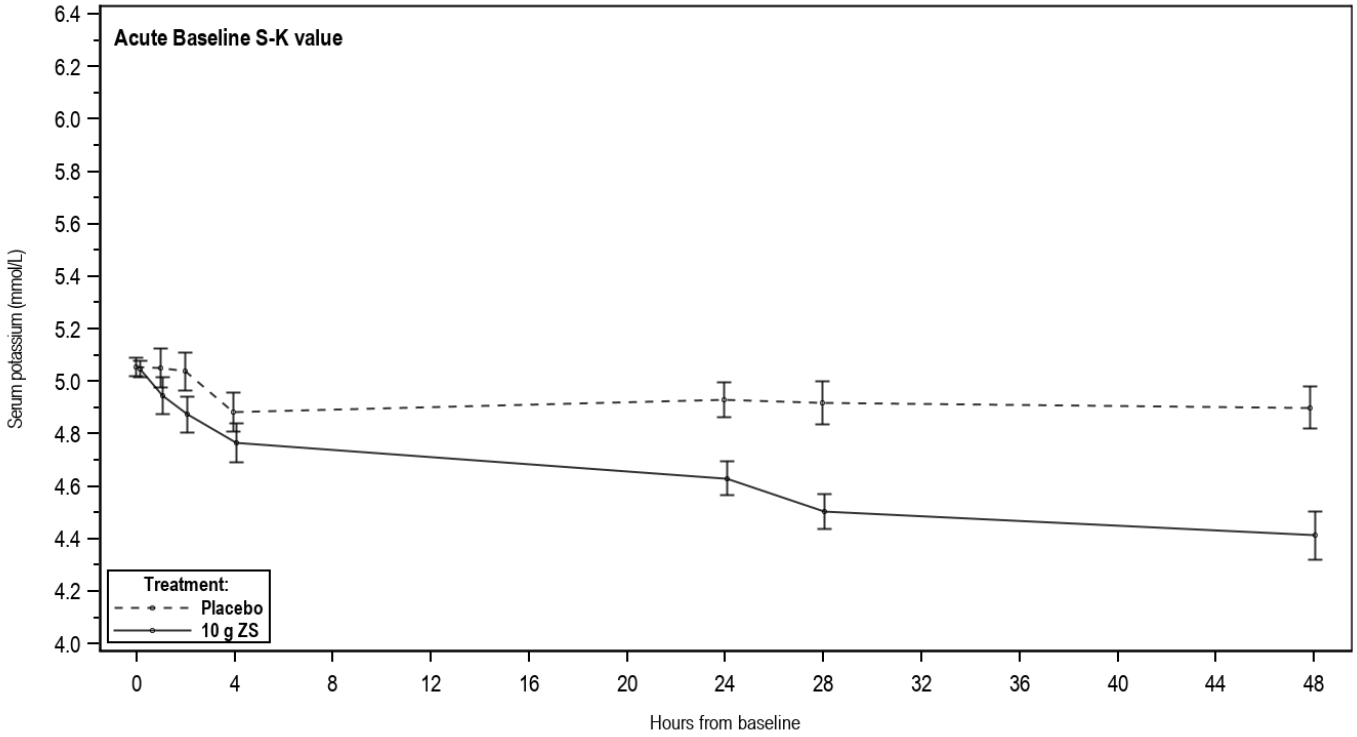


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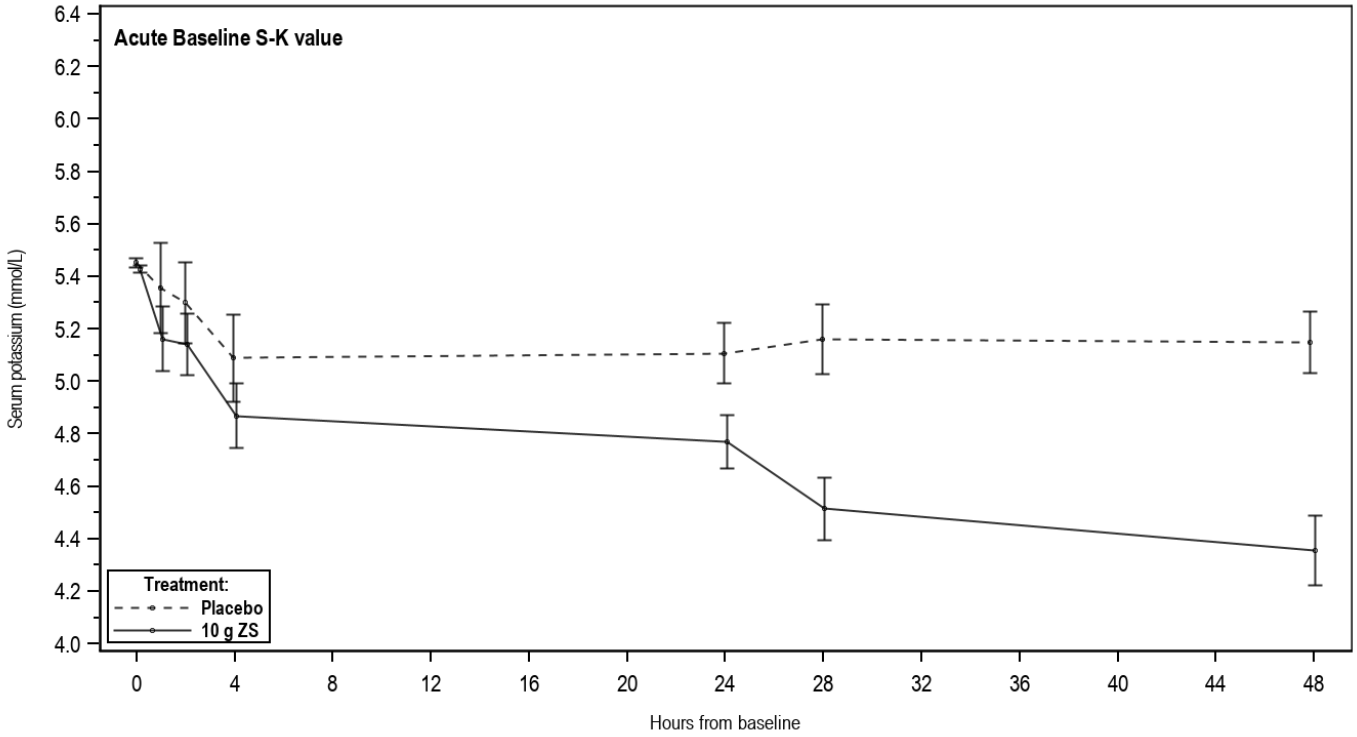


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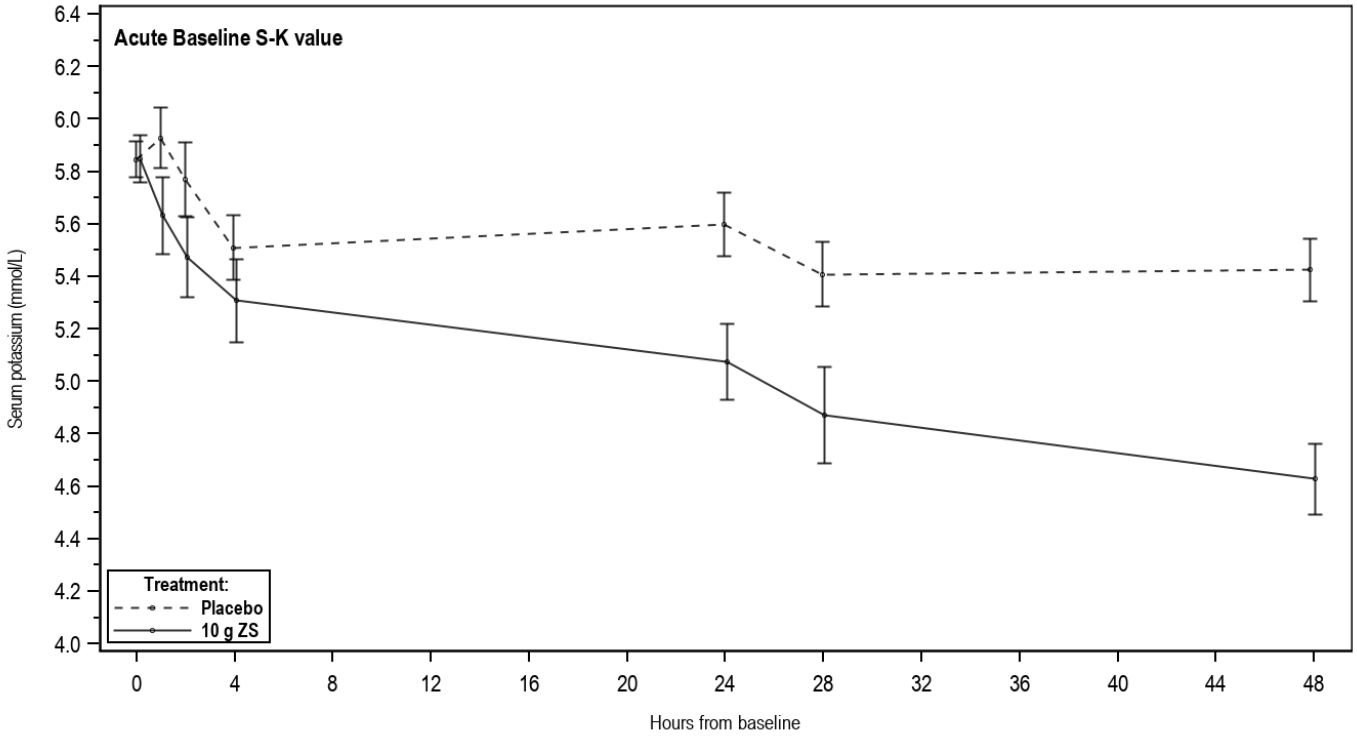


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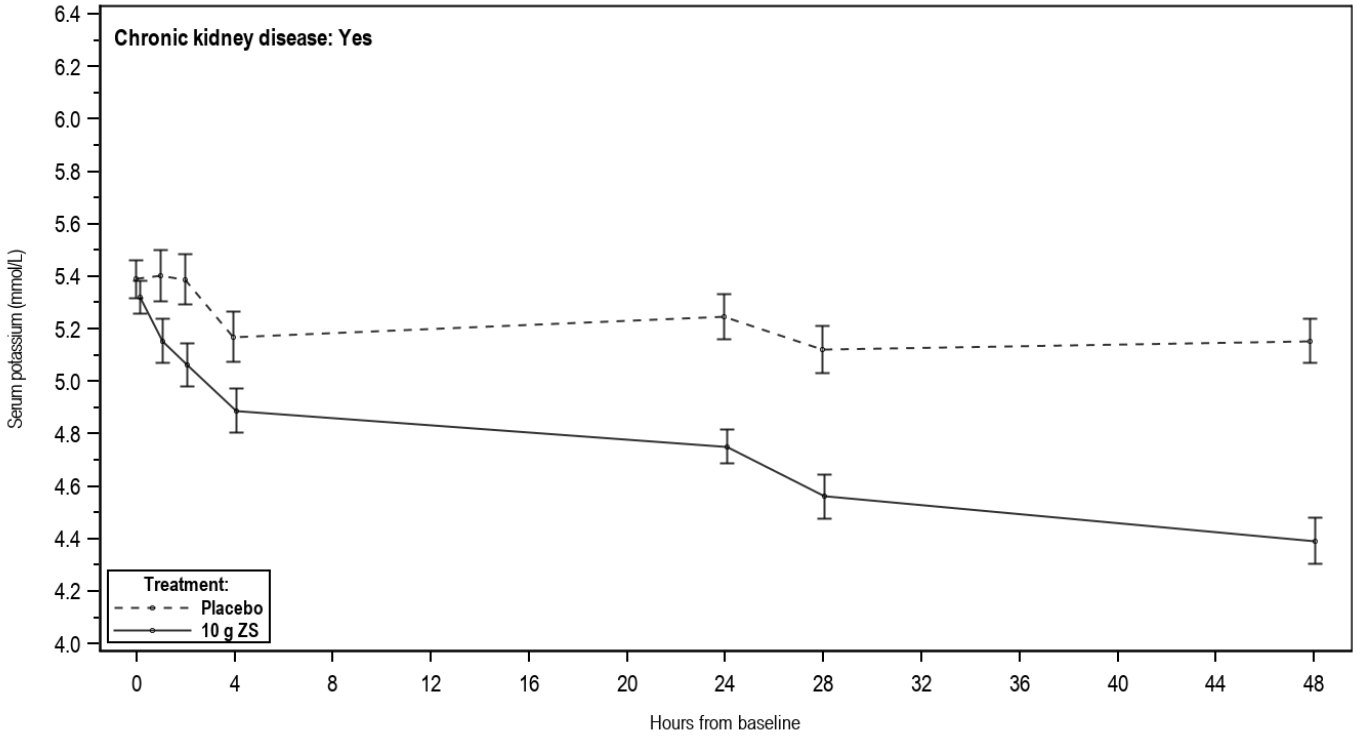


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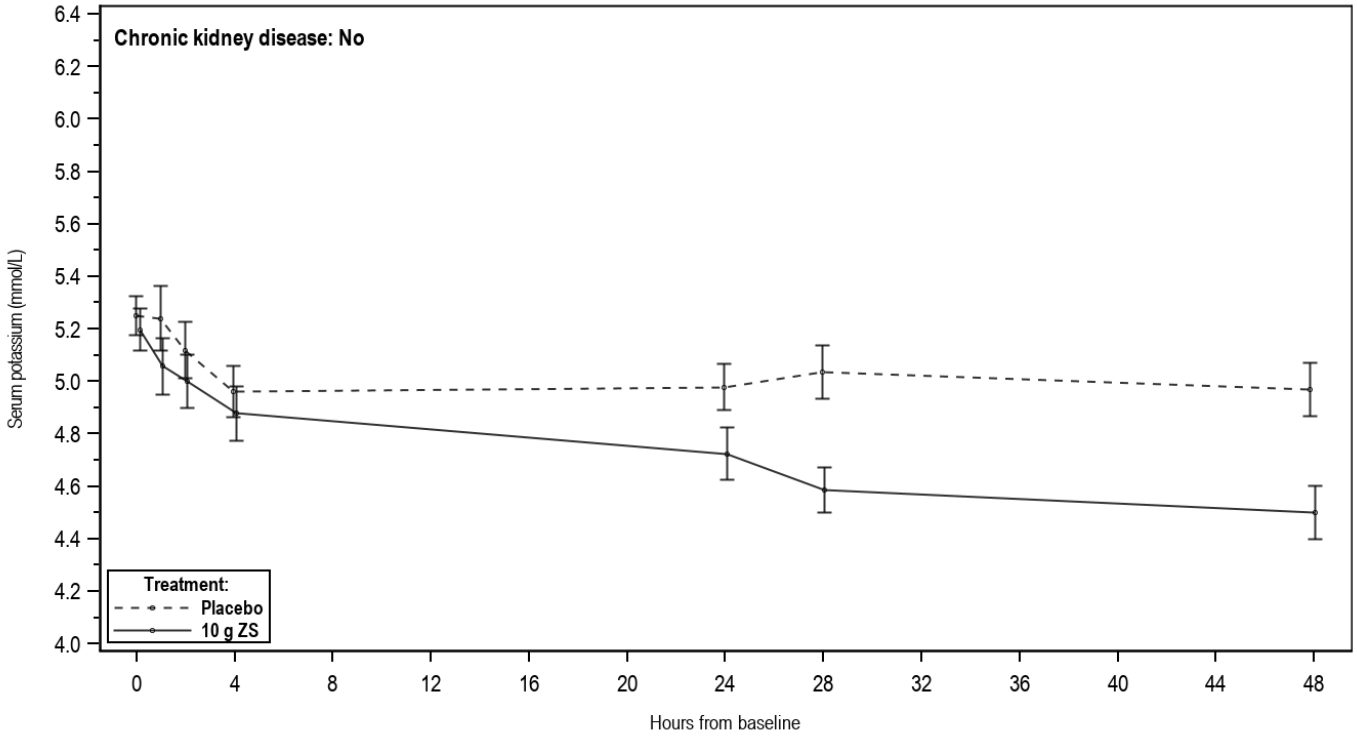


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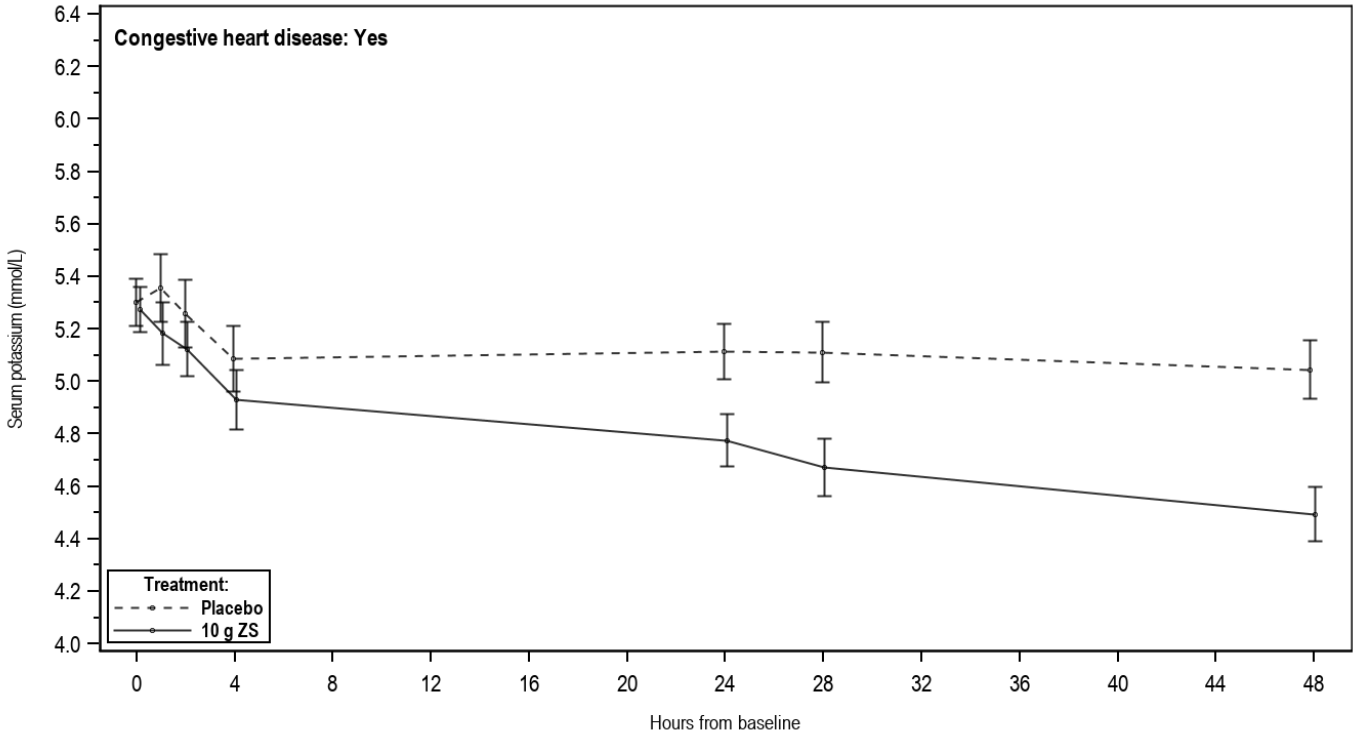


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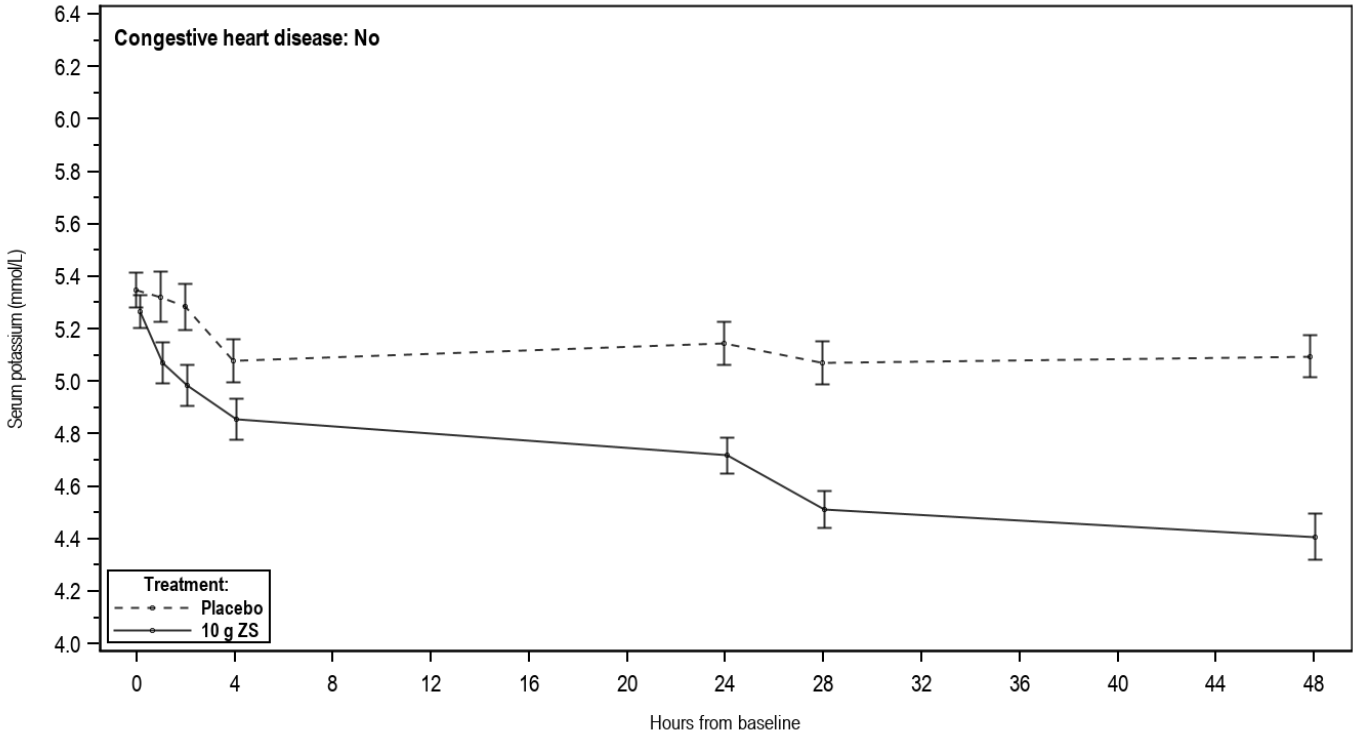


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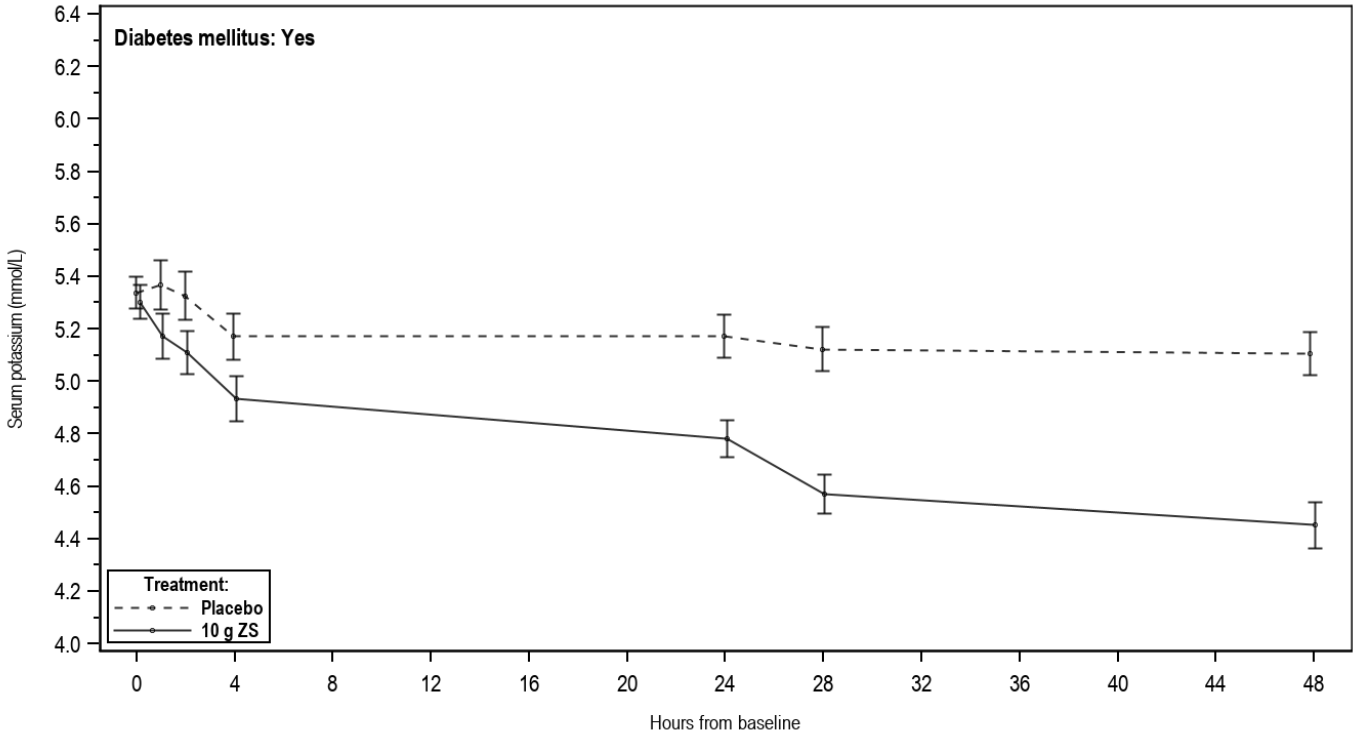


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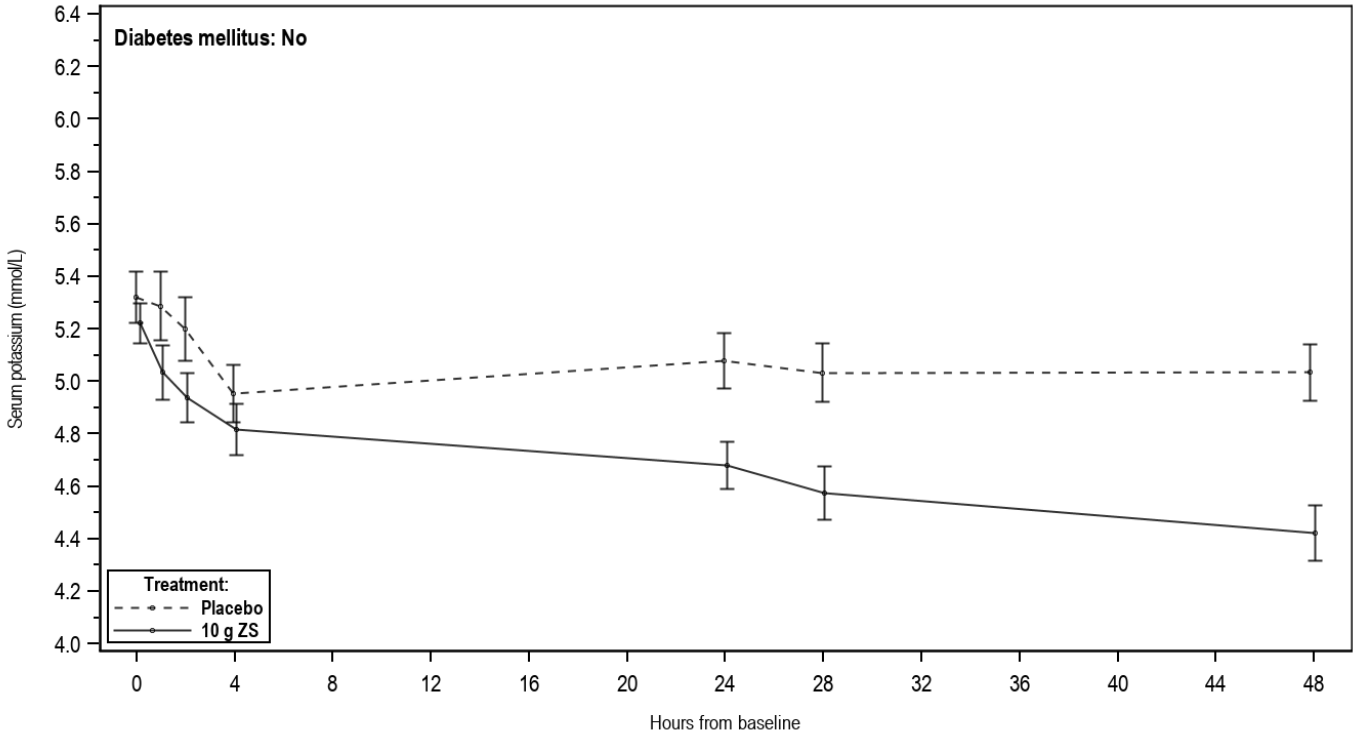


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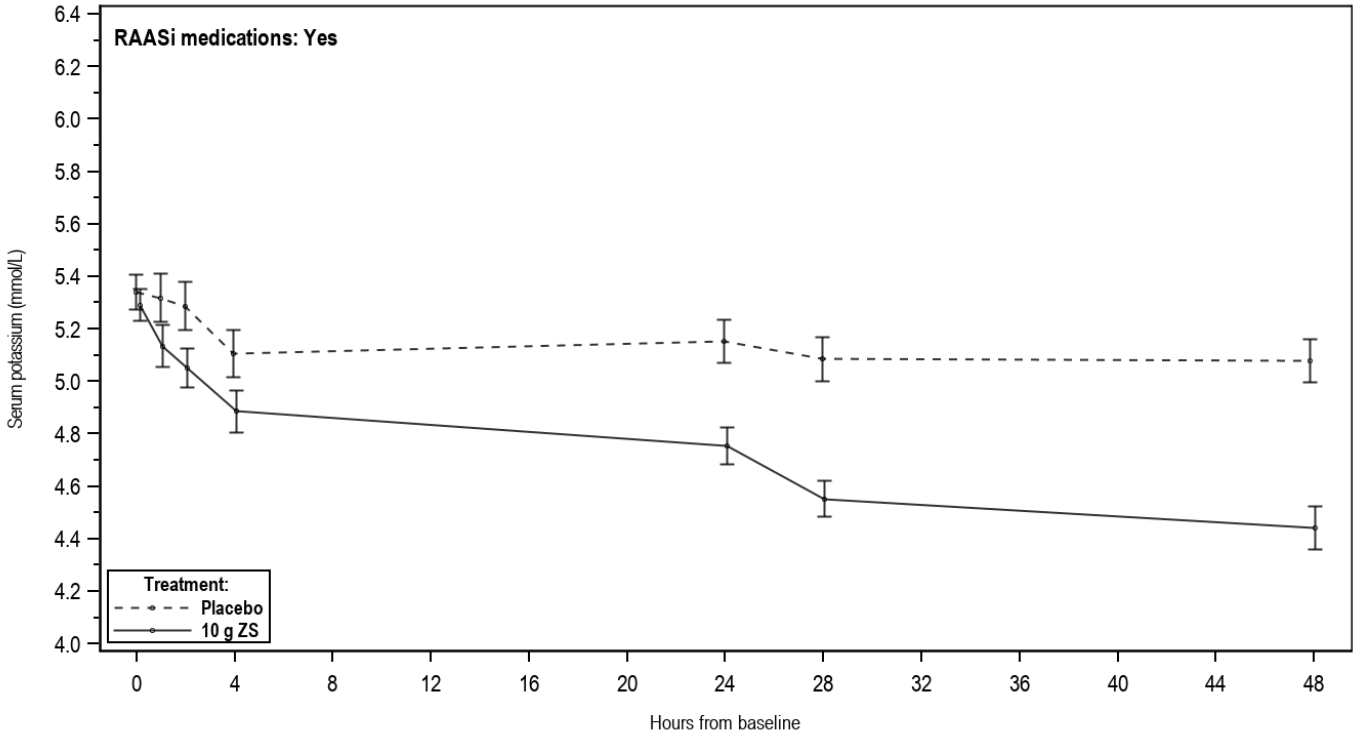


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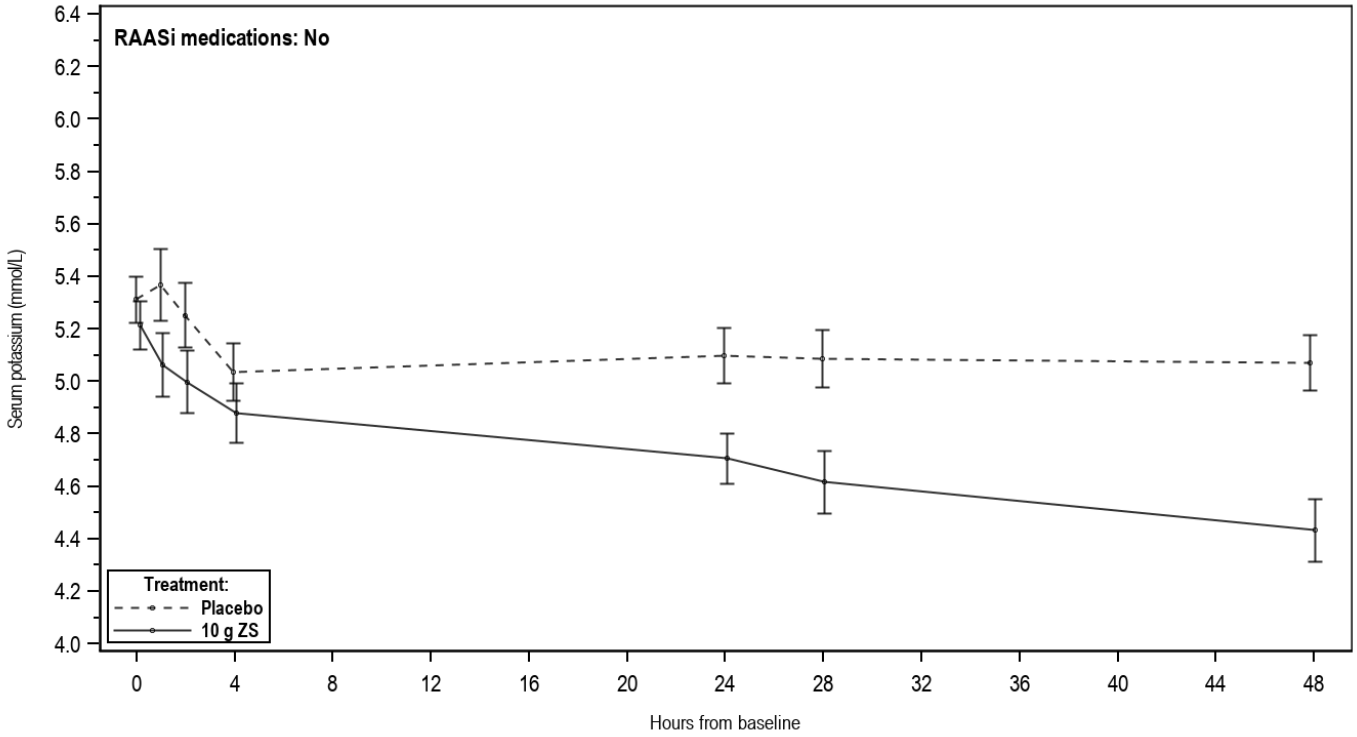


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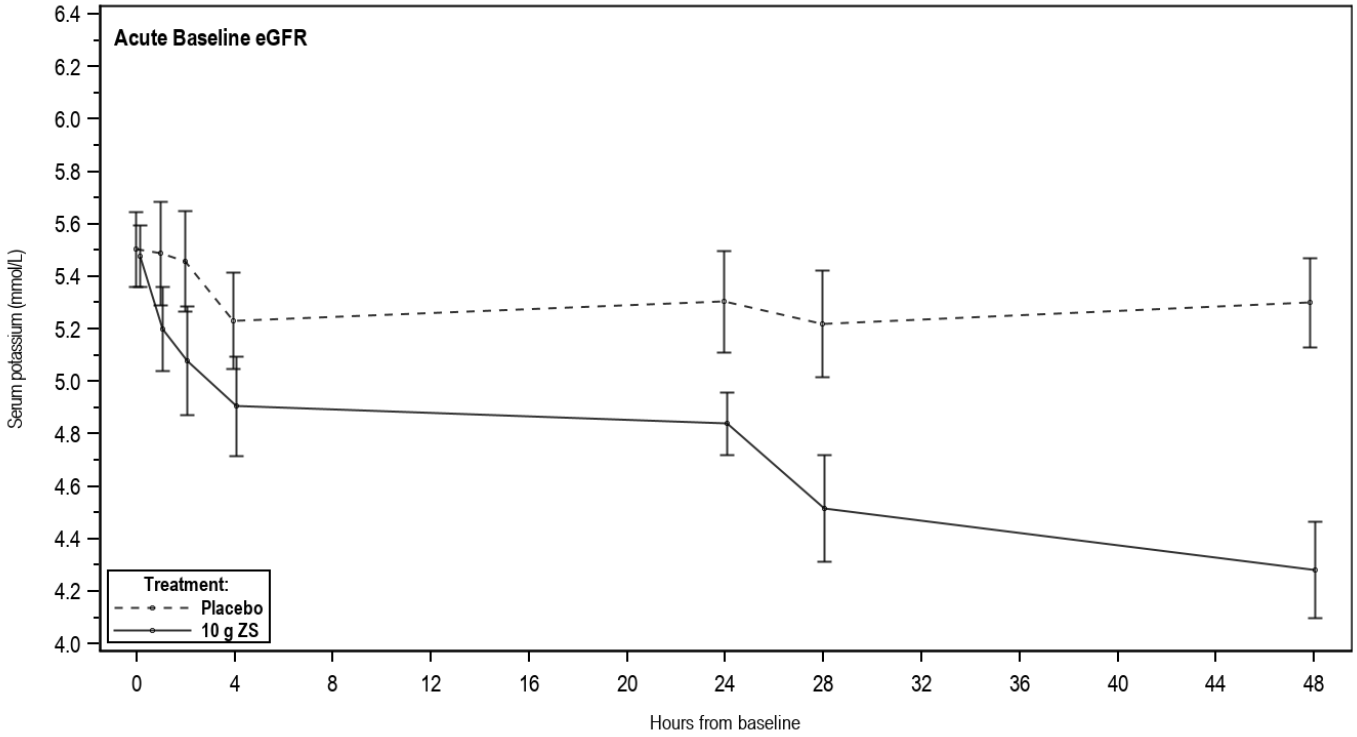


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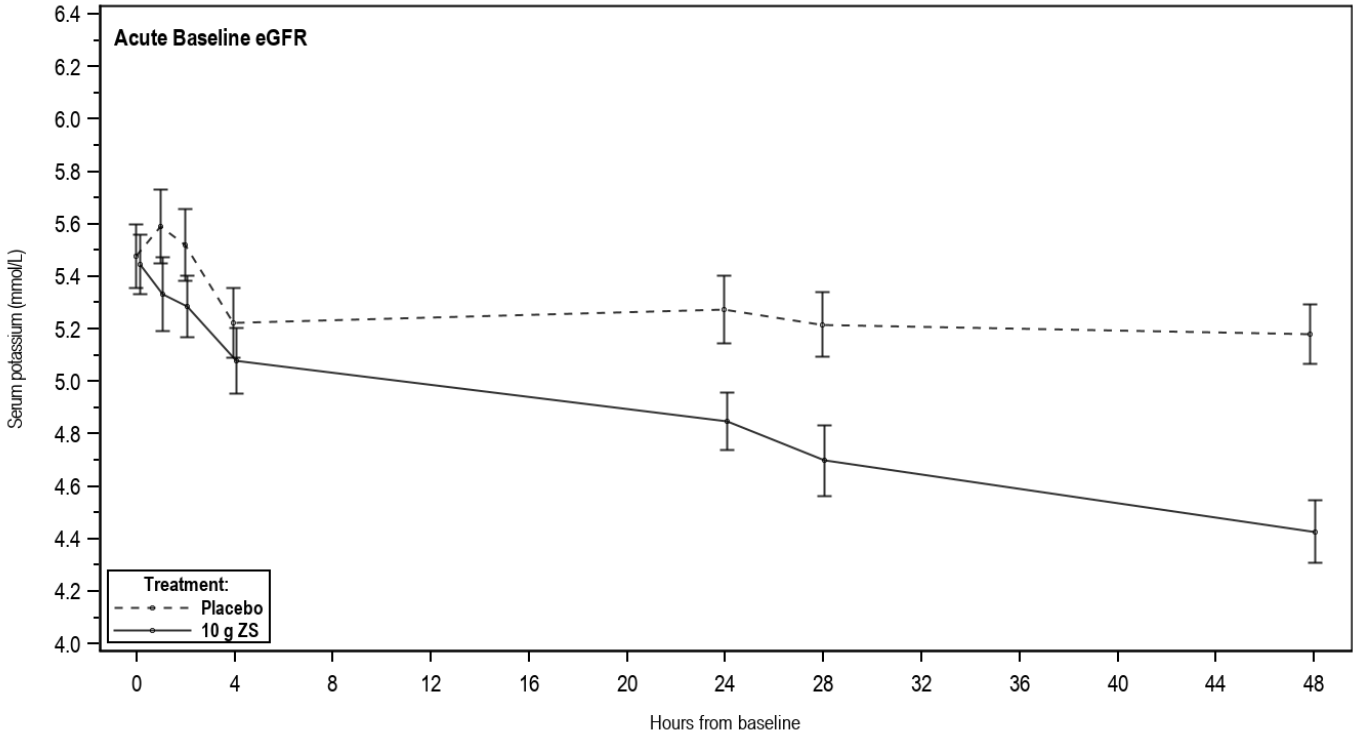


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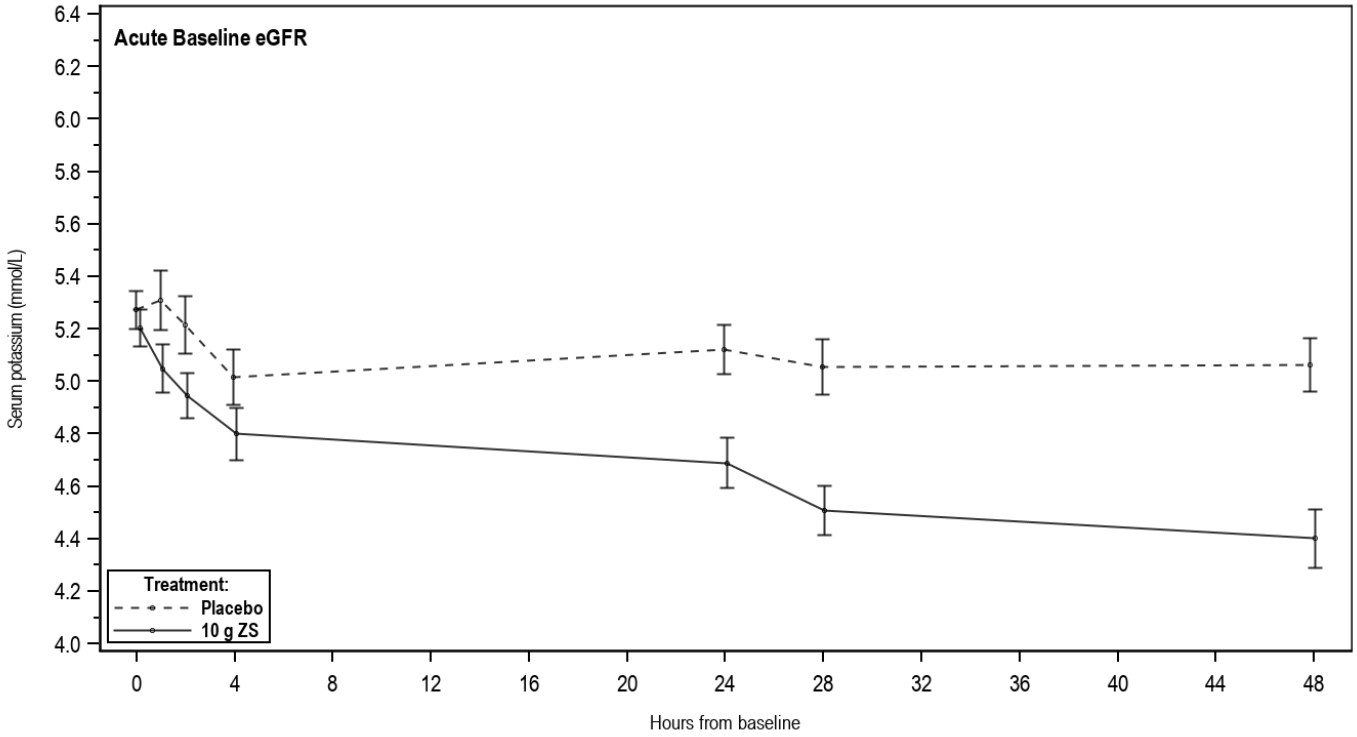


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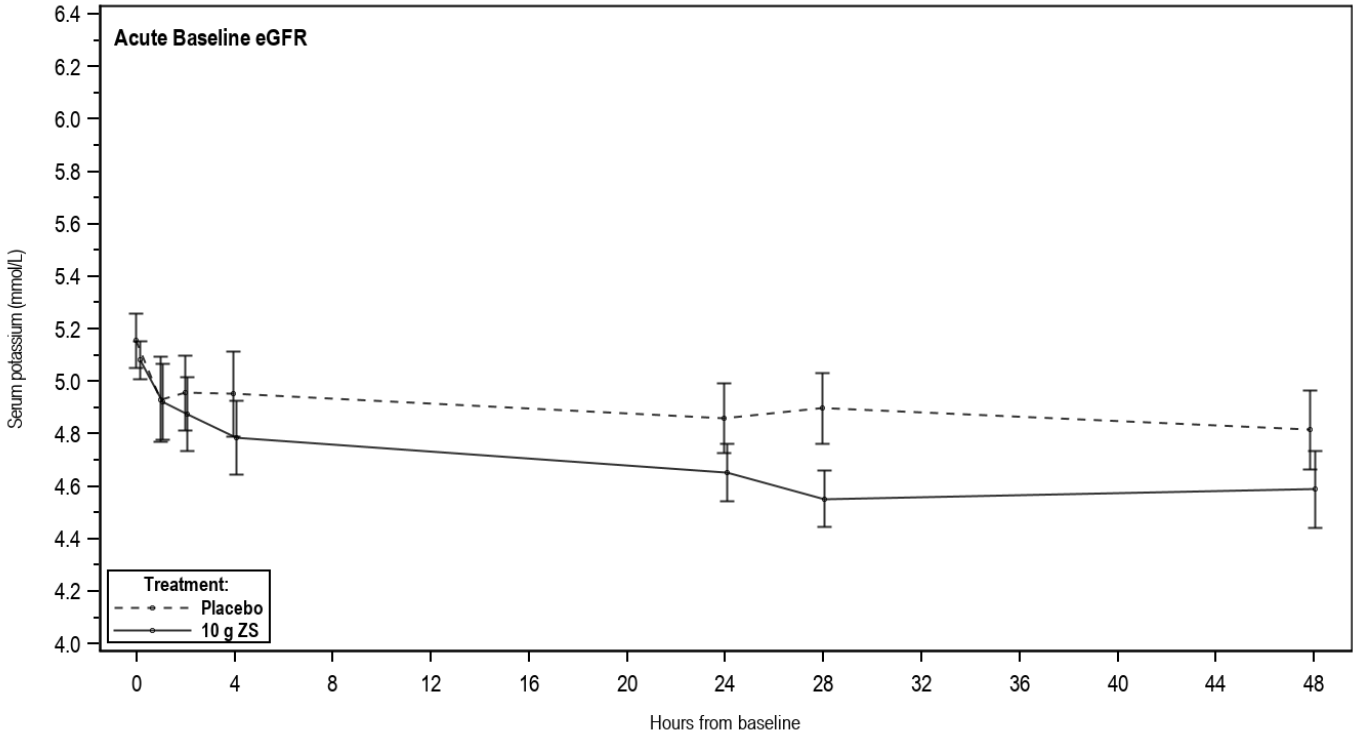


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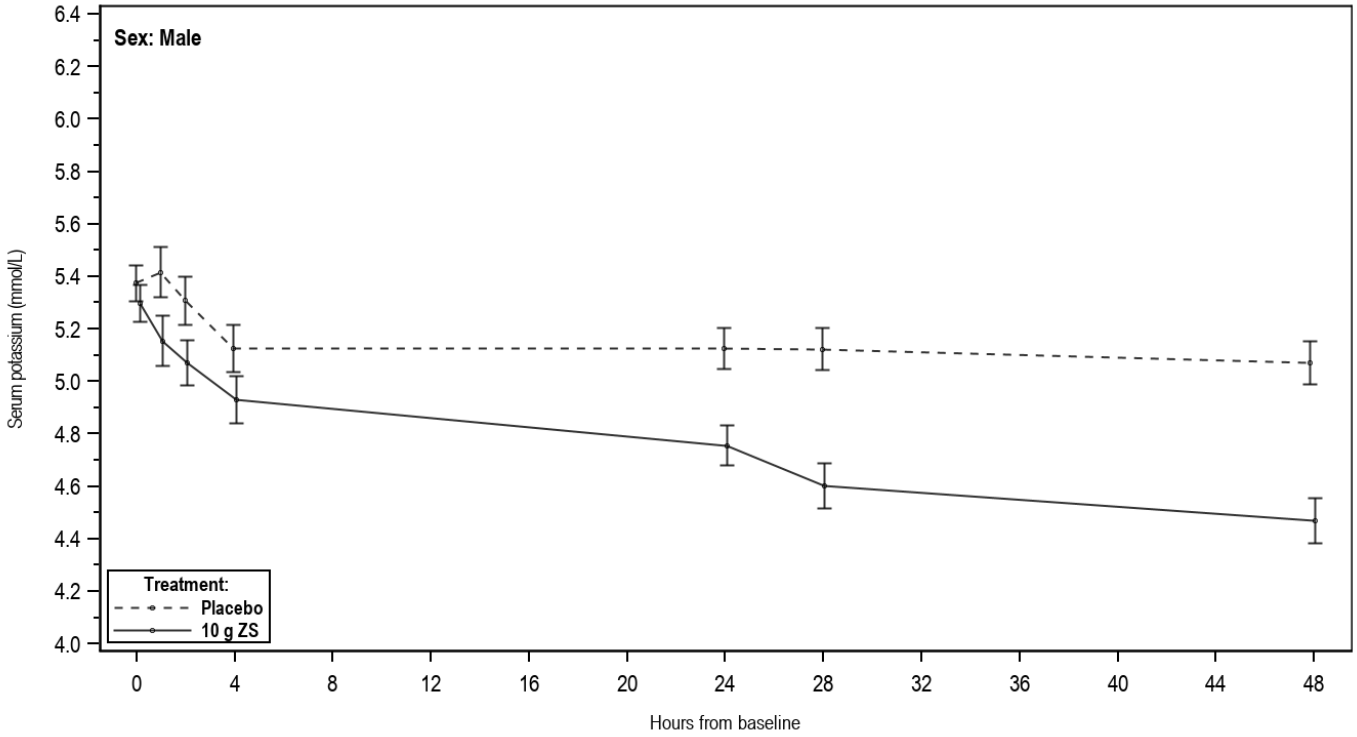


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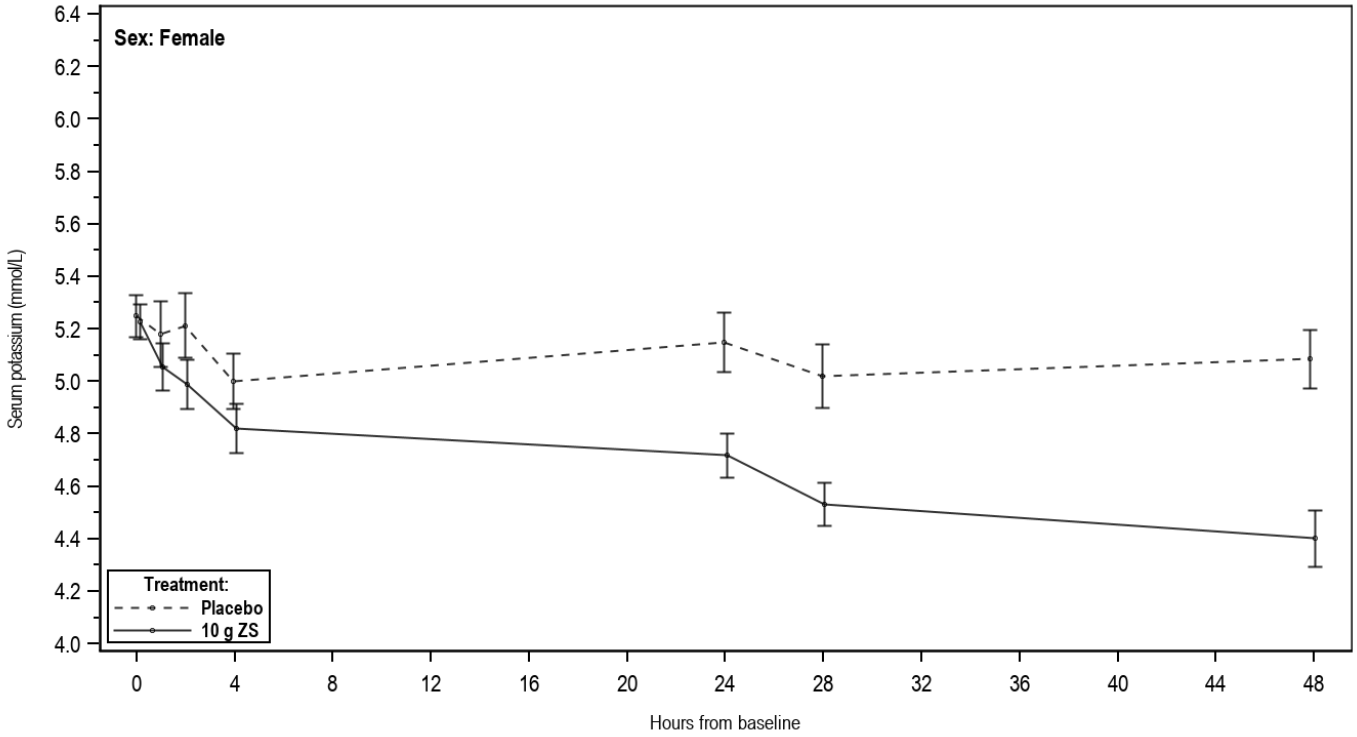


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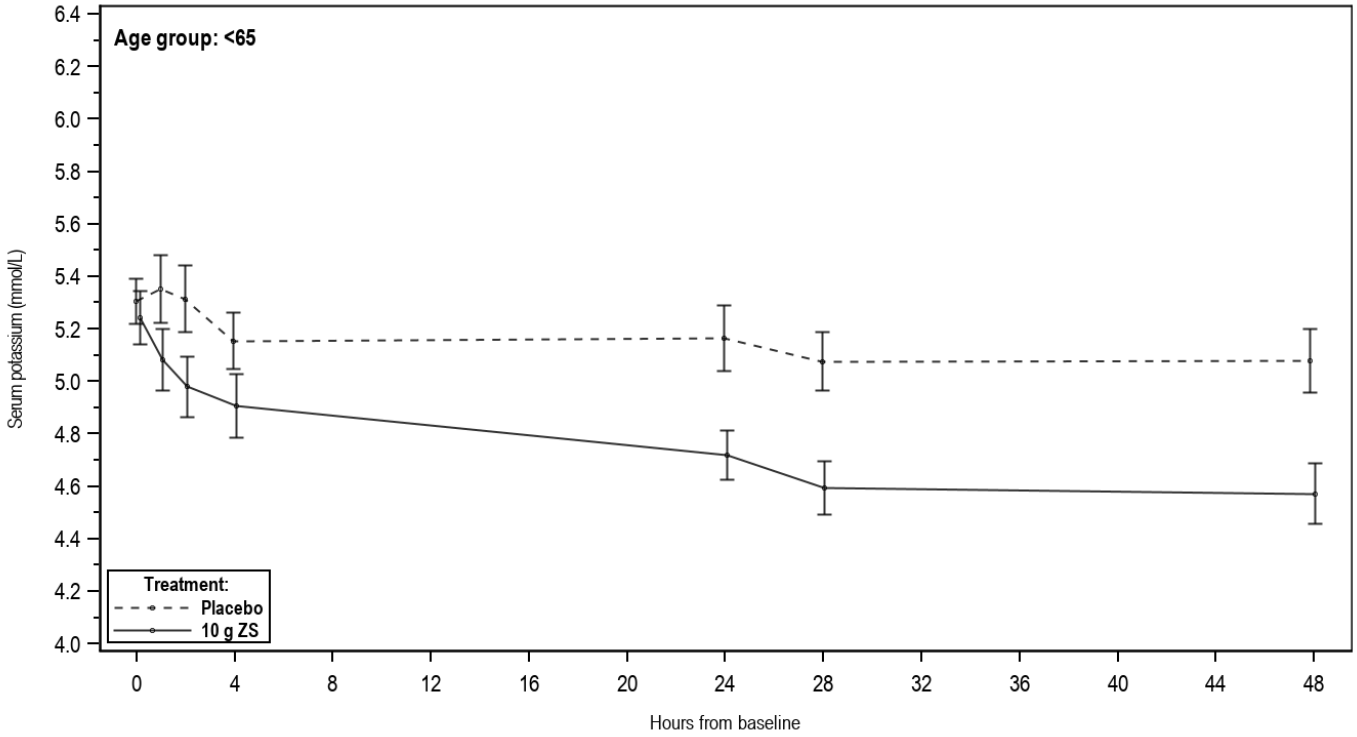


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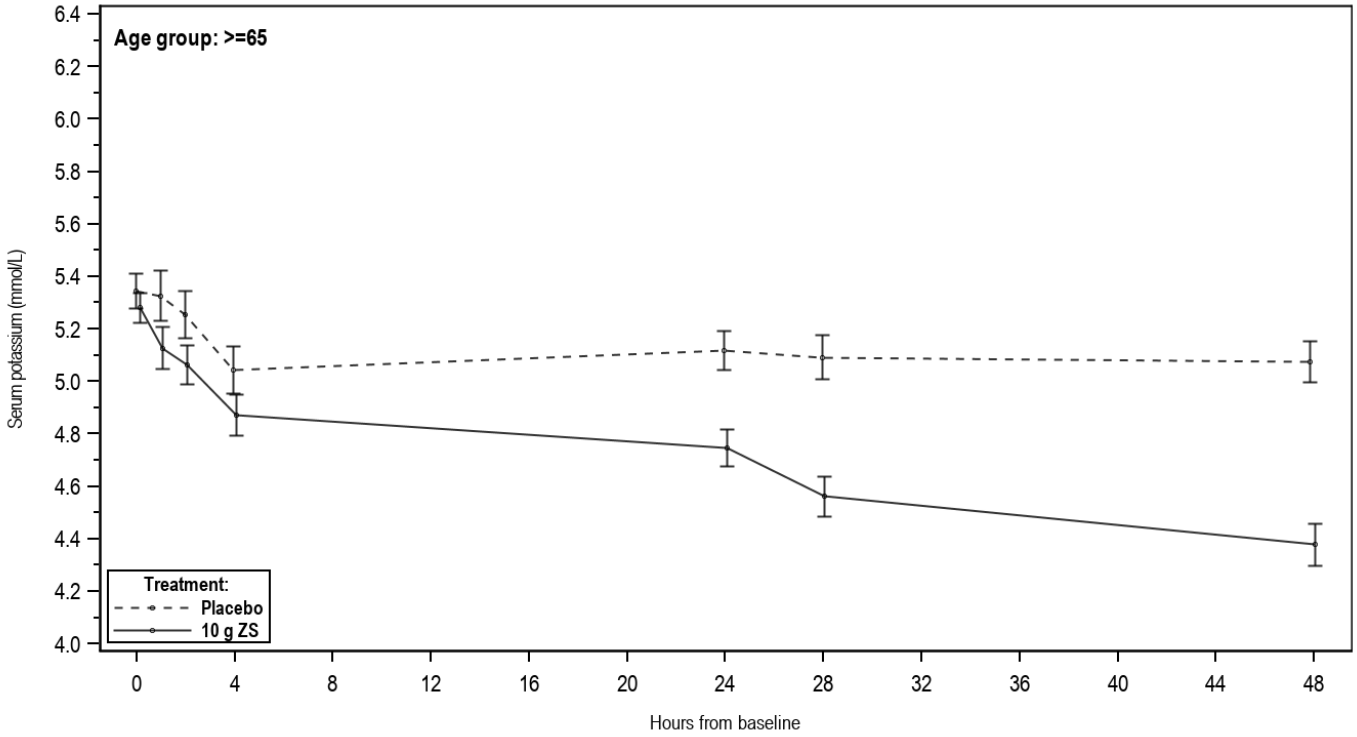


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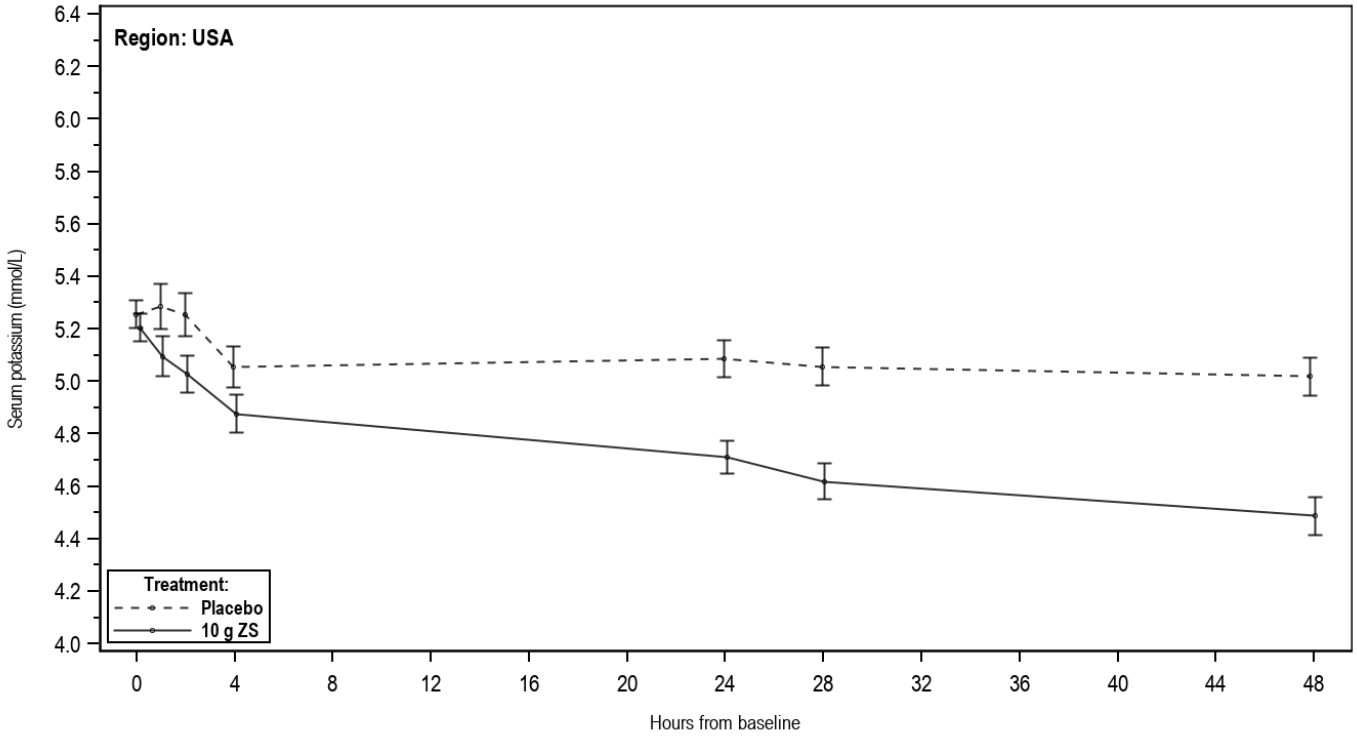


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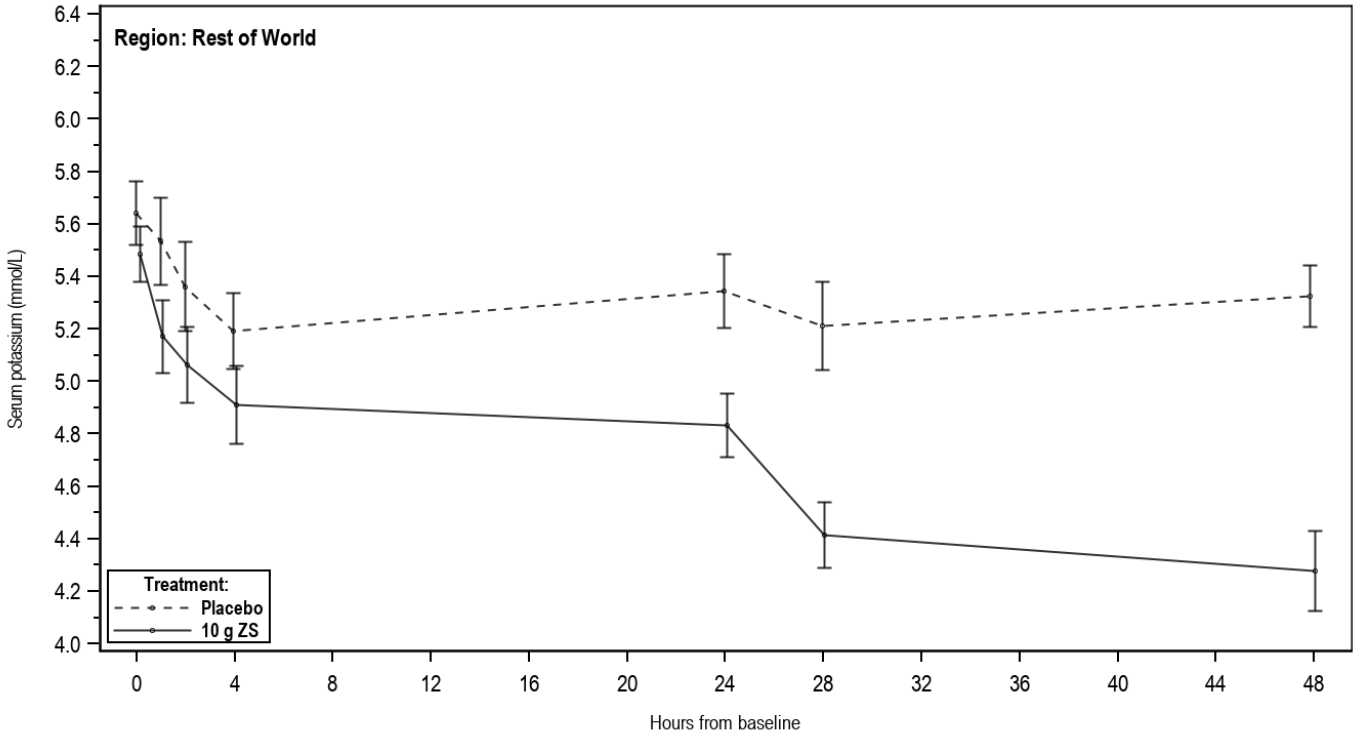


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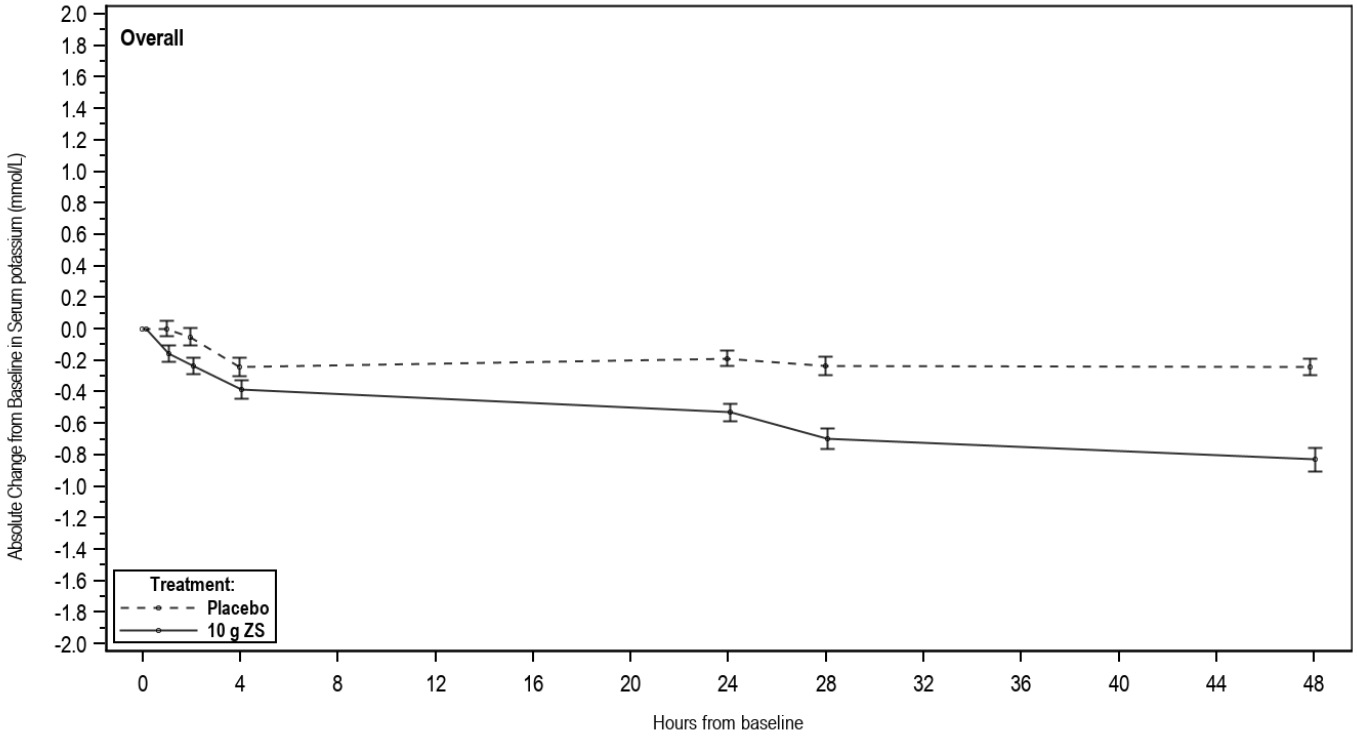


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Figure 3.1.2.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint)(95% Confidence Interval): absolute change from baseline, ZS 10g TID vs. combined placebo (Intent-to-treat population)

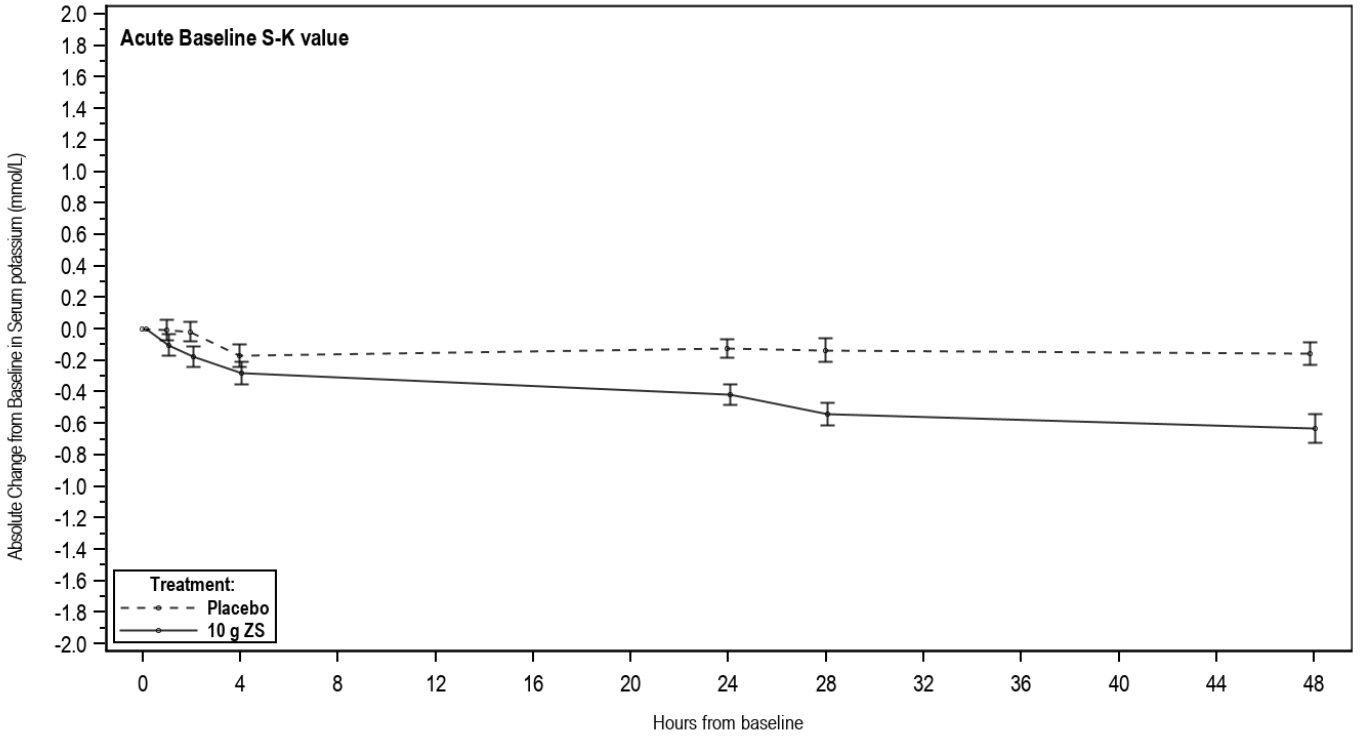


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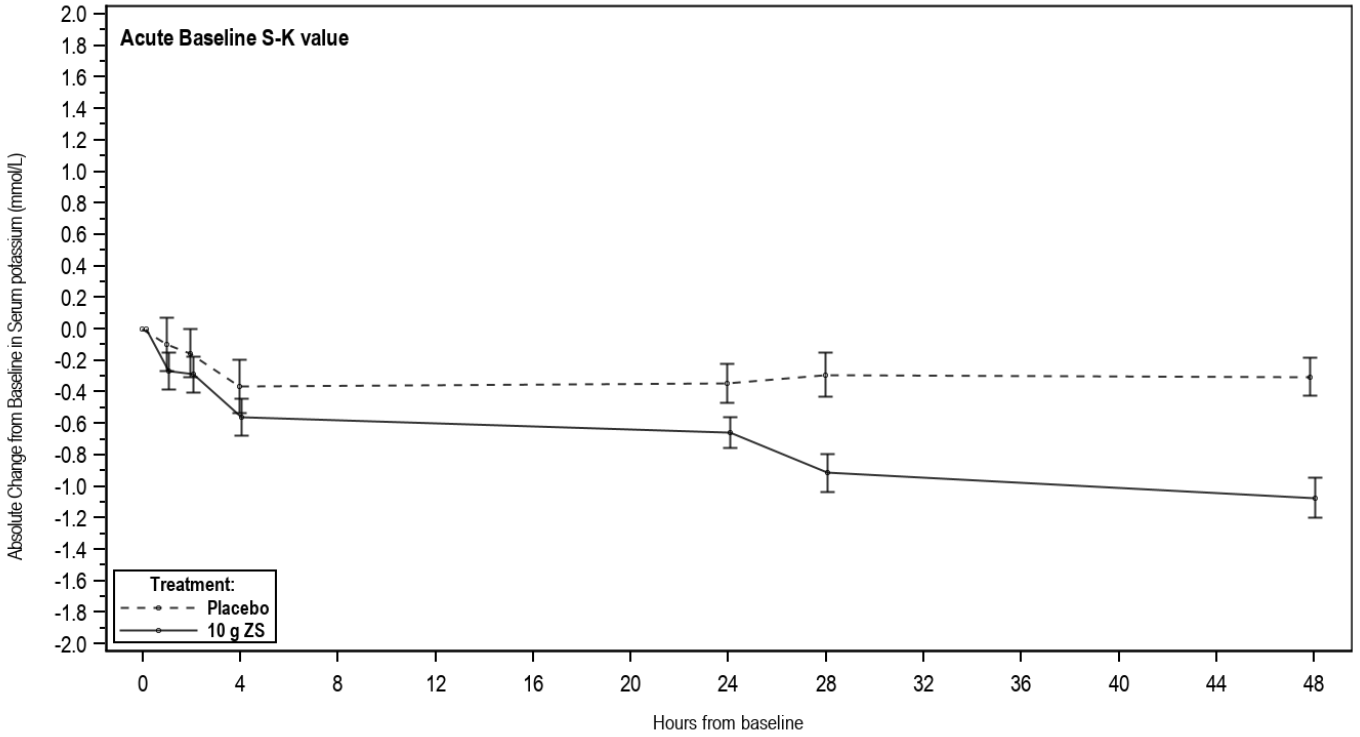


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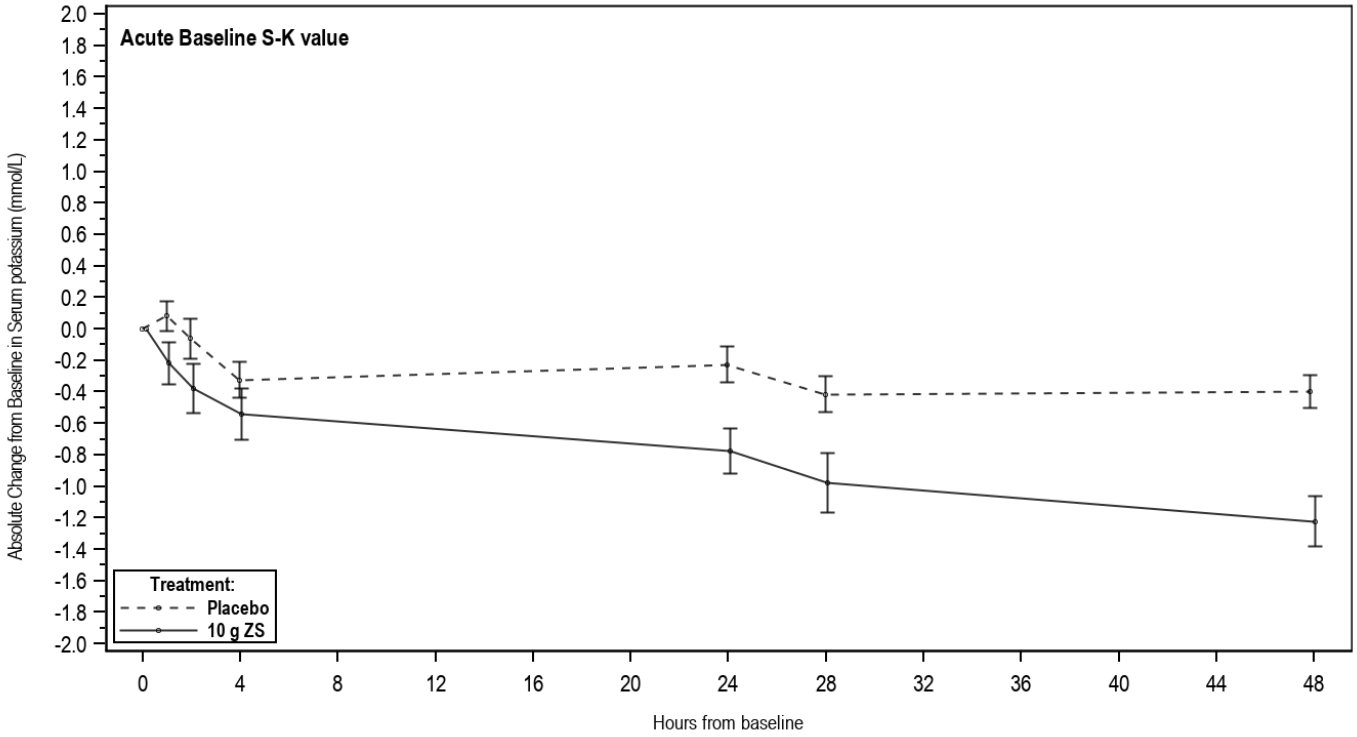


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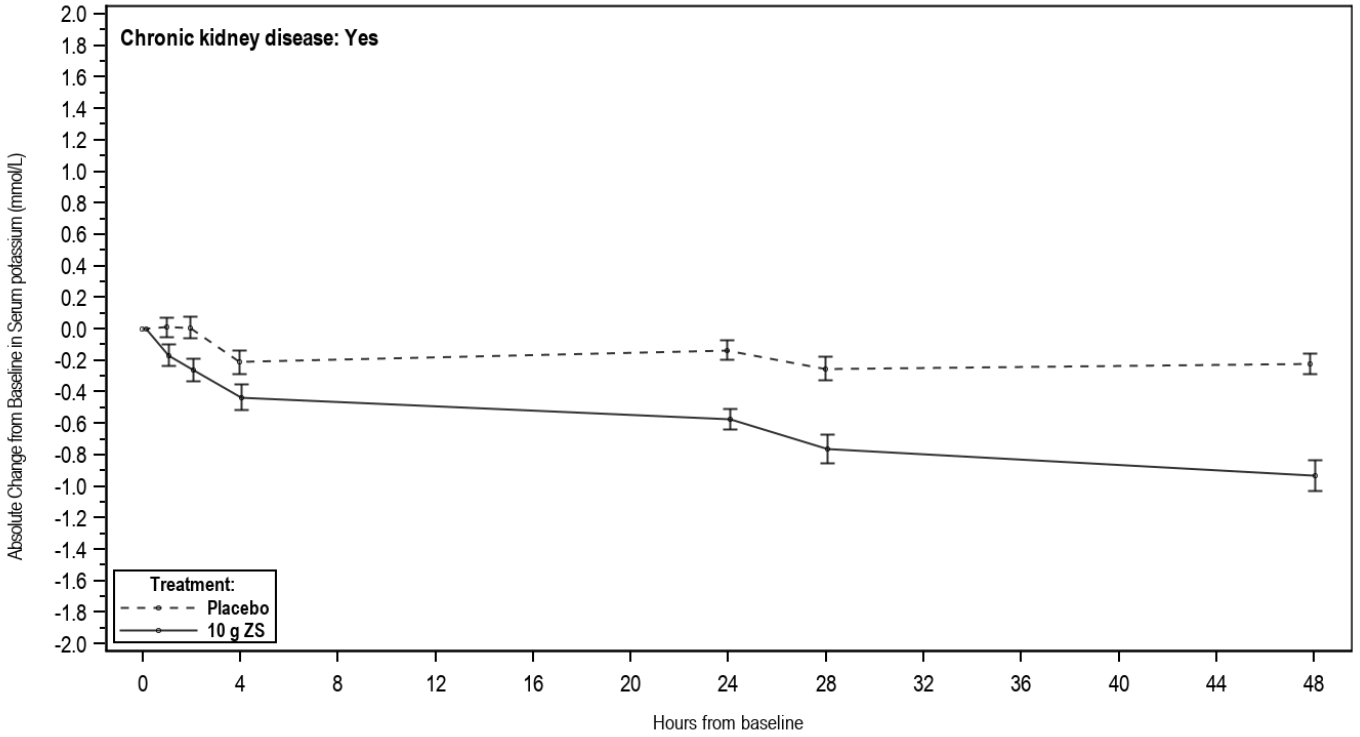


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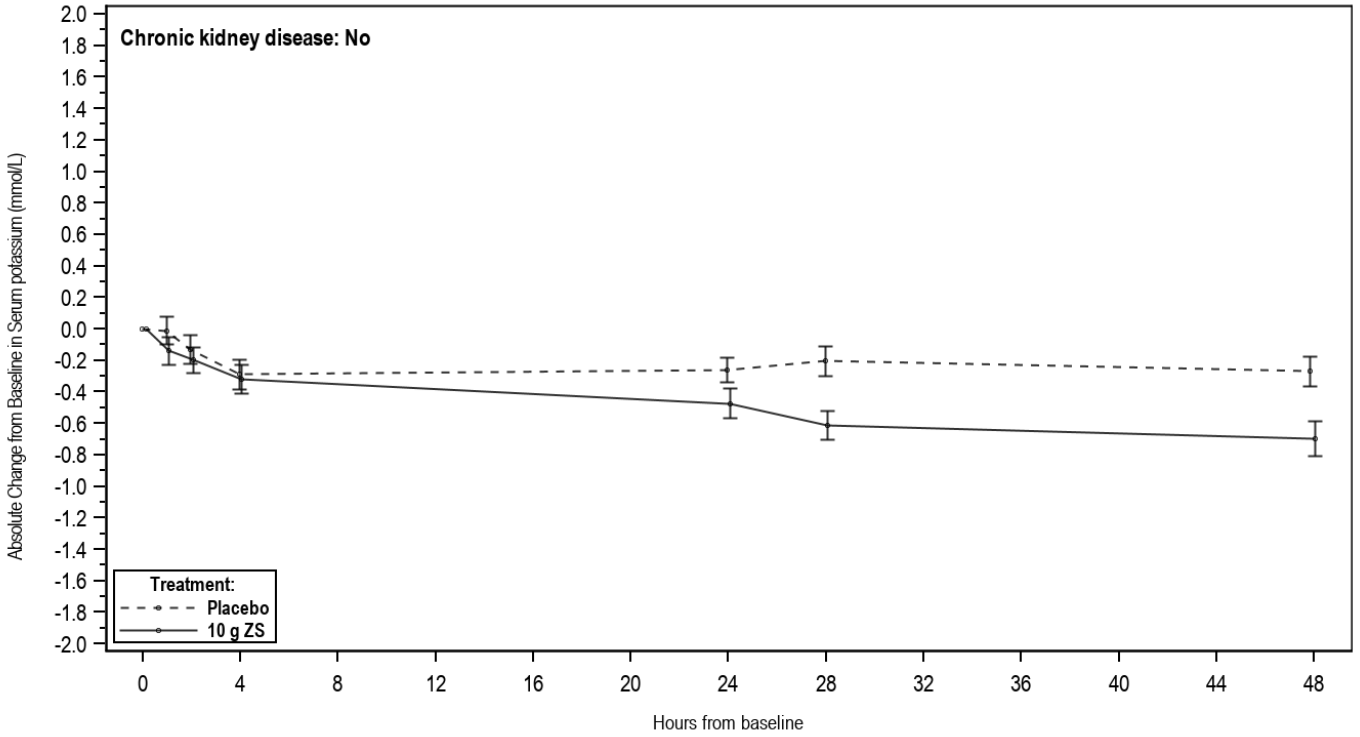


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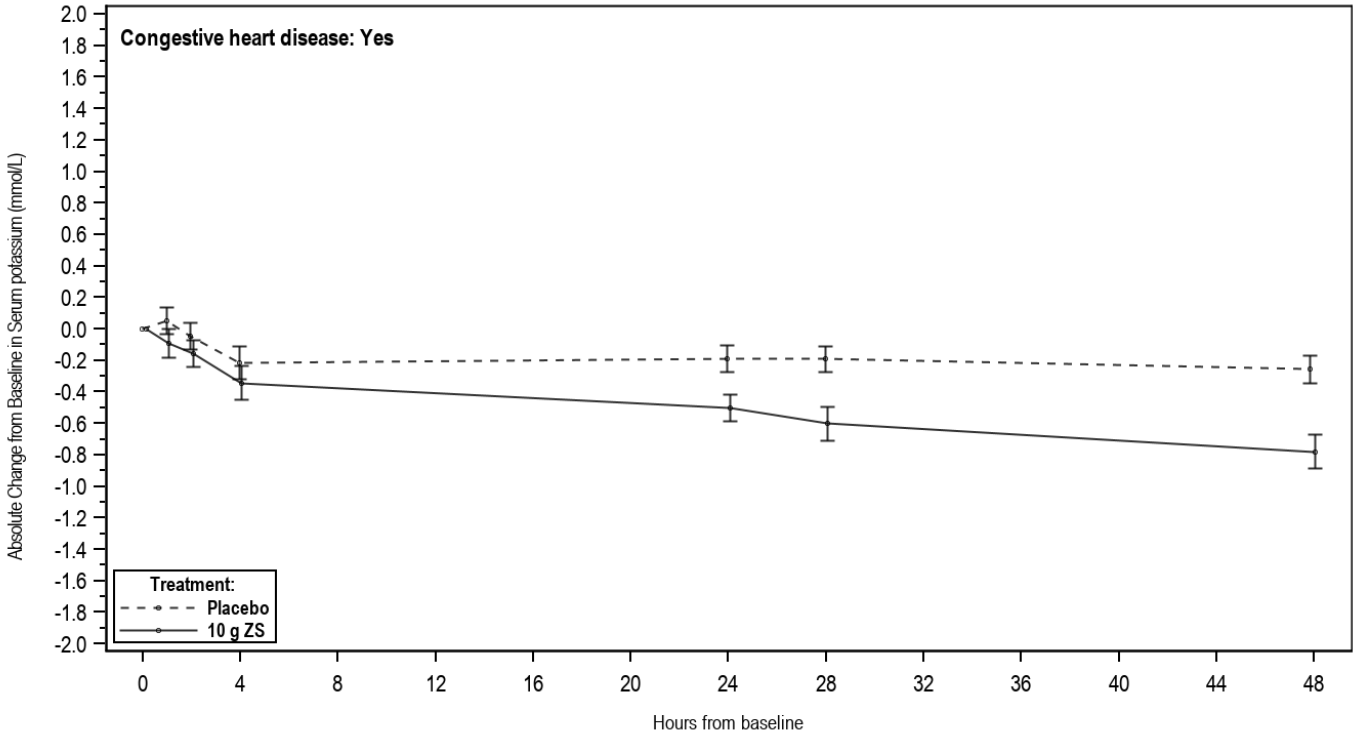


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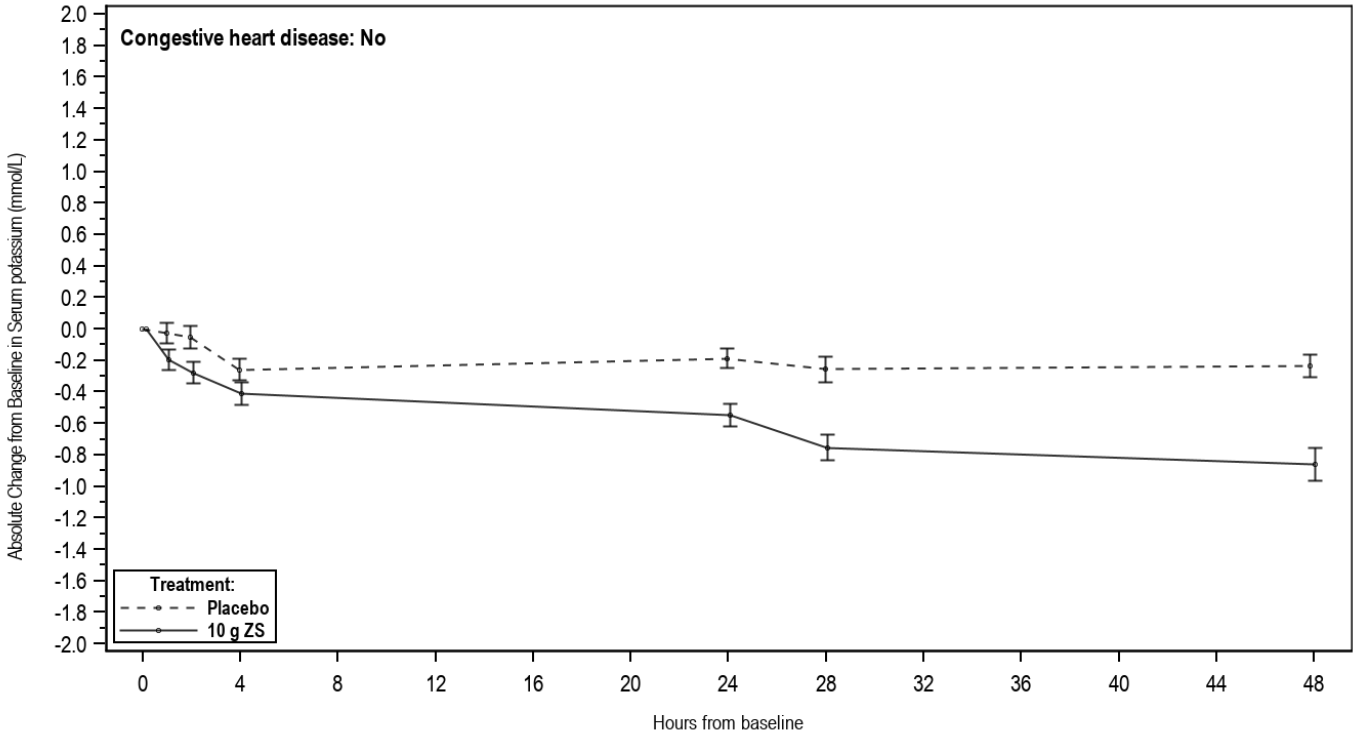


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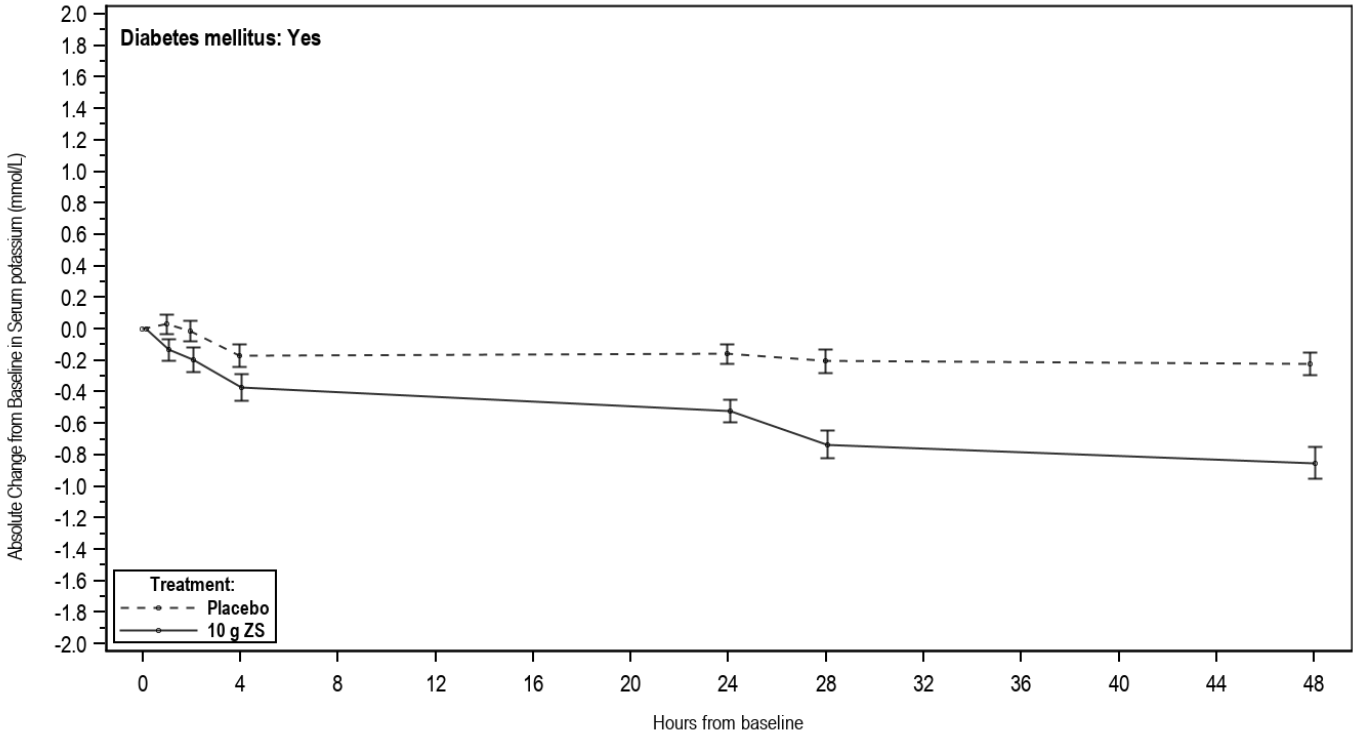


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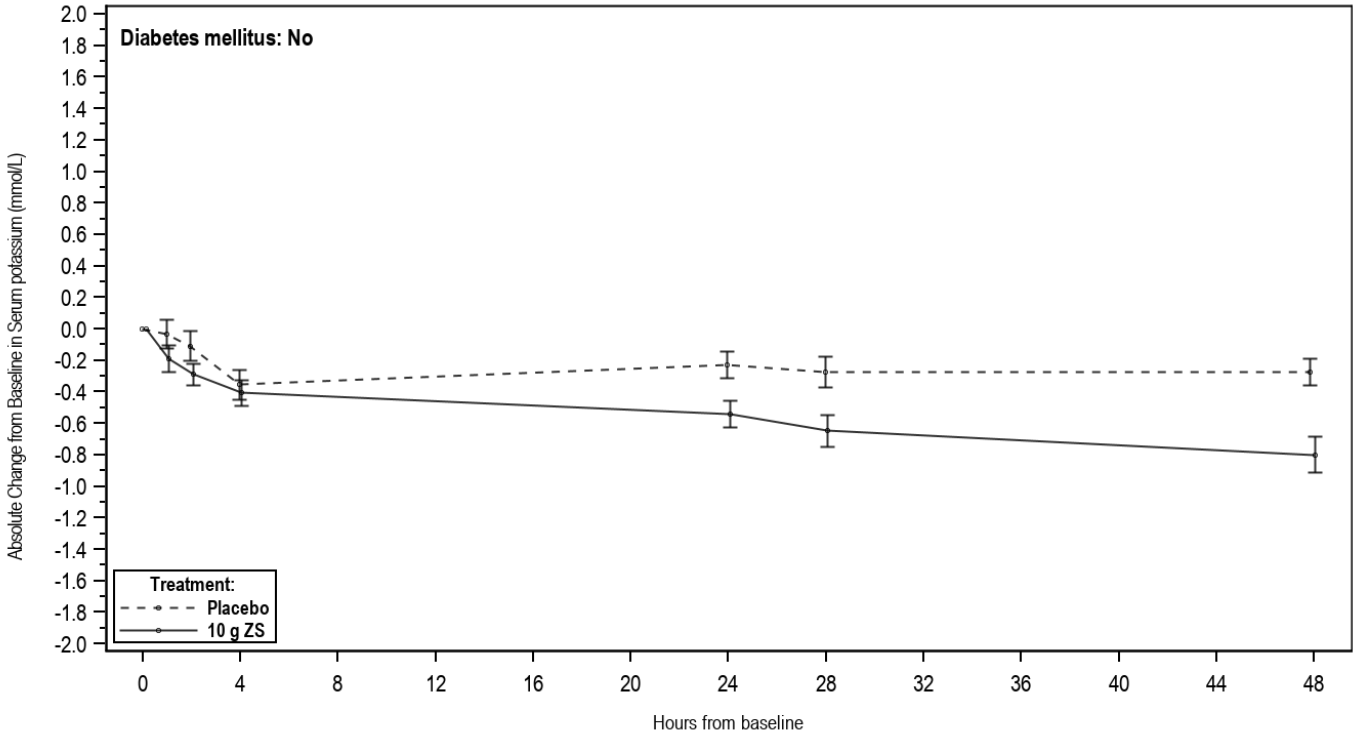


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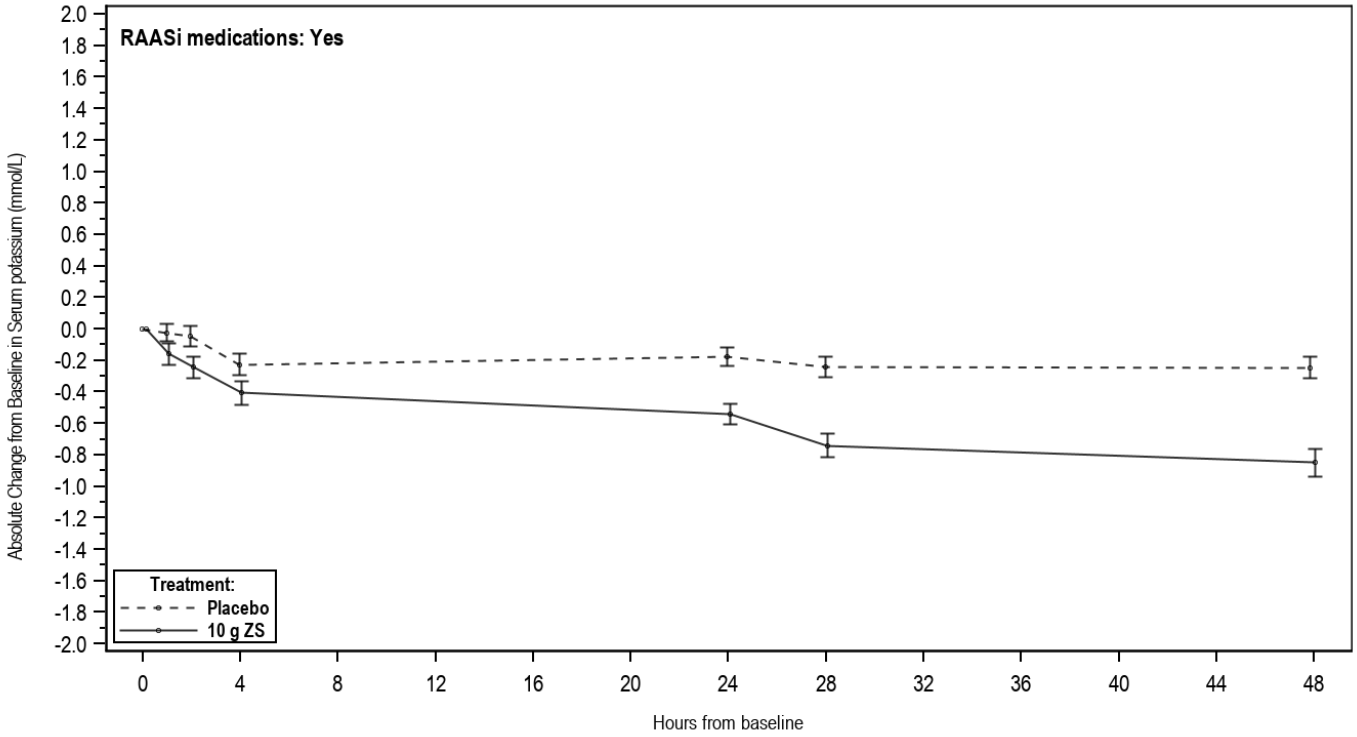


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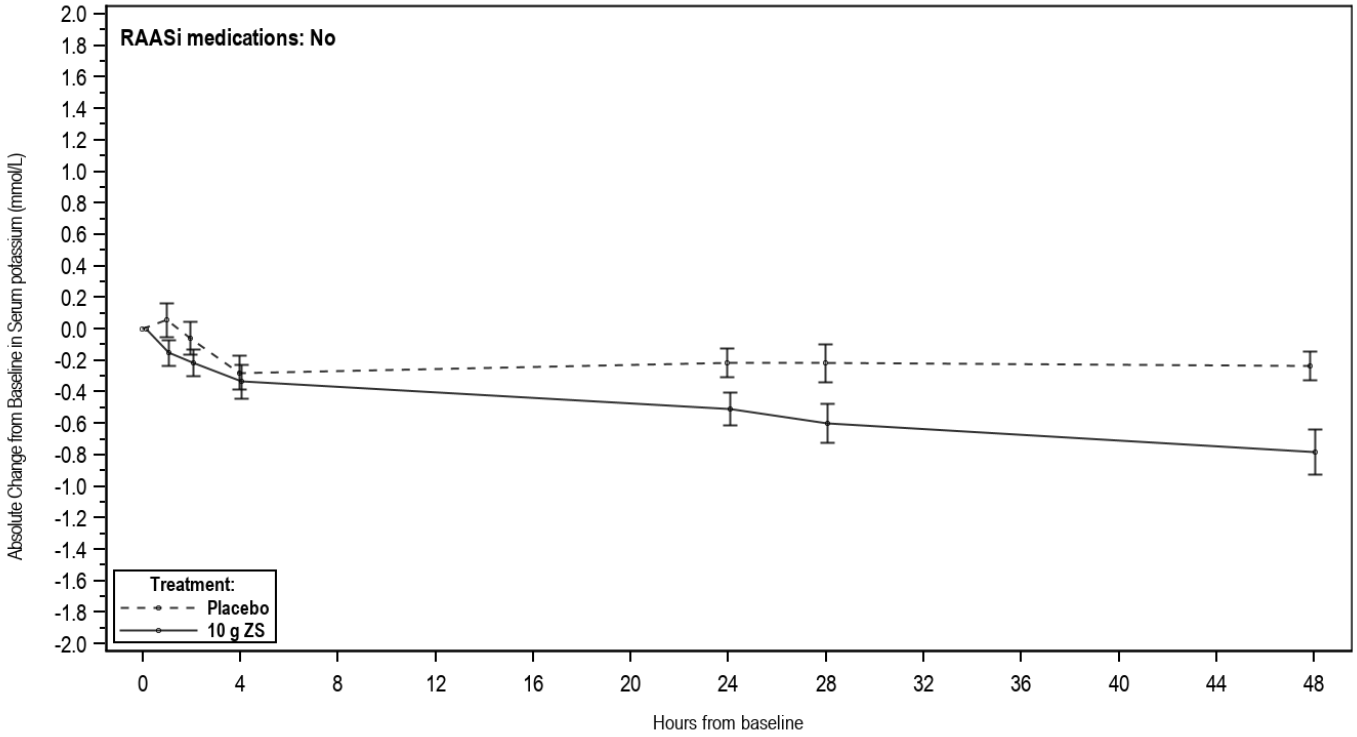


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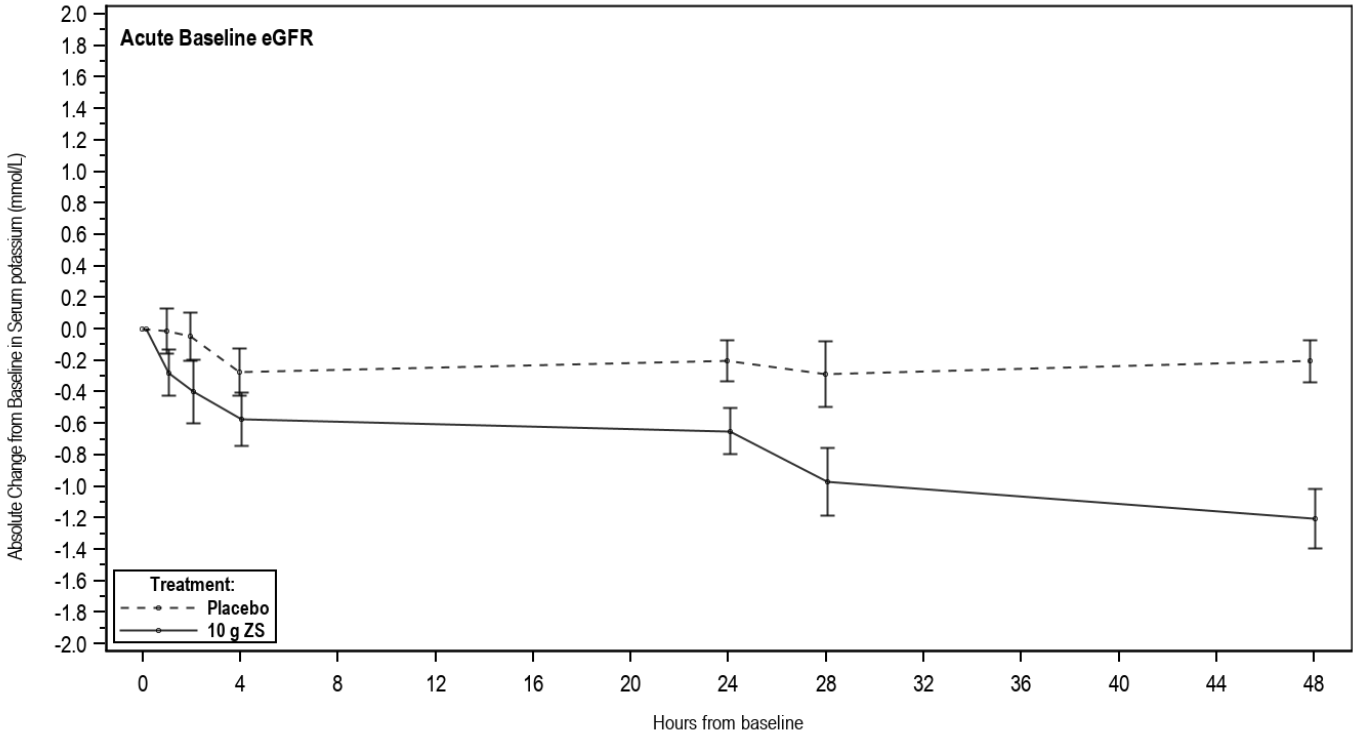


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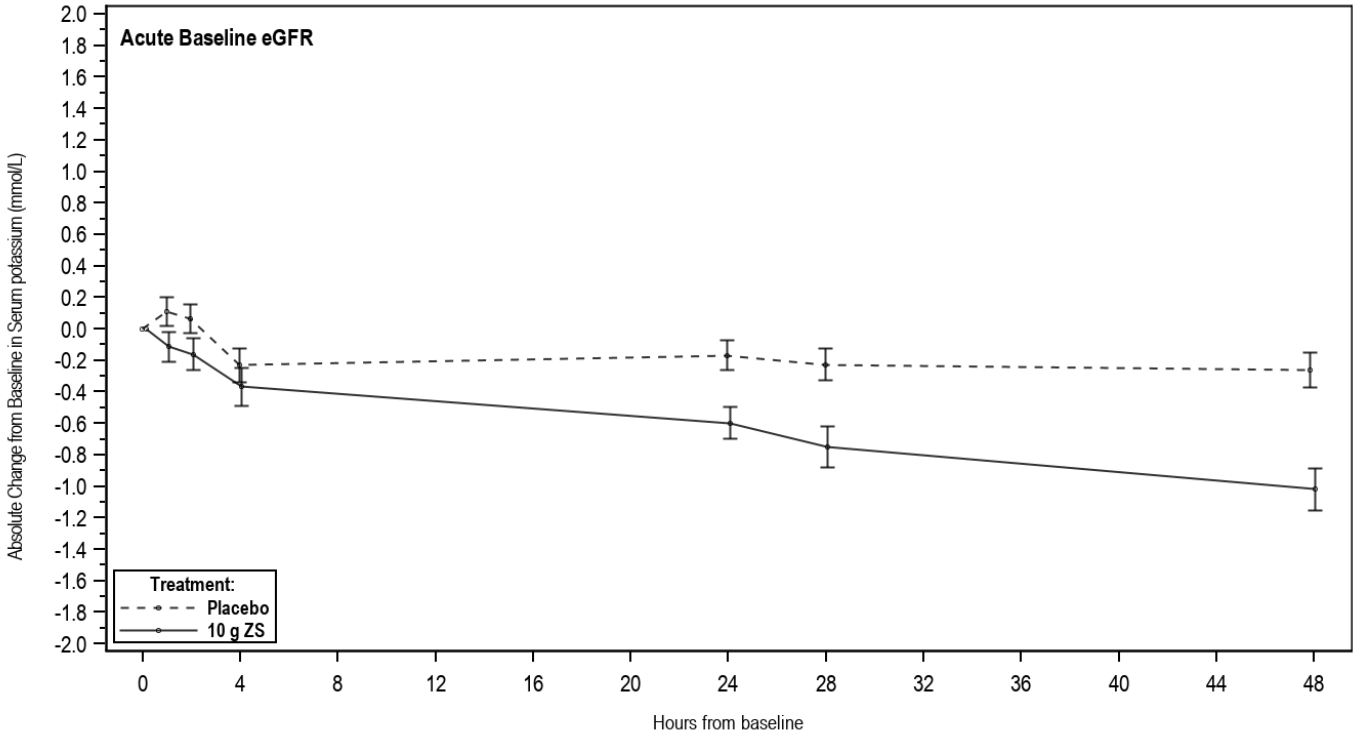


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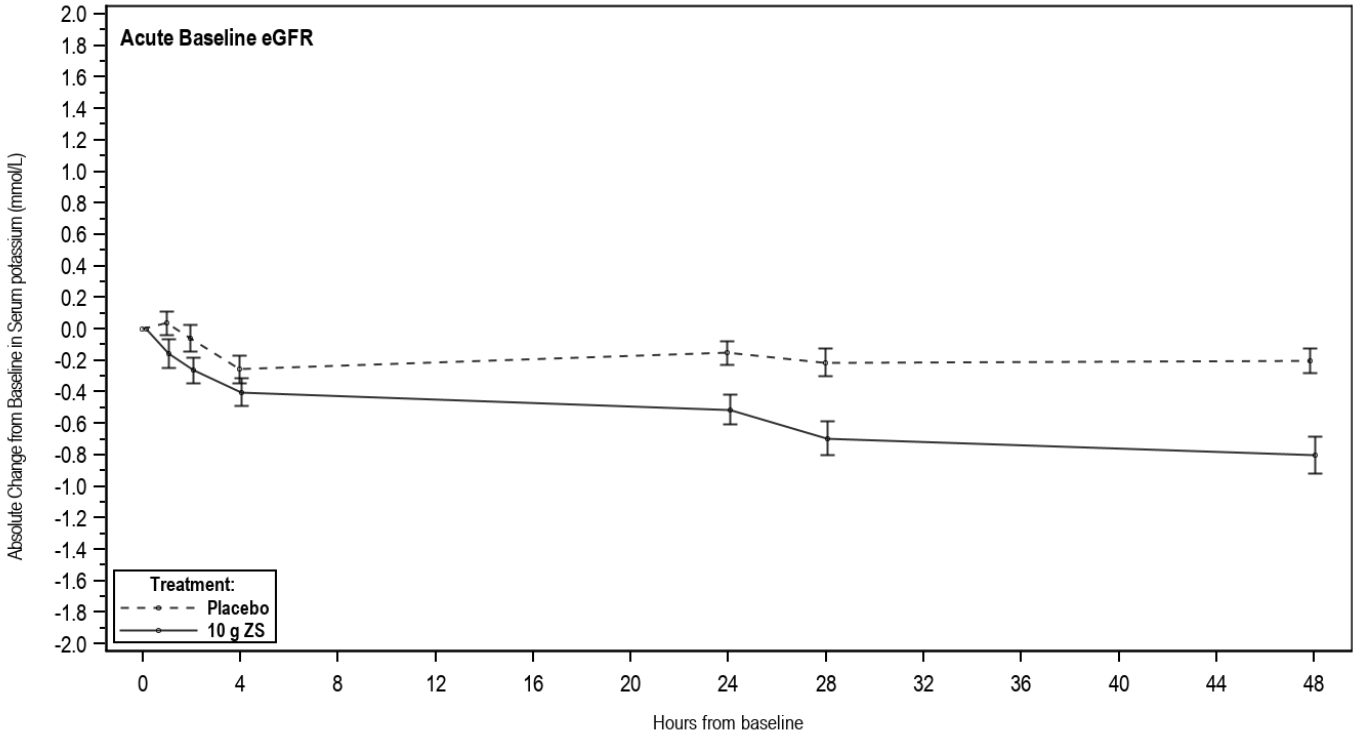


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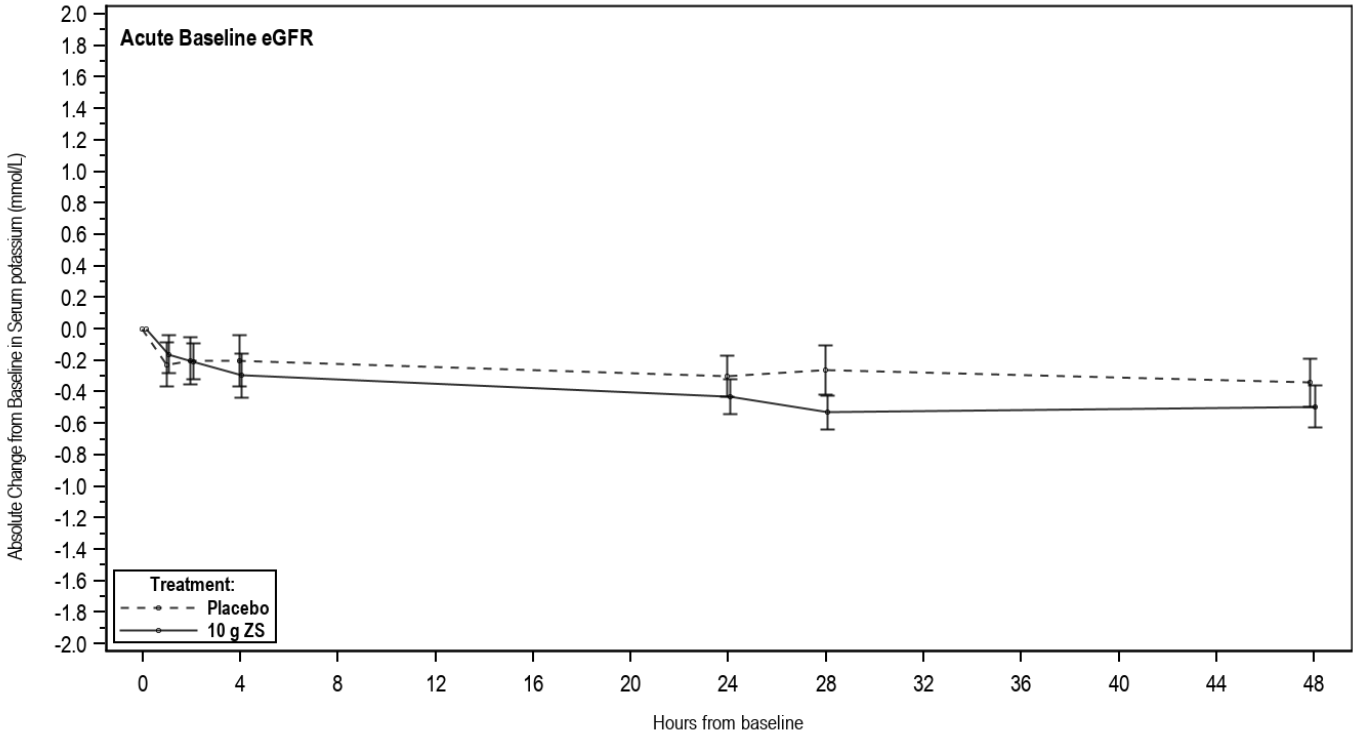


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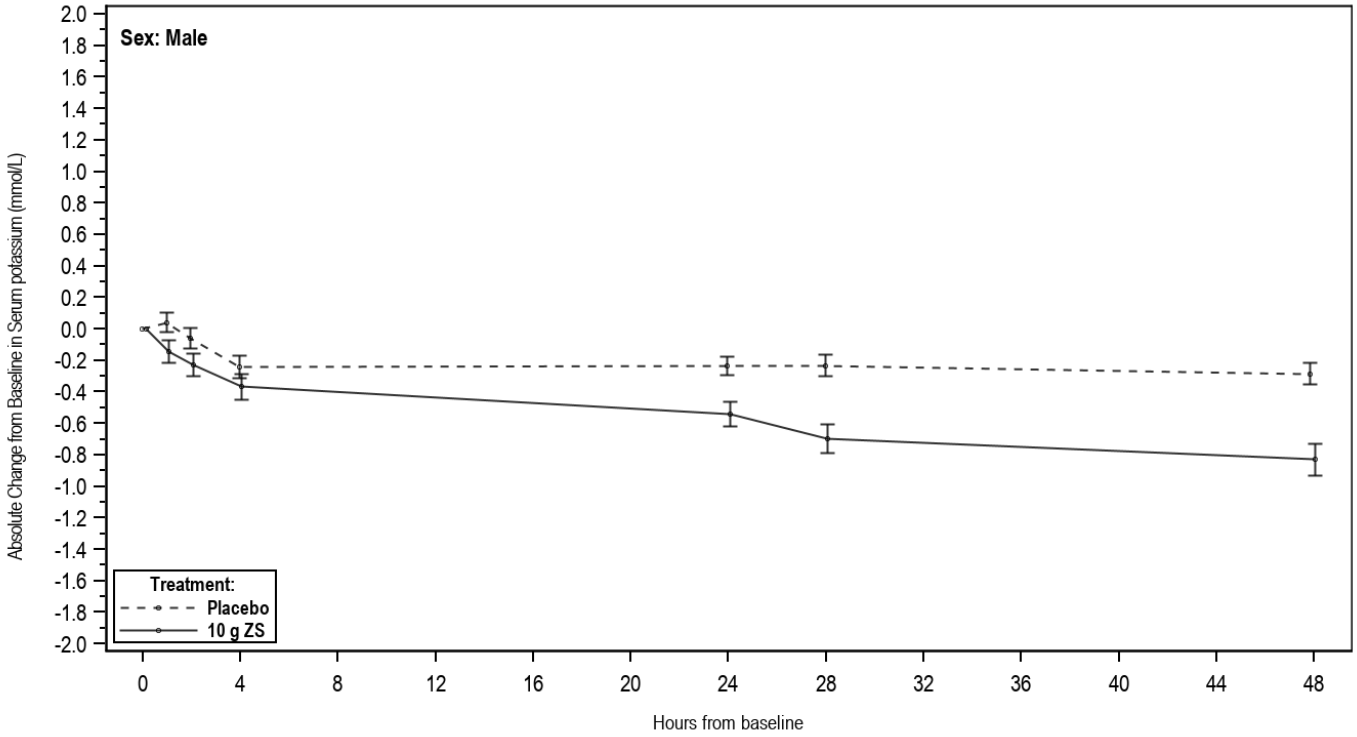


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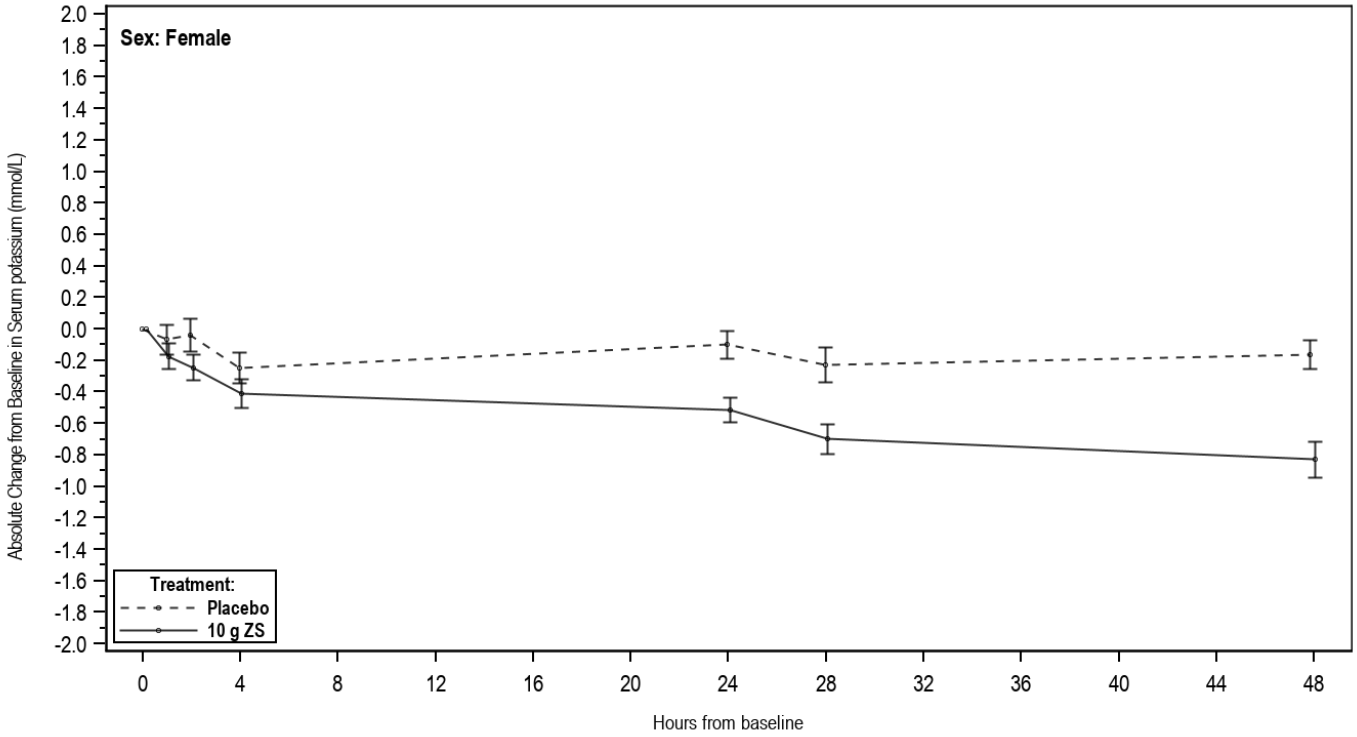


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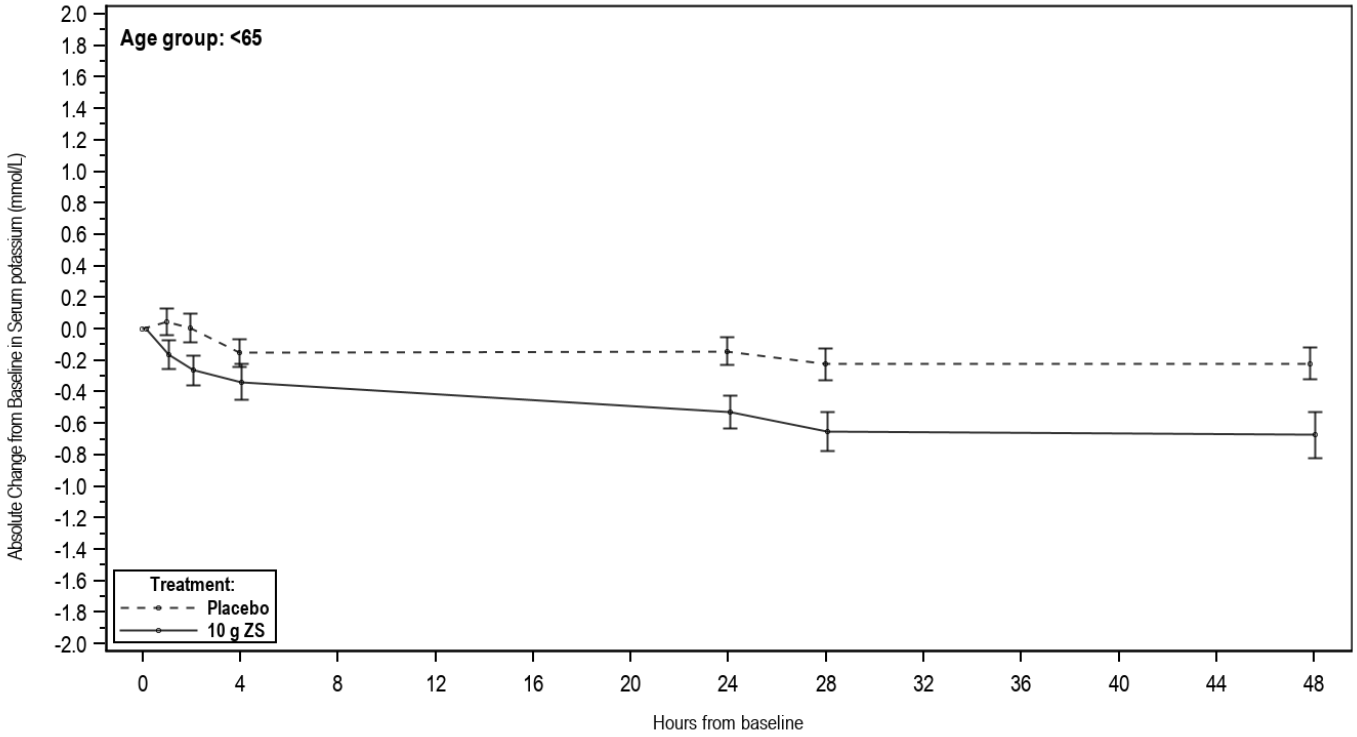


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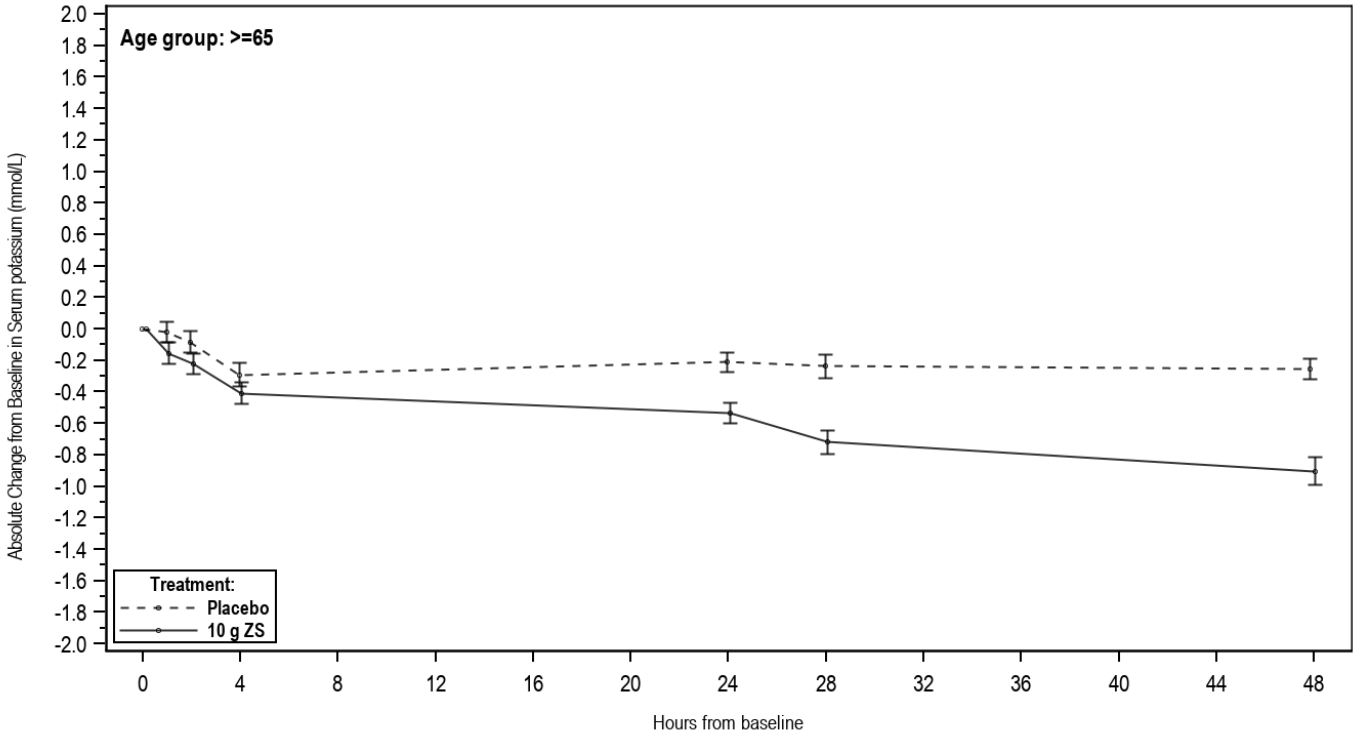


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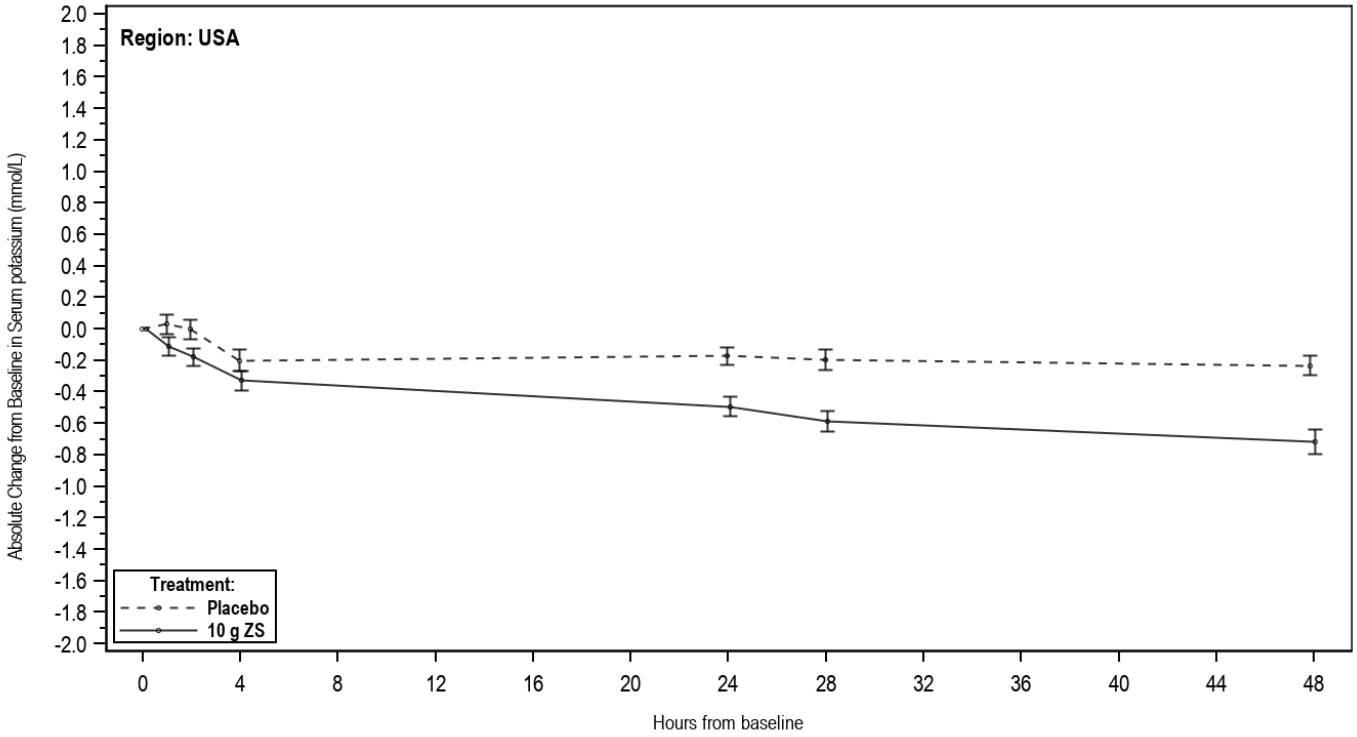


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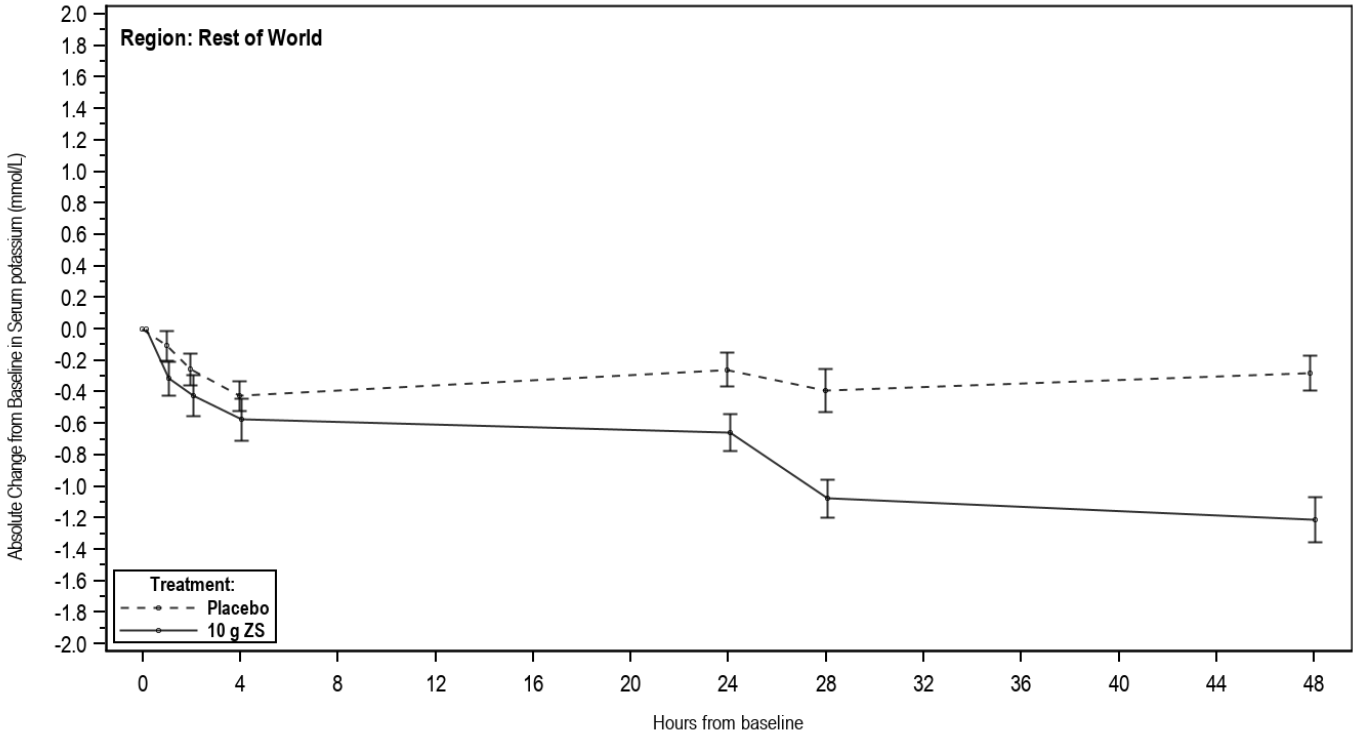


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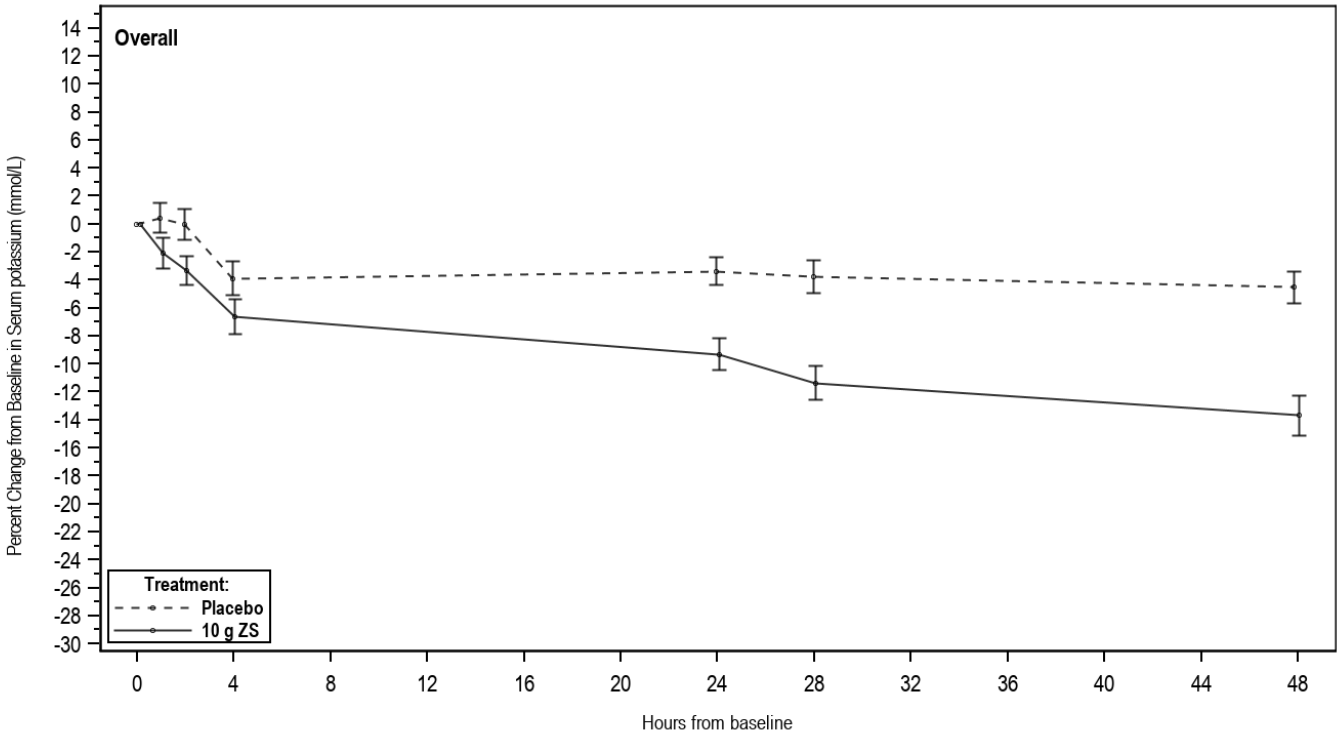


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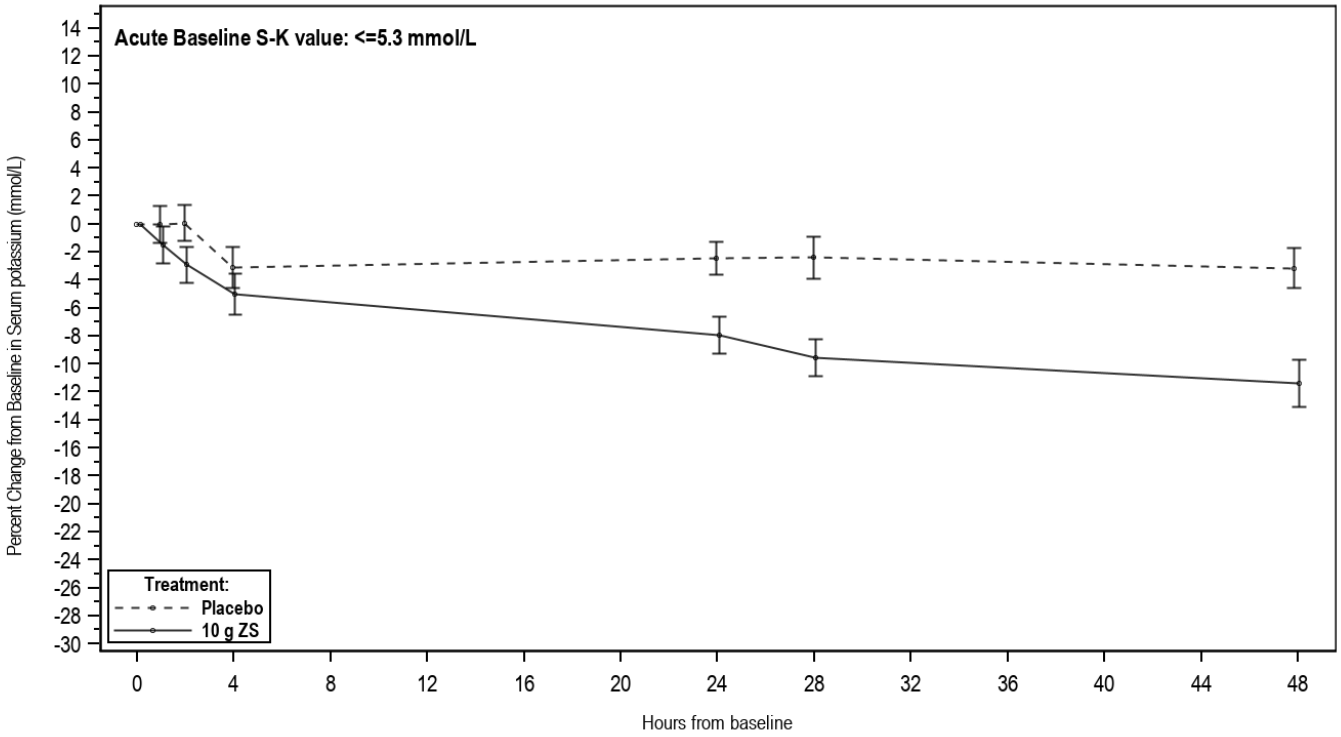


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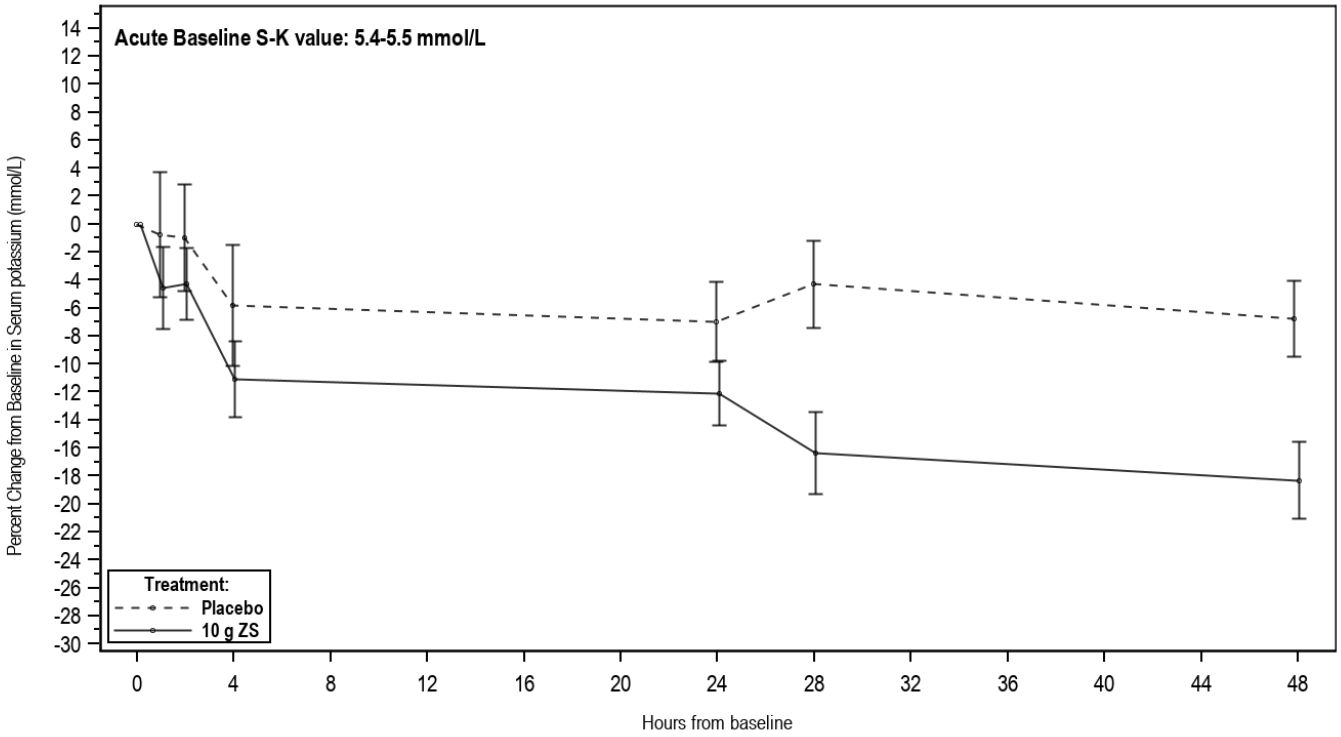


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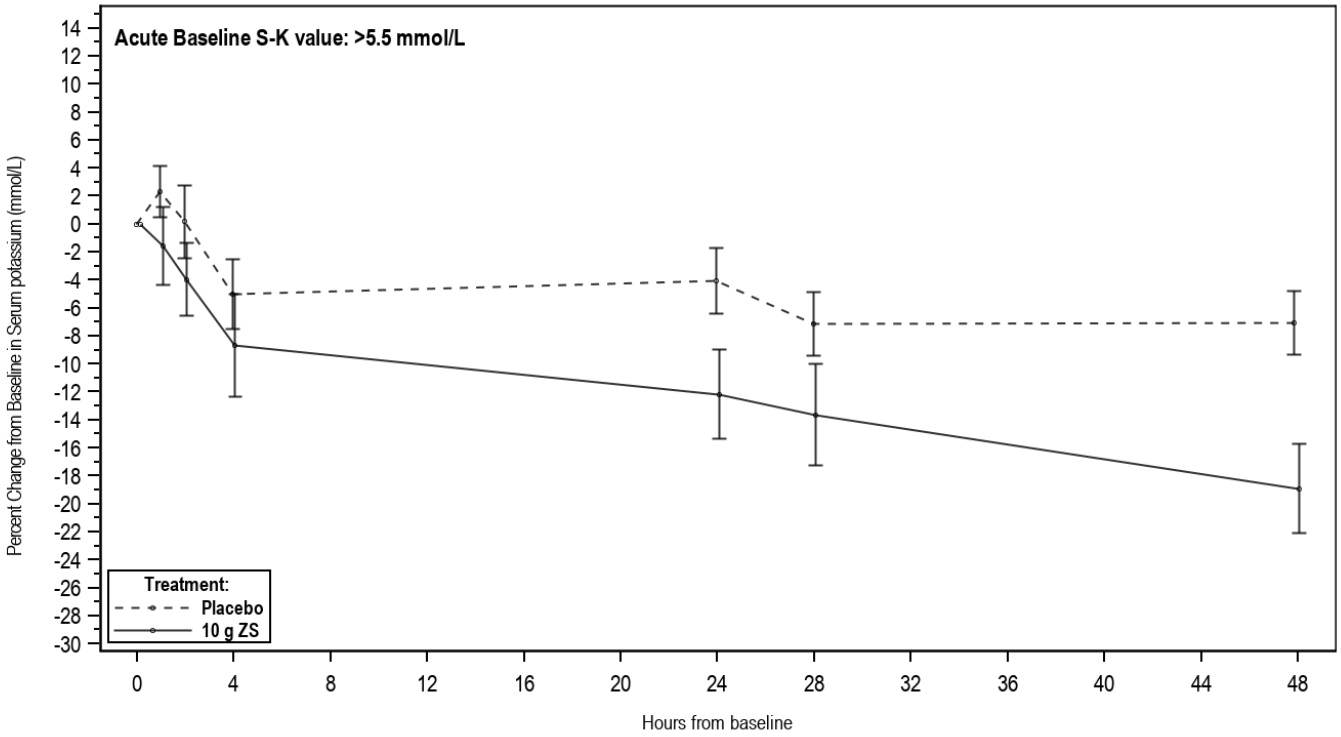
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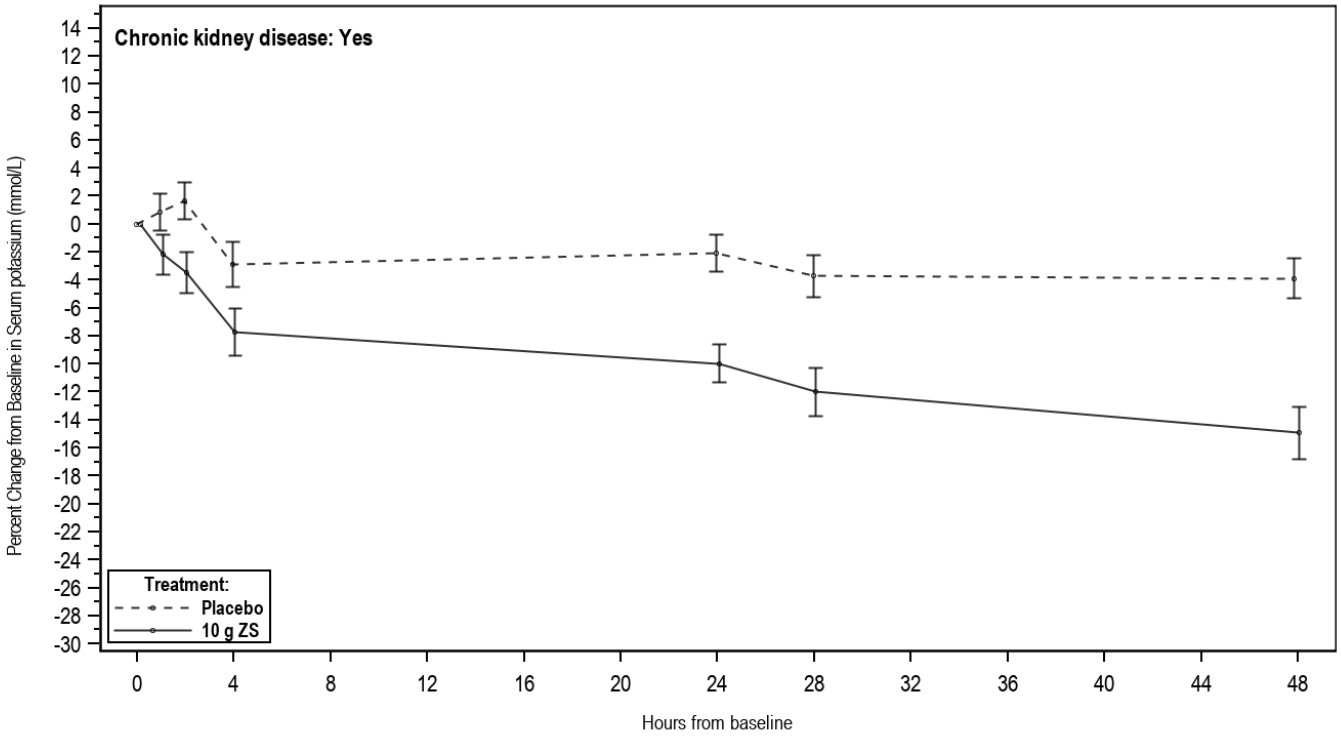


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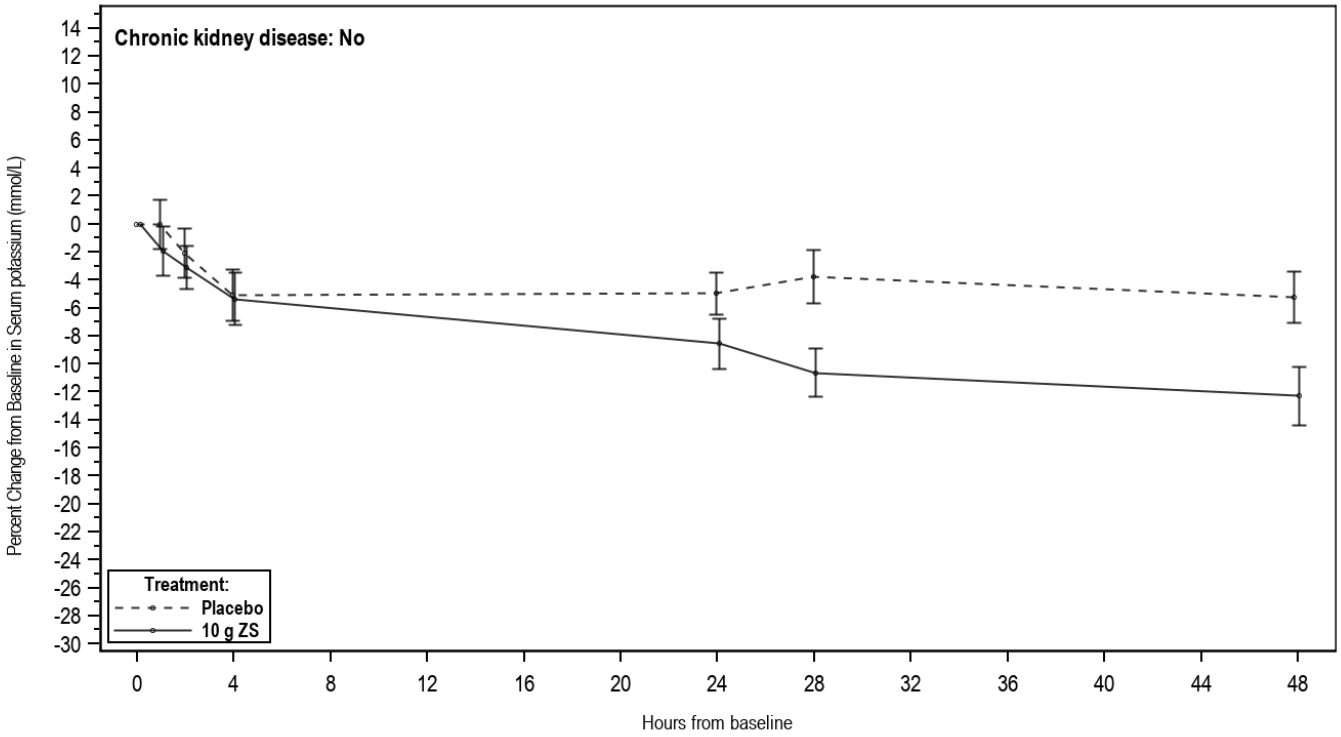


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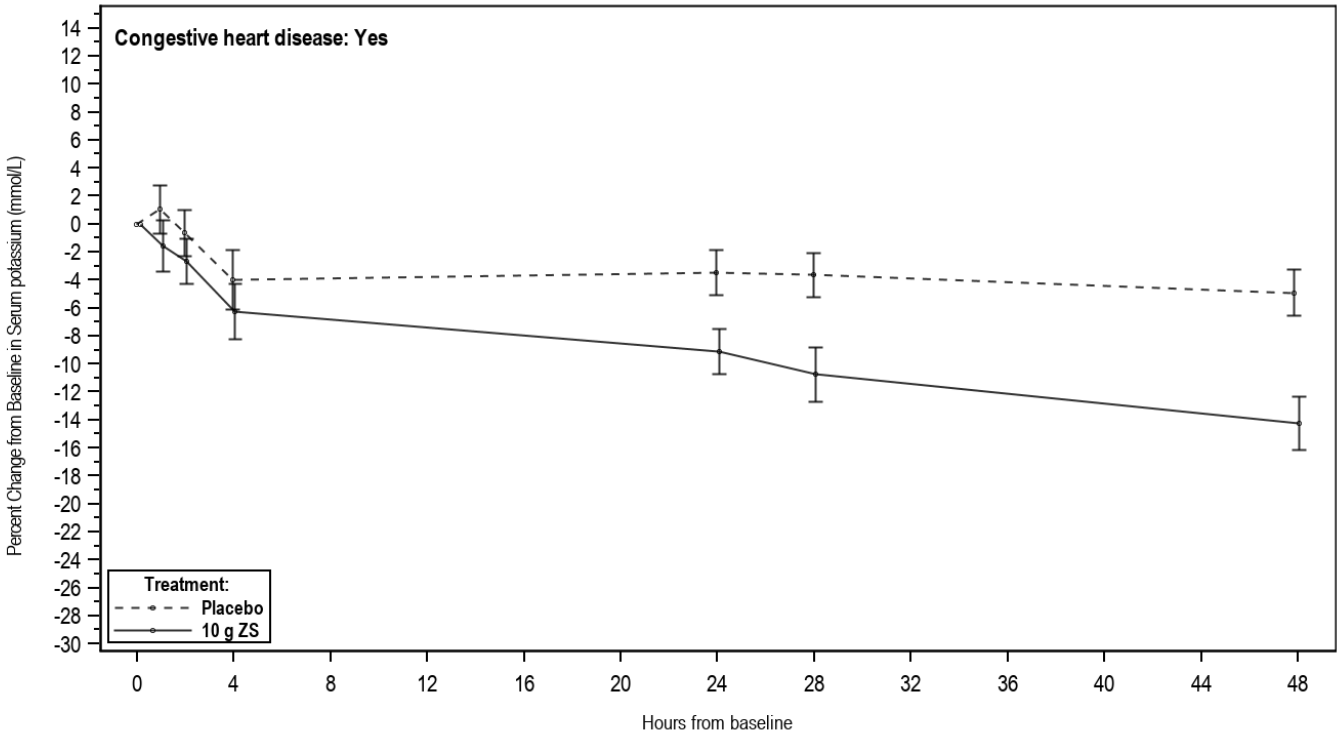


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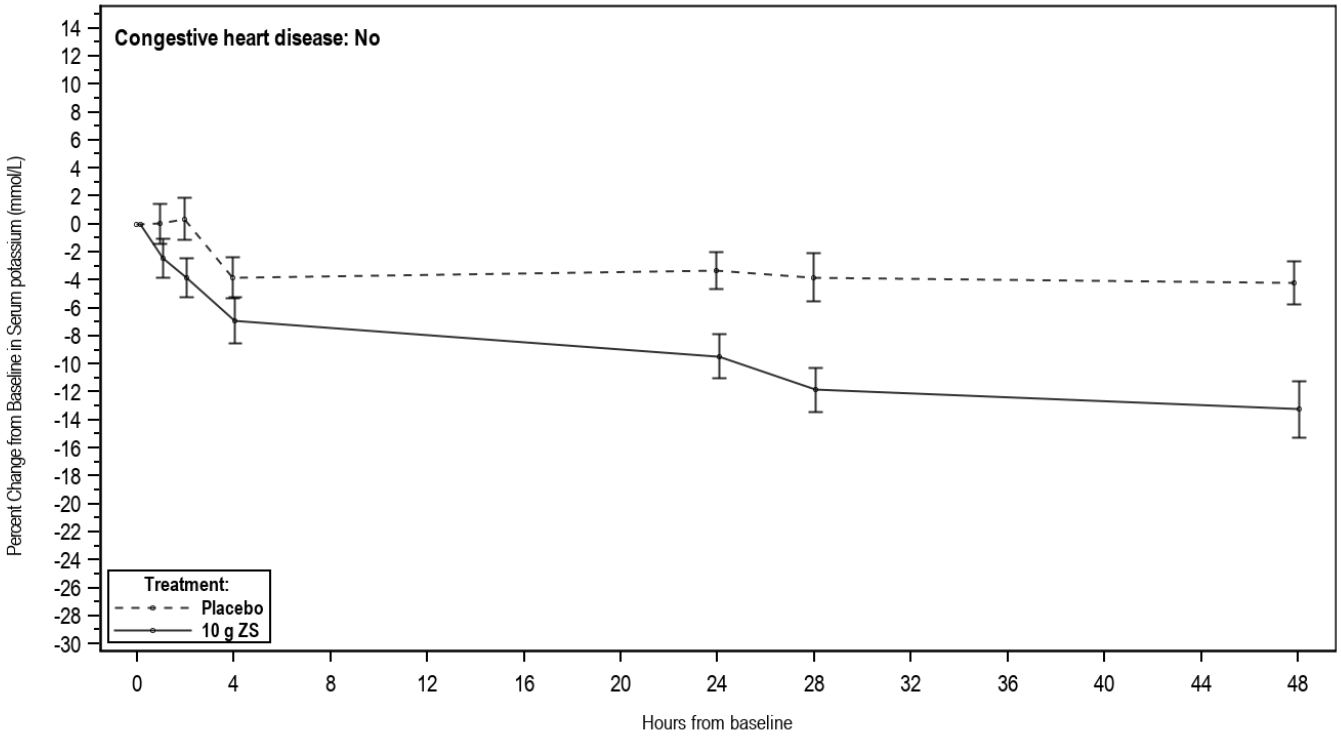


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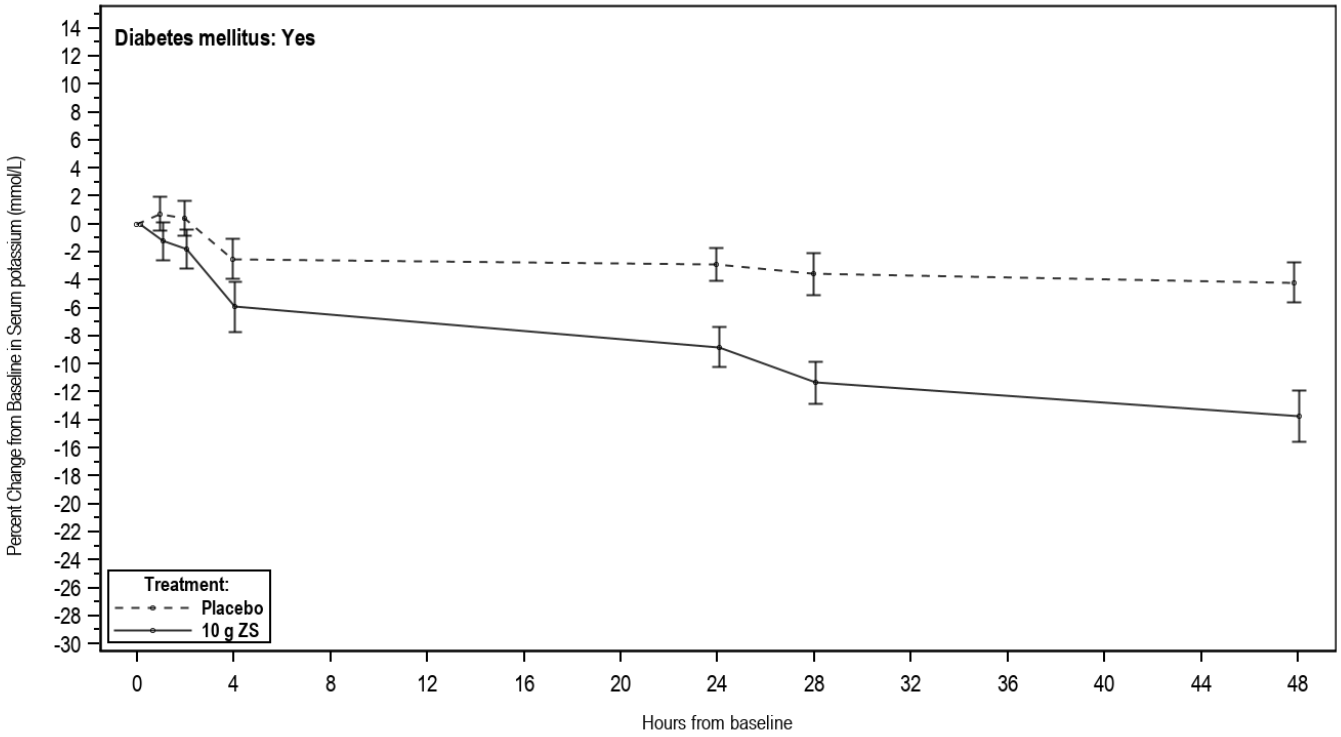


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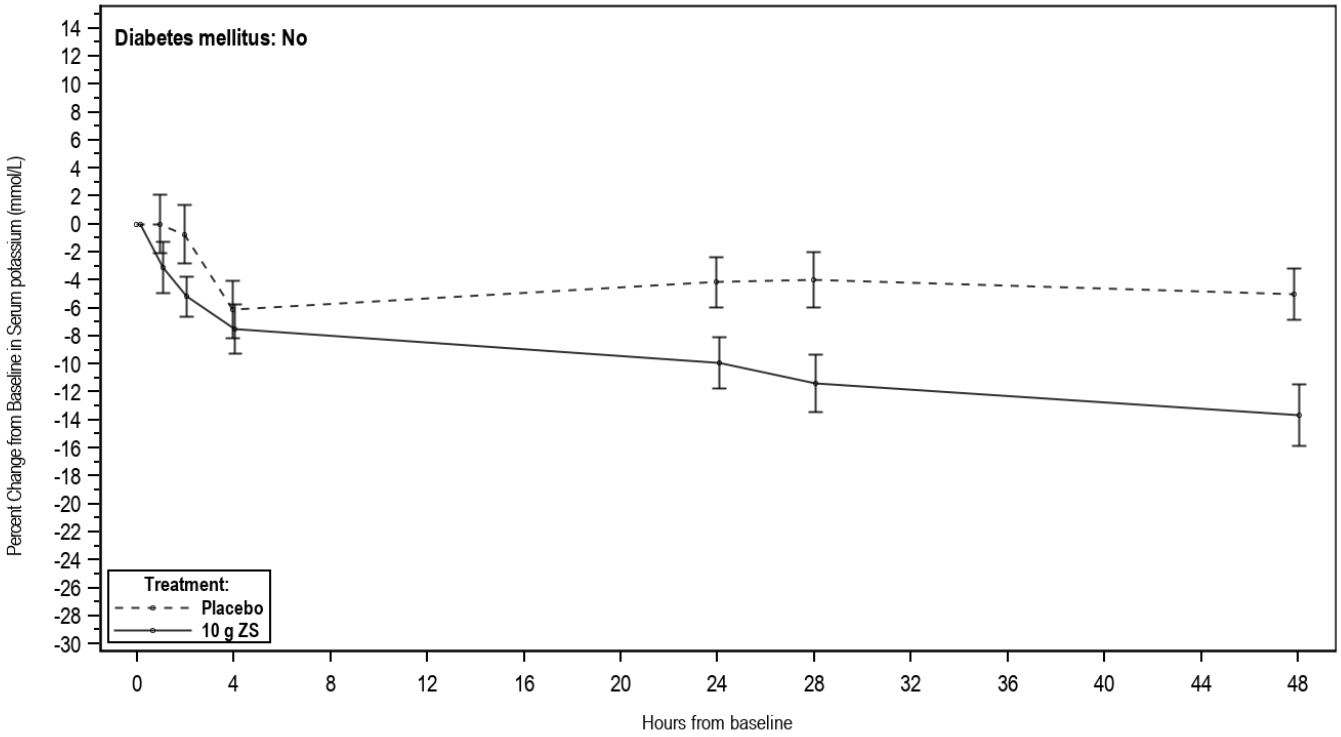


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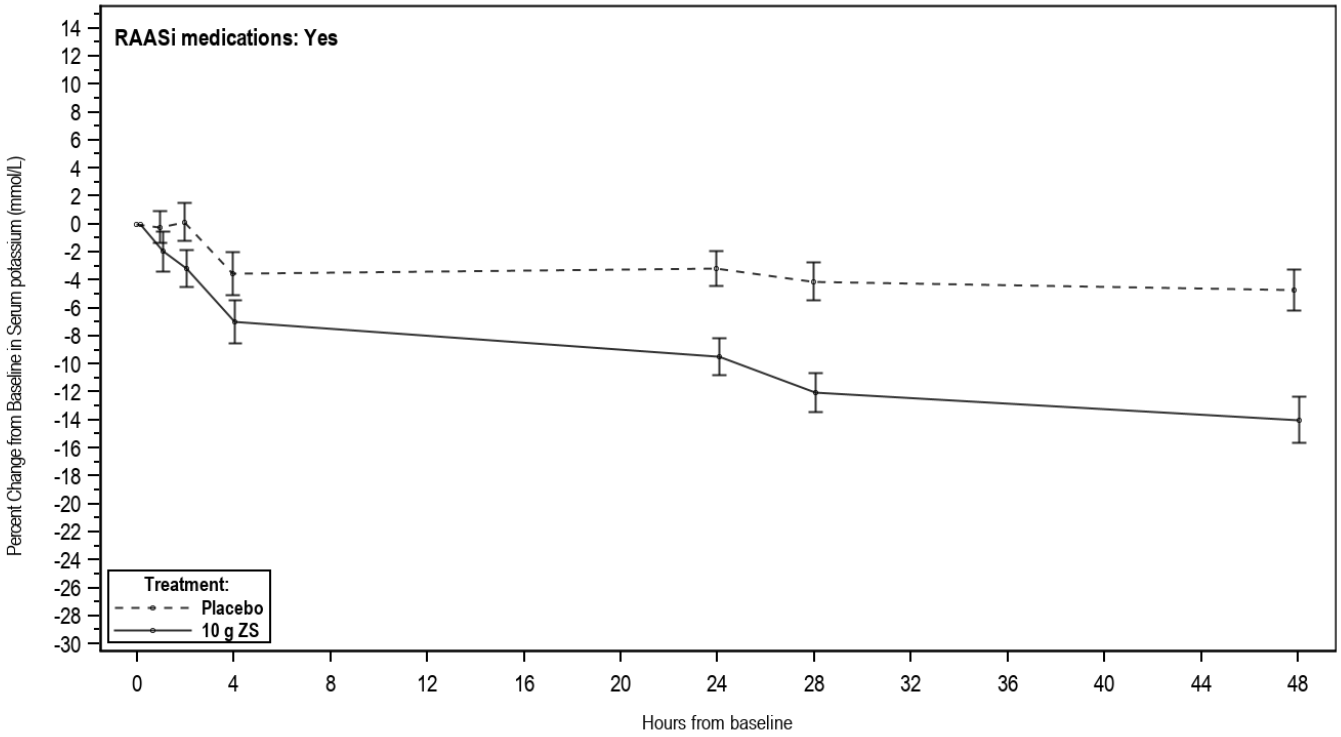


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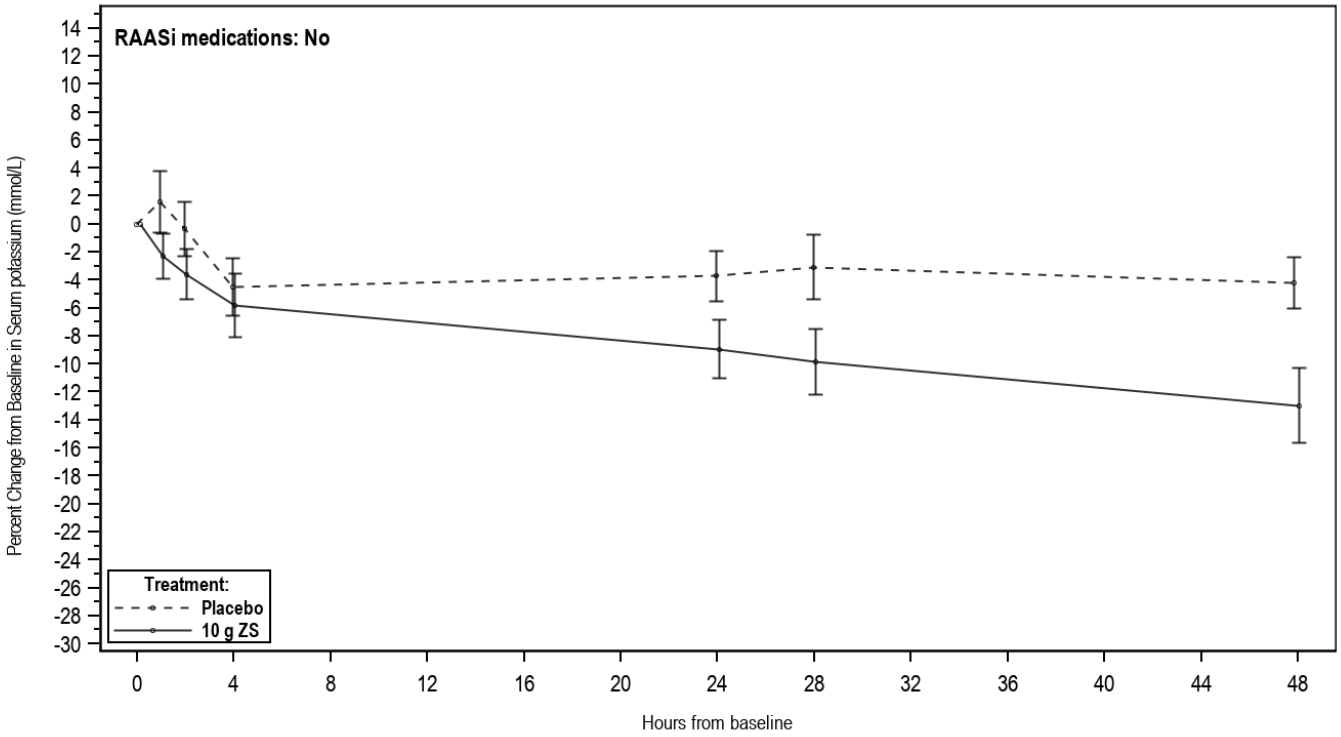


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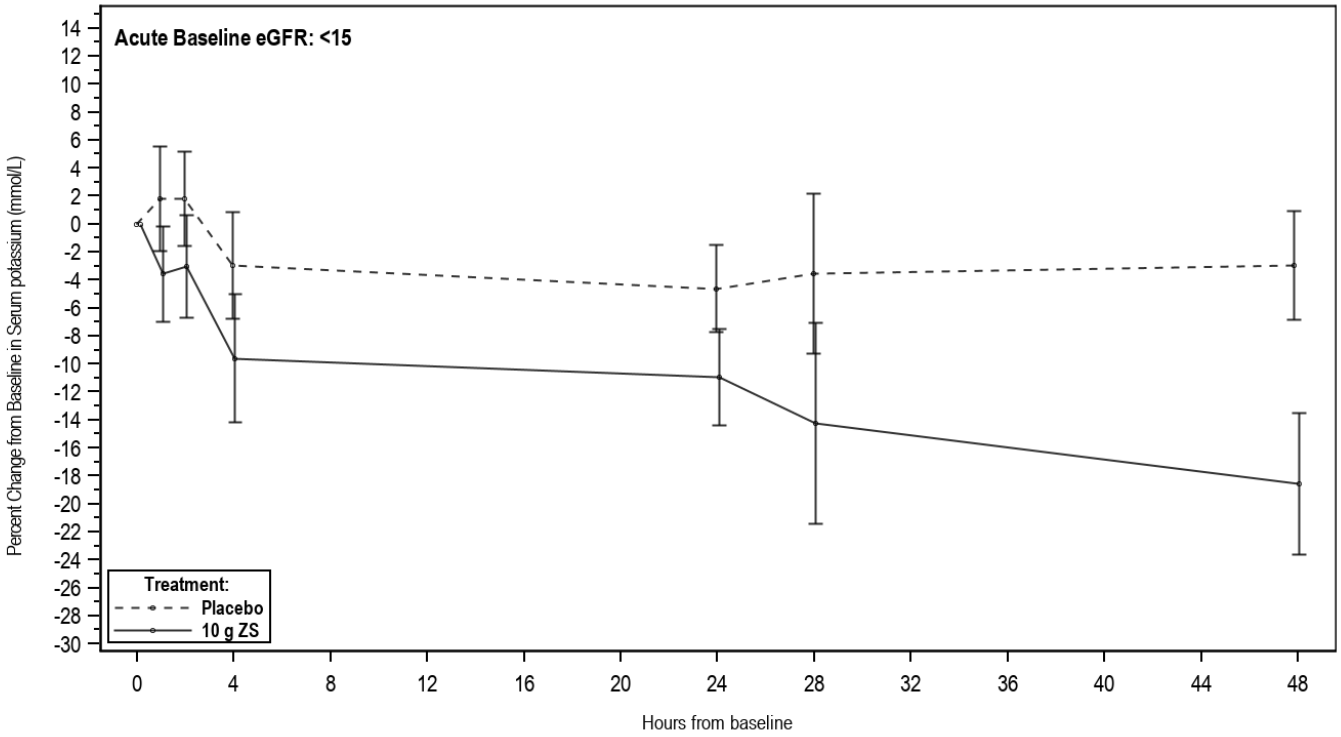


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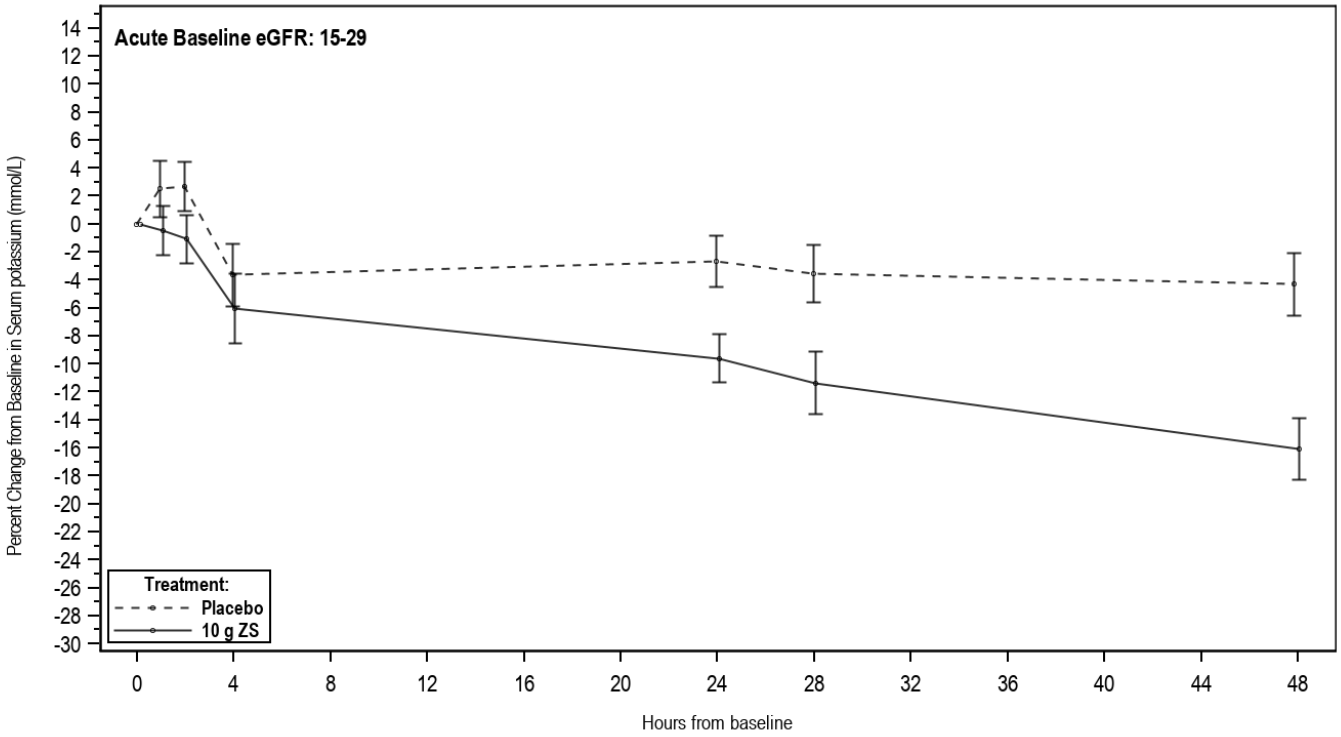


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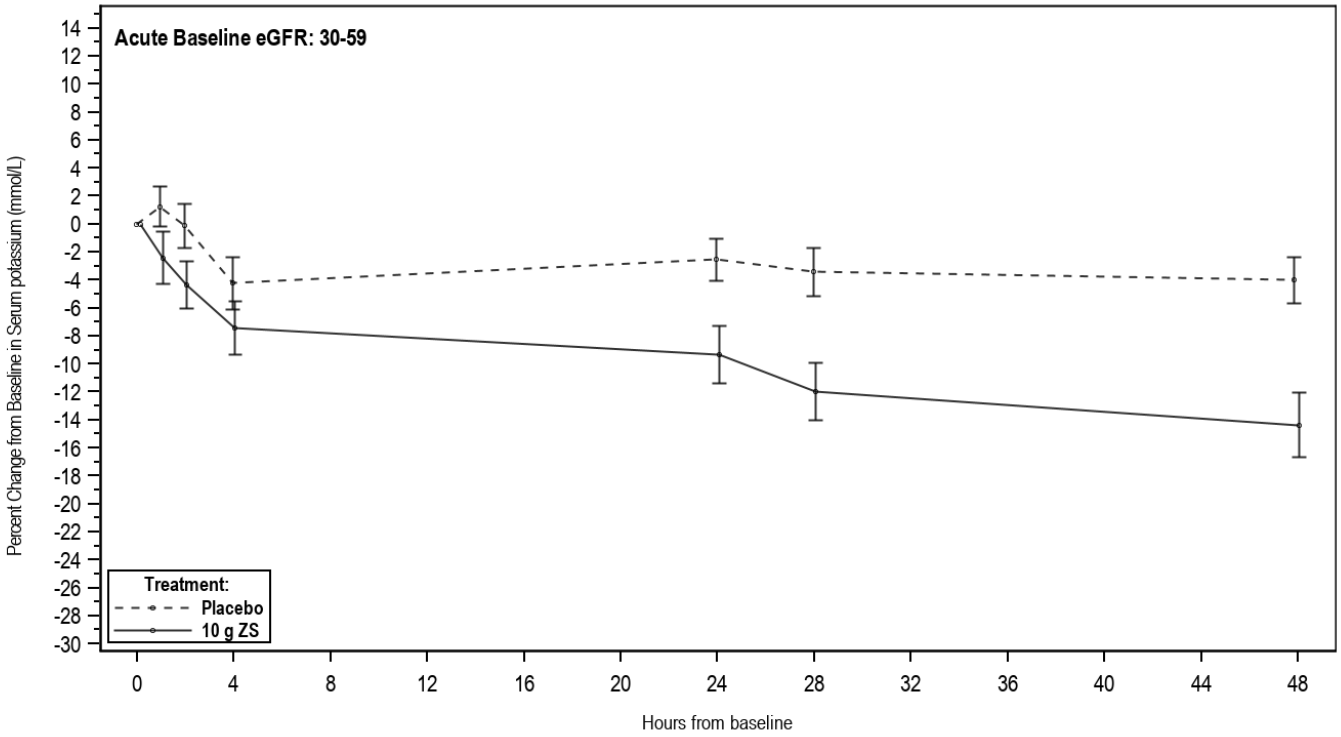


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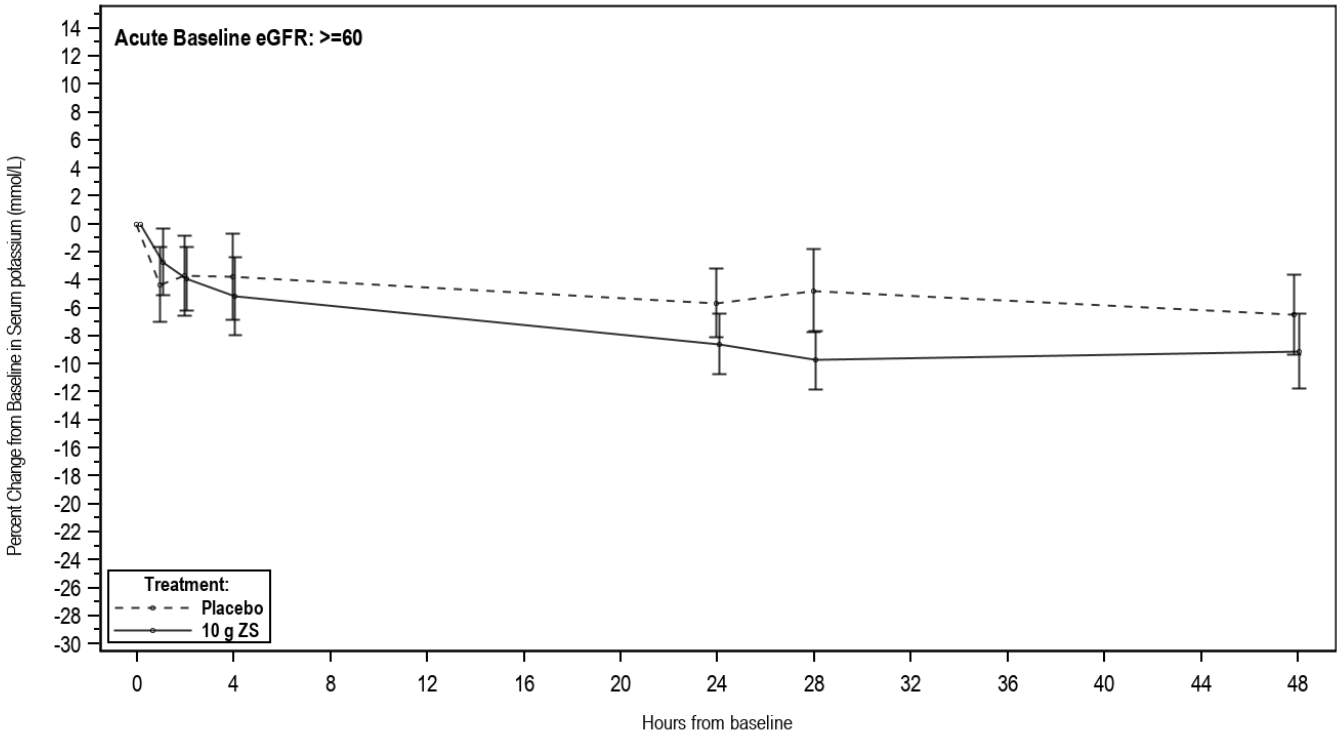


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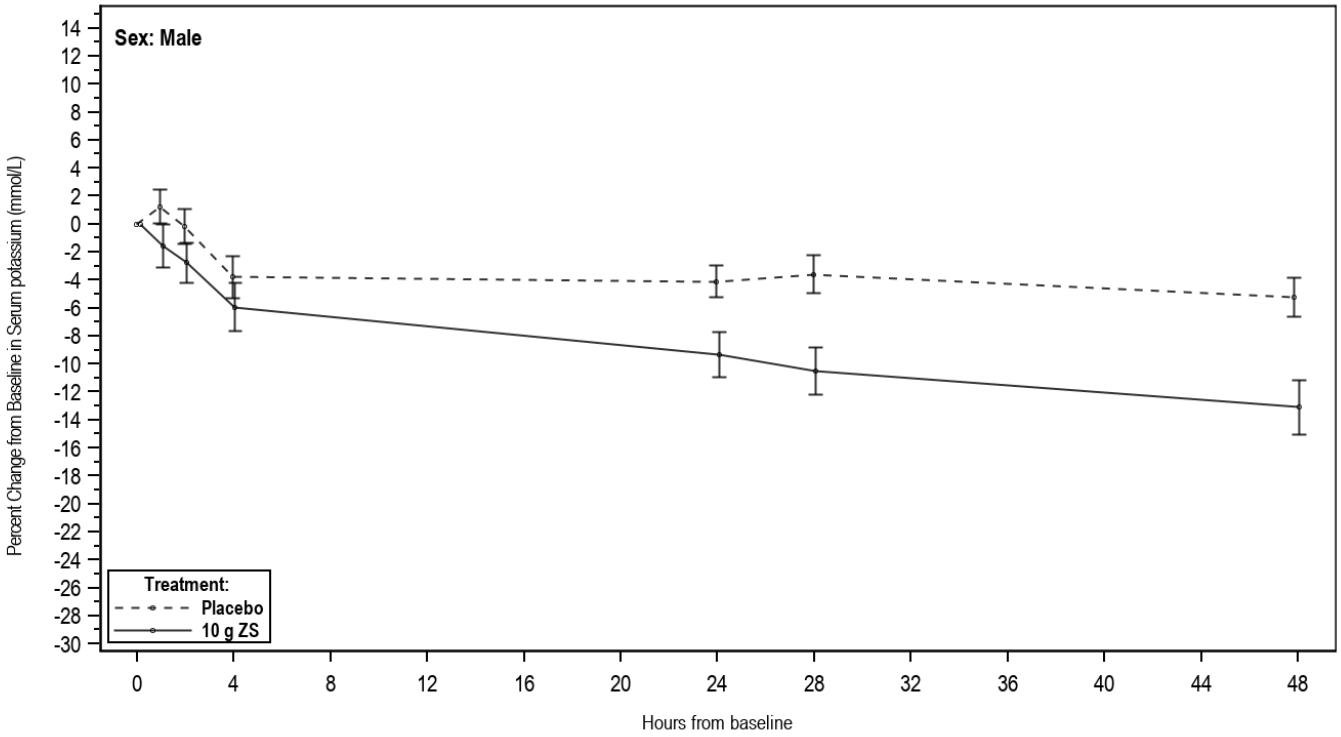


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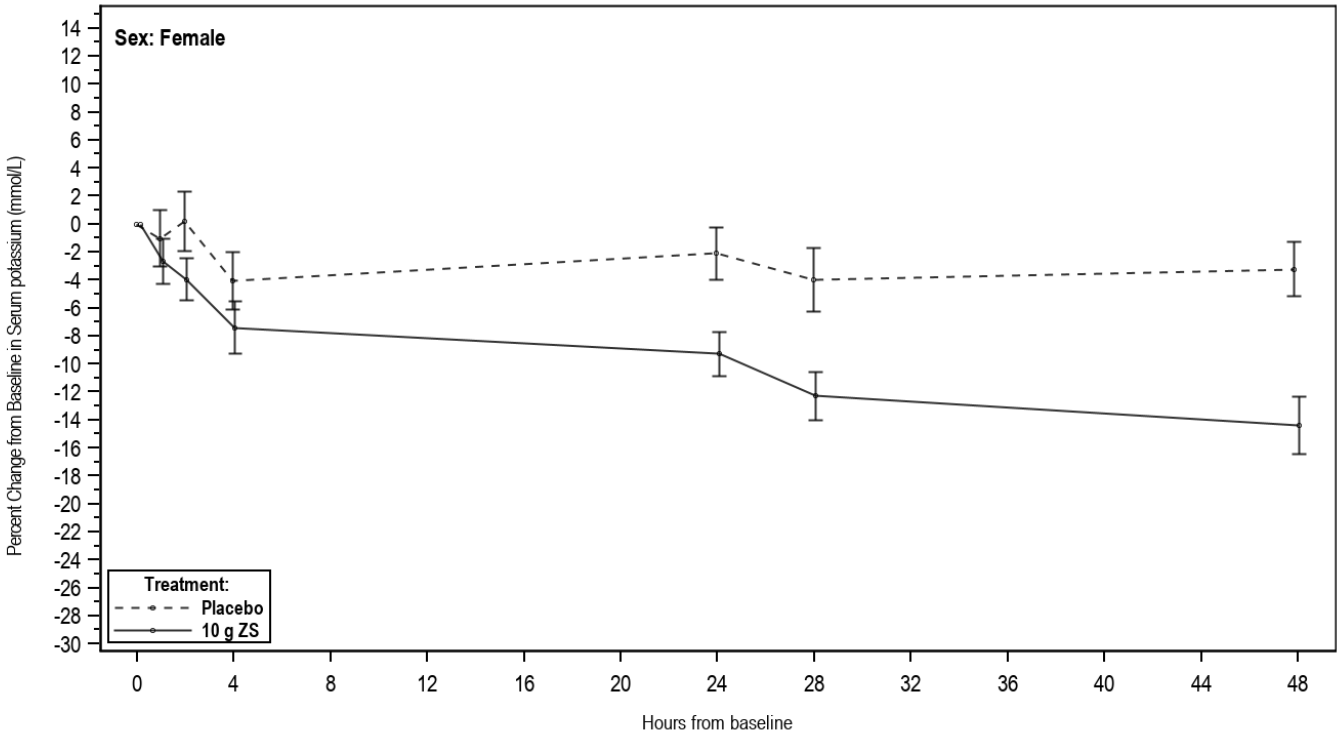


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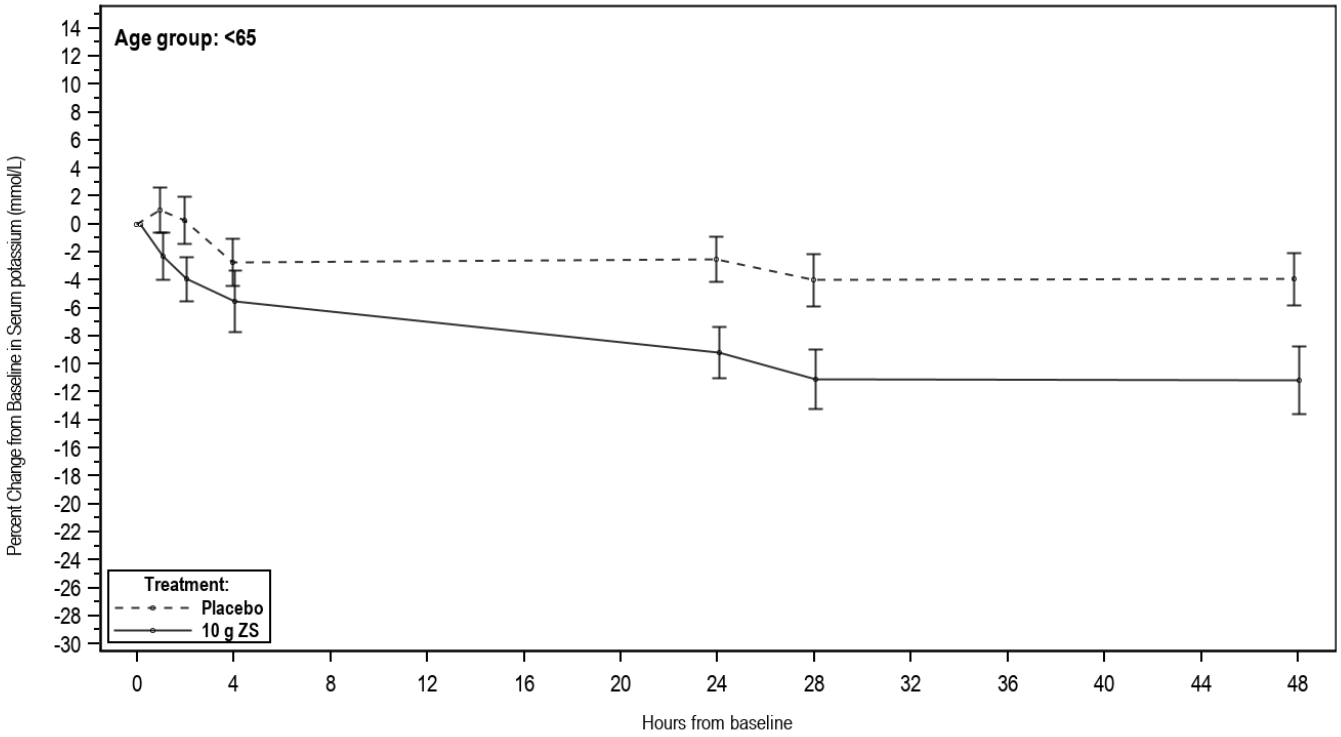


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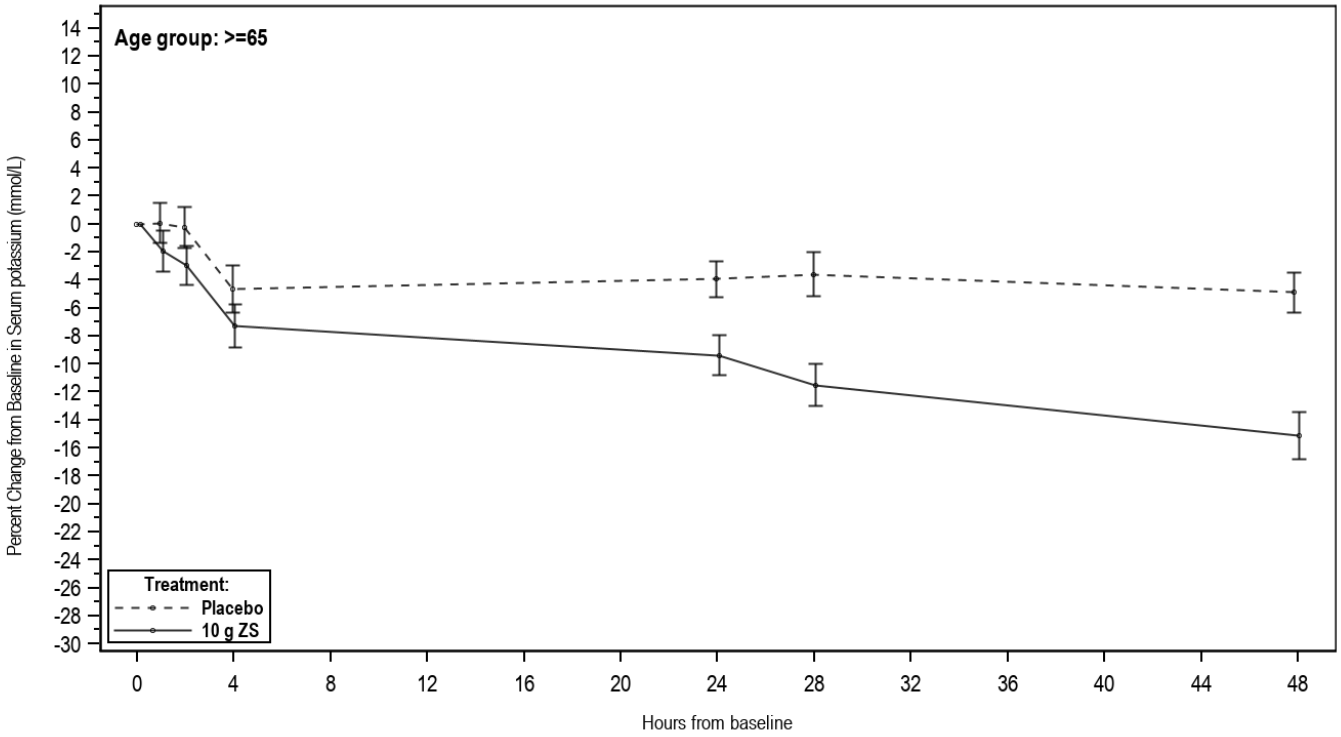


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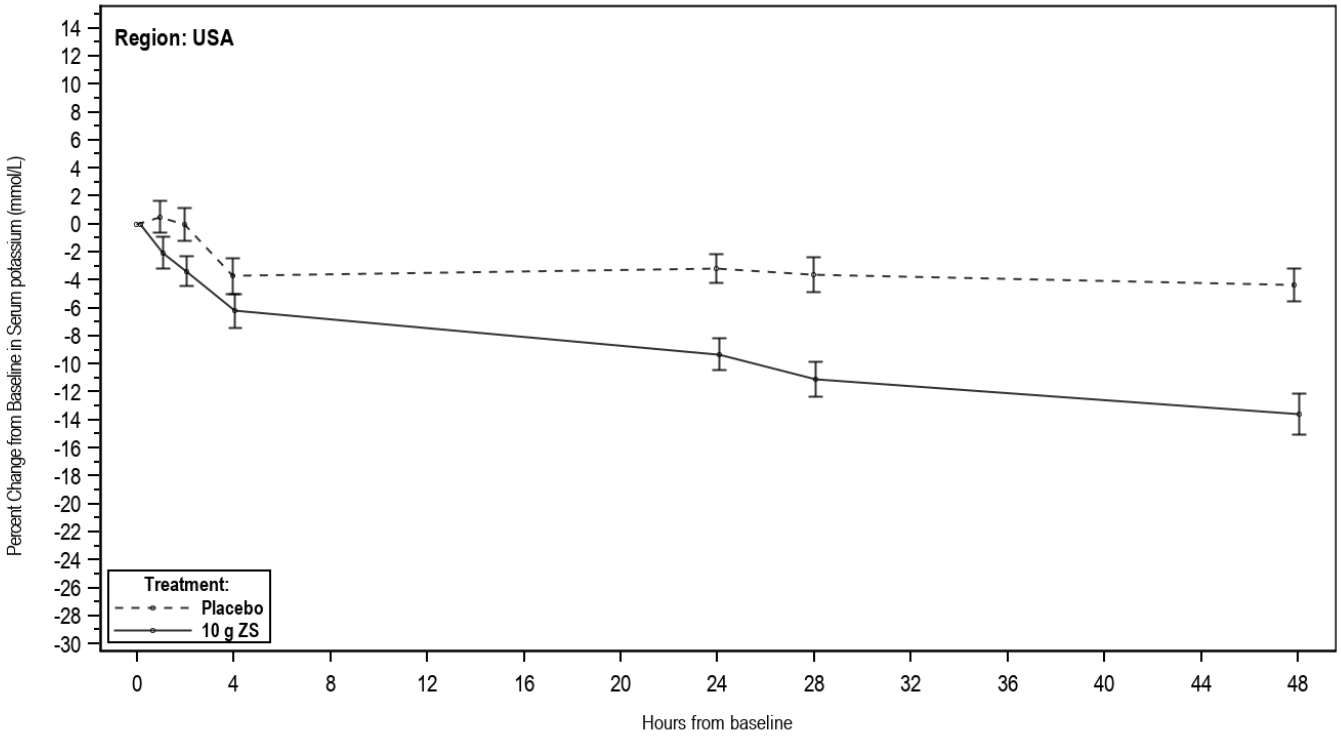


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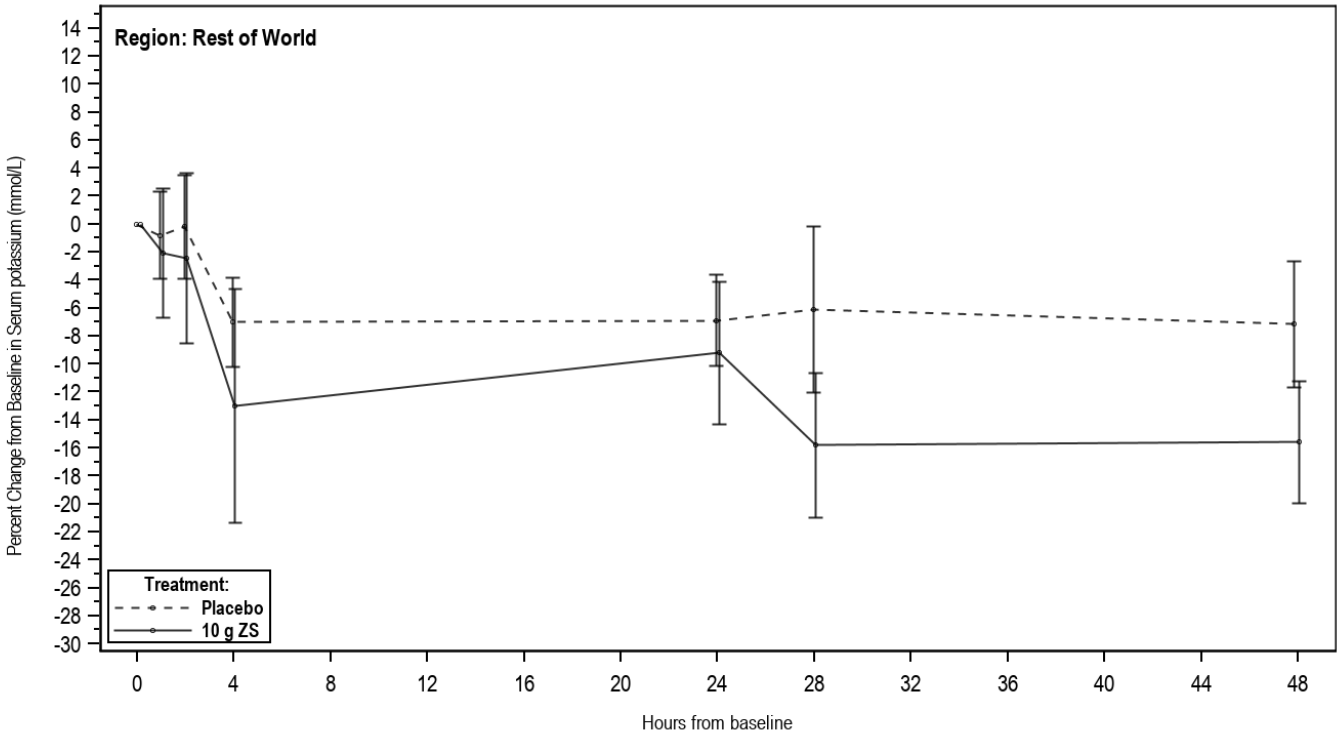


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Table 3.1.3.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)					10g ZS (N=203)								
Subgroup / Category	N	Patients with events [n(%)]	KM % at 24 hours	KM % at 48 hours	Median time (hours)	N	Patients with events [n(%)]	KM % at 24 hours	KM % at 48 hours	Median time (hours)	Hazard ratio (95% CI)	Hazard ratio p-value	Subgroup interaction test p-value	Study interaction test p-value
Overall	221	150 (67.9%)	51.23	32.02	24.5	203	190 (93.6%)	27.35	8.06	6.5	2.04 (1.64, 2.54)	<.0001		0.6981
Baseline S-K													0.8154	
<=5.3 mmol/L	126	80 (63.5%)	61.11	37.81	25.5	125	112 (89.6%)	36.48	11.39	23.3	2.06 (1.53, 2.76)	<.0001		
>5.3 - <=5.5 mmol/L	36	26 (72.2%)	38.89	30.56	4.0	42	42 (100.0%)	14.29	2.38	4.0	2.17 (1.30, 3.63)	0.0032		
>5.5 mmol/L	59	44 (74.6%)	37.11	18.50	14.0	36	36 (100.0%)	11.11	2.78	4.0	2.23 (1.41, 3.52)	0.0006		
Chronic kidney disease													0.1957	
Yes	128	83 (64.8%)	51.99	33.07	24.8	116	110 (94.8%)	24.56	6.82	4.1	2.36 (1.76, 3.16)	<.0001		
No	93	67 (72.0%)	50.20	29.17	24.1	87	80 (92.0%)	31.03	9.85	8.0	1.69 (1.21, 2.35)	0.0020		
Congestive heart disease													0.6465	
Yes	81	56 (69.1%)	51.85	28.92	24.6	75	72 (96.0%)	28.00	6.67	14.0	1.90 (1.33, 2.72)	0.0005		
No	140	94 (67.1%)	50.86	33.64	24.5	128	118 (92.2%)	26.99	9.53	4.0	2.09 (1.58, 2.77)	<.0001		
Diabetes mellitus													0.2843	
Yes	131	83 (63.4%)	57.01	38.16	25.7	116	109 (94.0%)	32.39	7.88	22.4	2.36 (1.75, 3.18)	<.0001		
No	90	67 (74.4%)	42.77	23.10	21.8	87	81 (93.1%)	20.69	8.62	4.0	1.70 (1.23, 2.36)	0.0015		
RAASi medications													0.1077	
Yes	147	93 (63.3%)	53.26	35.85	25.0	142	134 (94.4%)	29.98	6.81	4.1	2.31 (1.76, 3.03)	<.0001		
No	74	57 (77.0%)	47.26	25.08	23.8	61	56 (91.8%)	21.31	11.48	7.5	1.55 (1.05, 2.29)	0.0272		
Baseline eGFR													0.0140	
<15 ml/min/1.73m**2	26	15 (57.7%)	53.85	34.62	26.2	19	18 (94.7%)	0.00	0.00	3.9	4.25 (1.95, 9.24)	0.0003		
15- <30 ml/min/1.73m**2	56	35 (62.5%)	48.32	27.11	24.0	56	54 (96.4%)	35.71	7.14	22.9	2.06 (1.34, 3.19)	0.0011		
30- <60 ml/min/1.73m**2	100	69 (69.0%)	53.98	33.13	25.0	83	78 (94.0%)	24.10	6.20	4.1	2.10 (1.50, 2.94)	<.0001		
>=60 ml/min/1.73m**2	39	31 (79.5%)	46.15	25.64	23.8	45	40 (88.9%)	33.33	15.56	8.0	1.29 (0.79, 2.10)	0.3103		
Sex													0.0750	
Male	144	101 (70.1%)	50.84	30.81	24.5	117	108 (92.3%)	31.24	9.81	22.4	1.81 (1.37, 2.39)	<.0001		
Female	77	49 (63.6%)	51.95	34.84	25.0	86	82 (95.3%)	22.09	5.81	4.0	2.53 (1.75, 3.67)	<.0001		
Age (years)													0.3914	
<65 years	76	46 (60.5%)	60.50	38.19	27.4	66	57 (86.4%)	29.63	14.04	7.7	2.17 (1.44, 3.26)	0.0002		
>=65 years	145	104 (71.7%)	46.32	28.71	23.7	137	133 (97.1%)	26.28	5.84	4.1	1.92 (1.47, 2.49)	<.0001		

Hazard ratio derived from Cox proportional hazard model with treatment group and study.
For subgroup interaction analysis, the subgroup variable (if not already present) and an interaction term for subgroup*treatment group were added.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
NR: median not reached

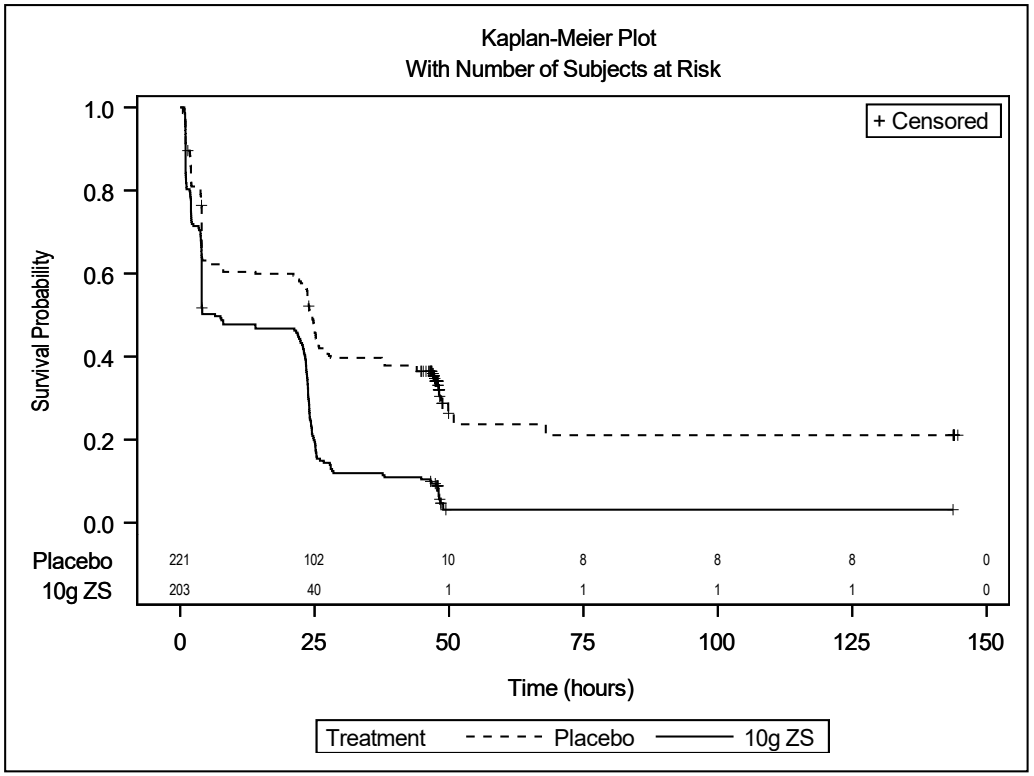
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Figure 3.1.3.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Overall



Plots shown for subgroups where interaction p-value is <=0.05

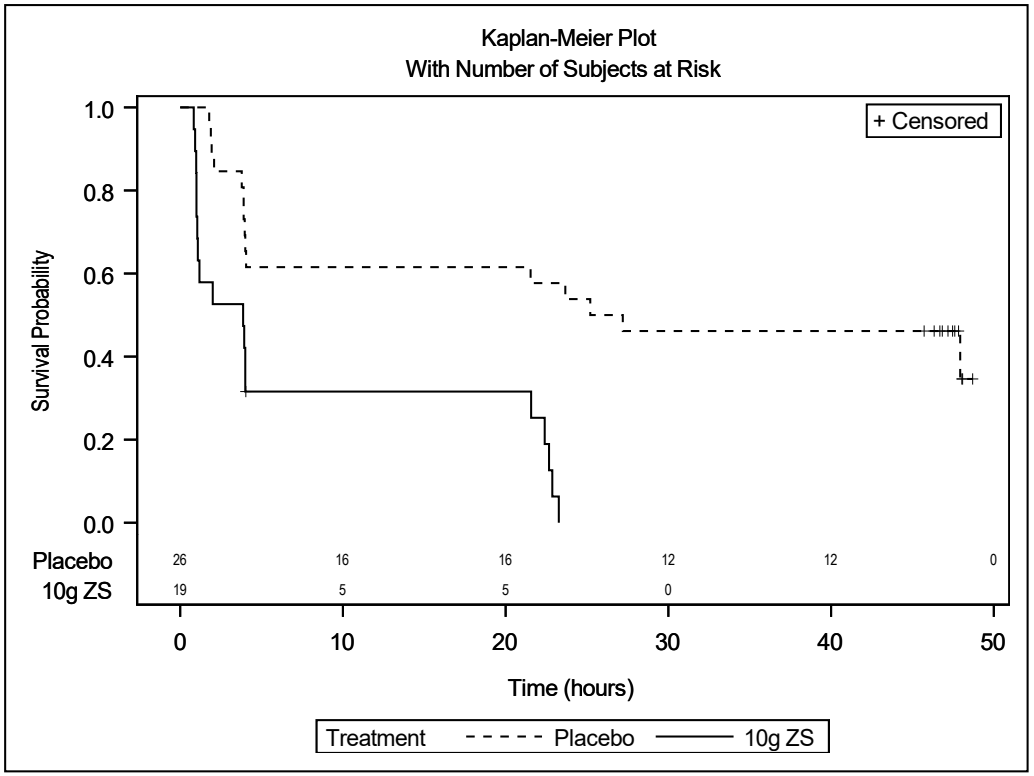
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Baseline eGFR: <15 ml/min/1.73m2**



Plots shown for subgroups where interaction p-value is <=0.05

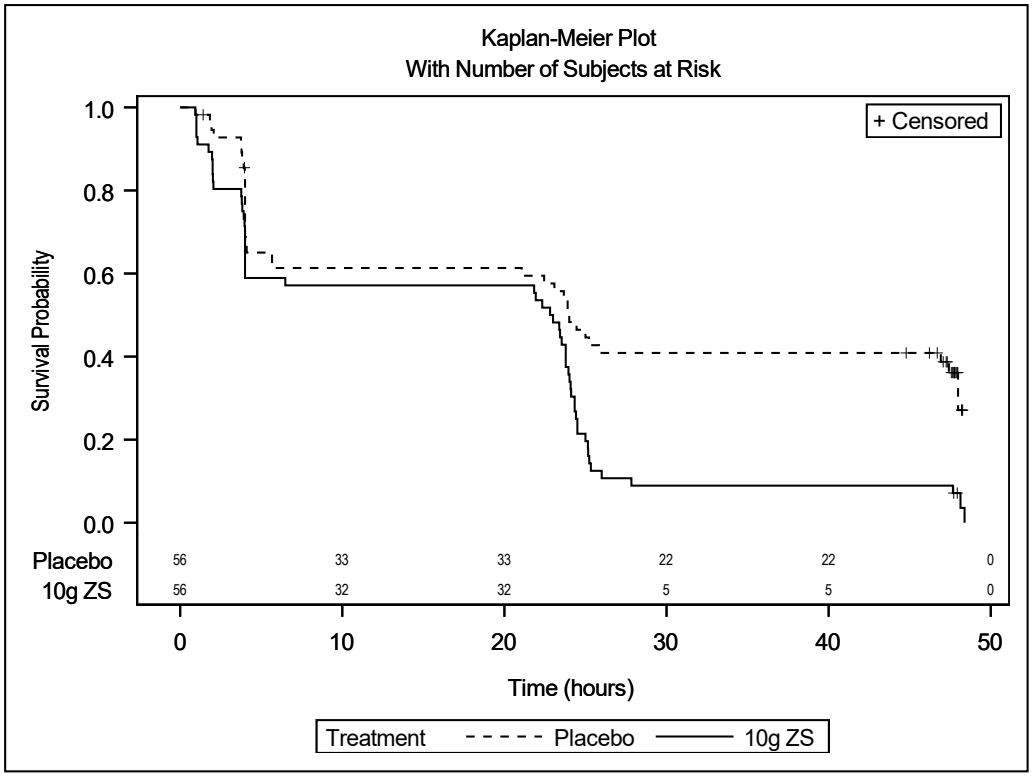
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Baseline eGFR: 15- <30 ml/min/1.73m2**



Plots shown for subgroups where interaction p-value is <=0.05

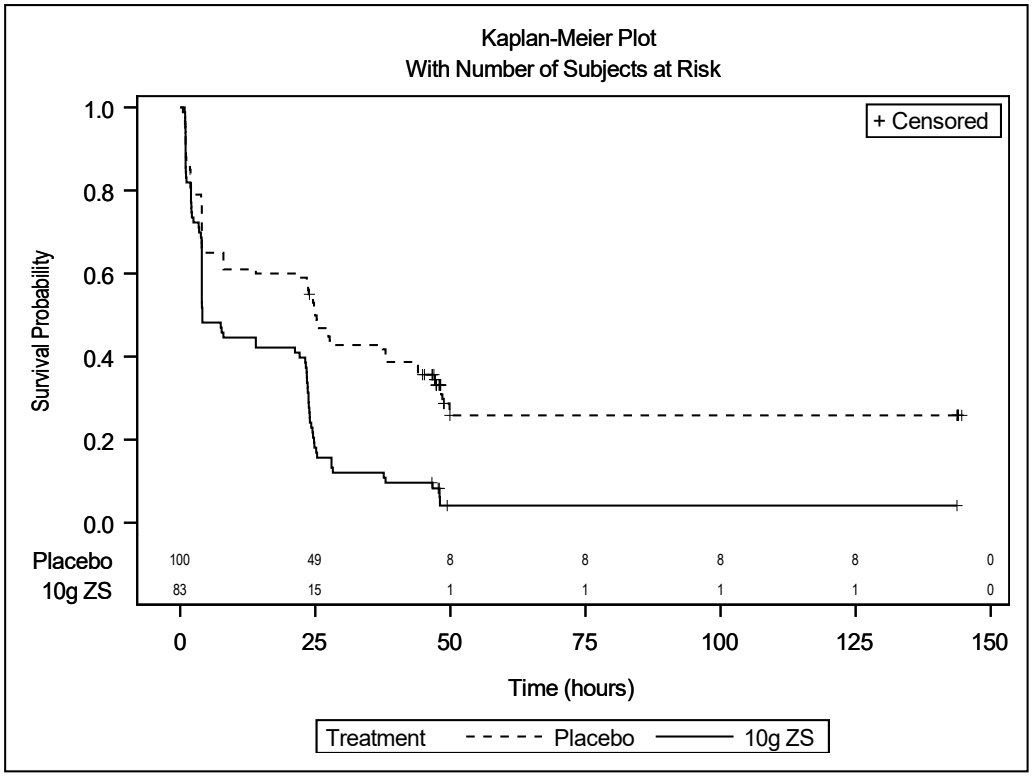
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Figure 3.1.3.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: 30- <60 ml/min/1.73m2**



Plots shown for subgroups where interaction p-value is <=0.05

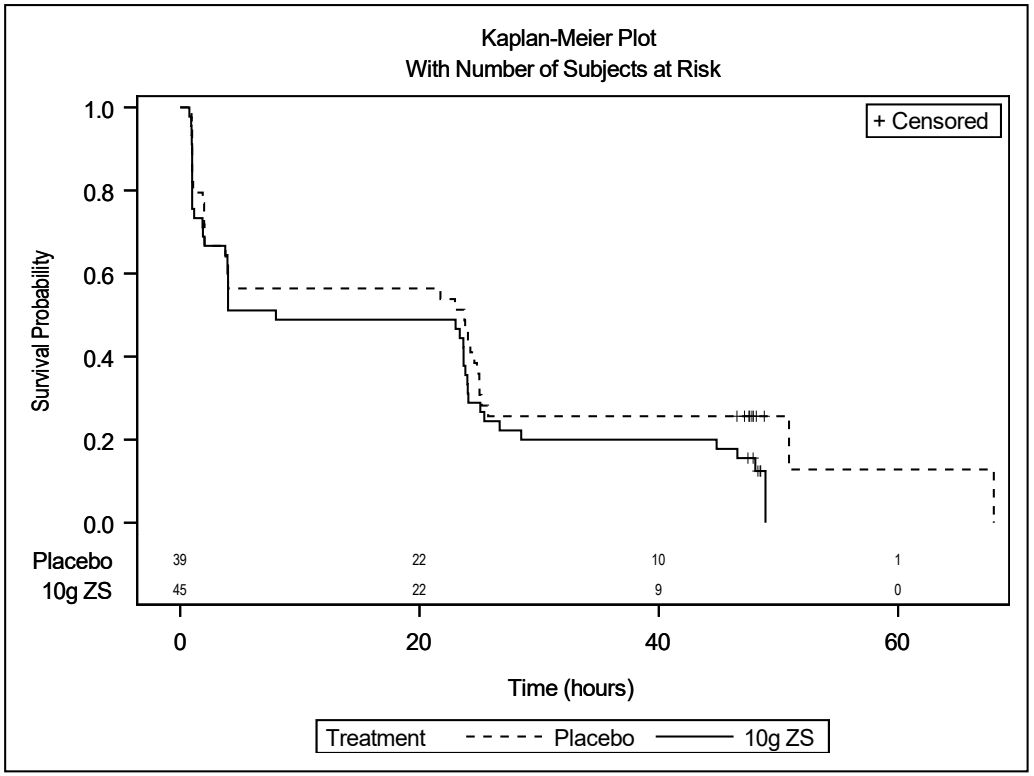
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Figure 3.1.3.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: >=60 ml/min/1.73m2**



Plots shown for subgroups where interaction p-value is <=0.05

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Table 3.1.4.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)					10g ZS (N=203)								
Subgroup / Category	N	Patients with events [n(%)]	KM % at 24 hours	KM % at 48 hours	Median time (hours)	N	Patients with events [n(%)]	KM % at 24 hours	KM % at 48 hours	Median time (hours)	Hazard ratio (95% CI)	Hazard ratio p-value	Subgroup interaction test p-value	Study interaction test p-value
Overall	221	173 (78.3%)	31.75	20.97	3.8	203	201 (99.0%)	9.03	1.34	1.0	1.87 (1.52, 2.31)	<.0001		0.3321
Baseline S-K													0.0810	
<=5.3 mmol/L	126	117 (92.9%)	11.90	6.35	1.0	125	124 (99.2%)	2.55	0.00	0.9	1.39 (1.07, 1.80)	0.0143		
>5.3 - <=5.5 mmol/L	36	28 (77.8%)	36.11	25.00	4.0	42	42 (100.0%)	9.52	2.38	4.0	2.03 (1.23, 3.37)	0.0060		
>5.5 mmol/L	59	28 (47.5%)	72.12	51.39	48.3	36	35 (97.2%)	30.56	4.17	22.1	3.56 (2.12, 5.98)	<.0001		
Chronic kidney disease													0.0965	
Yes	128	90 (70.3%)	39.52	29.42	4.0	116	114 (98.3%)	8.88	1.78	1.9	2.16 (1.62, 2.87)	<.0001		
No	93	83 (89.2%)	21.01	9.73	1.9	87	87 (100.0%)	9.20	1.15	1.0	1.48 (1.09, 2.02)	0.0131		
Congestive heart disease													0.6873	
Yes	81	60 (74.1%)	34.57	25.93	2.0	75	75 (100.0%)	9.33	1.33	2.0	1.72 (1.21, 2.45)	0.0025		
No	140	113 (80.7%)	30.05	17.94	3.9	128	126 (98.4%)	8.87	1.21	1.0	1.91 (1.47, 2.50)	<.0001		
Diabetes mellitus													0.7971	
Yes	131	101 (77.1%)	36.40	22.16	4.0	116	115 (99.1%)	12.39	0.88	2.0	1.99 (1.50, 2.64)	<.0001		
No	90	72 (80.0%)	24.94	19.27	1.9	87	86 (98.9%)	4.60	2.30	1.0	1.67 (1.21, 2.31)	0.0017		
RAASi medications													0.5382	
Yes	147	110 (74.8%)	33.52	23.35	2.0	142	140 (98.6%)	11.56	1.93	2.0	1.75 (1.36, 2.27)	<.0001		
No	74	63 (85.1%)	28.38	15.61	4.0	61	61 (100.0%)	3.28	0.00	1.0	2.35 (1.60, 3.45)	<.0001		
Baseline eGFR													0.1305	
<15 ml/min/1.73m**2	26	15 (57.7%)	53.85	42.31	25.8	19	18 (94.7%)	6.32	0.00	4.0	2.96 (1.38, 6.32)	0.0051		
15- <30 ml/min/1.73m**2	56	33 (58.9%)	48.82	38.36	23.9	56	55 (98.2%)	16.07	2.68	4.0	2.36 (1.52, 3.67)	0.0001		
30- <60 ml/min/1.73m**2	100	86 (86.0%)	23.96	15.62	2.0	83	83 (100.0%)	7.23	1.20	1.0	1.73 (1.27, 2.36)	0.0006		
>=60 ml/min/1.73m**2	39	39 (100.0%)	12.82	0.00	1.0	45	45 (100.0%)	4.44	0.00	0.9	1.31 (0.84, 2.06)	0.2318		
Sex													0.4070	
Male	144	108 (75.0%)	35.55	23.32	4.0	117	115 (98.3%)	12.29	2.63	2.0	2.01 (1.53, 2.64)	<.0001		
Female	77	65 (84.4%)	24.68	16.88	1.9	86	86 (100.0%)	4.65	0.00	1.0	1.60 (1.15, 2.24)	0.0056		
Age (years)													0.2854	
<65 years	76	59 (77.6%)	35.48	21.60	4.0	66	65 (98.5%)	9.57	0.00	1.0	2.15 (1.47, 3.13)	<.0001		
>=65 years	145	114 (78.6%)	29.78	21.27	2.0	137	136 (99.3%)	8.76	1.95	1.0	1.71 (1.32, 2.21)	<.0001		

Hazard ratio derived from Cox proportional hazard model with treatment group and study.
For subgroup interaction analysis, the subgroup variable (if not already present) and an interaction term for subgroup*treatment group were added.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
NR: median not reached

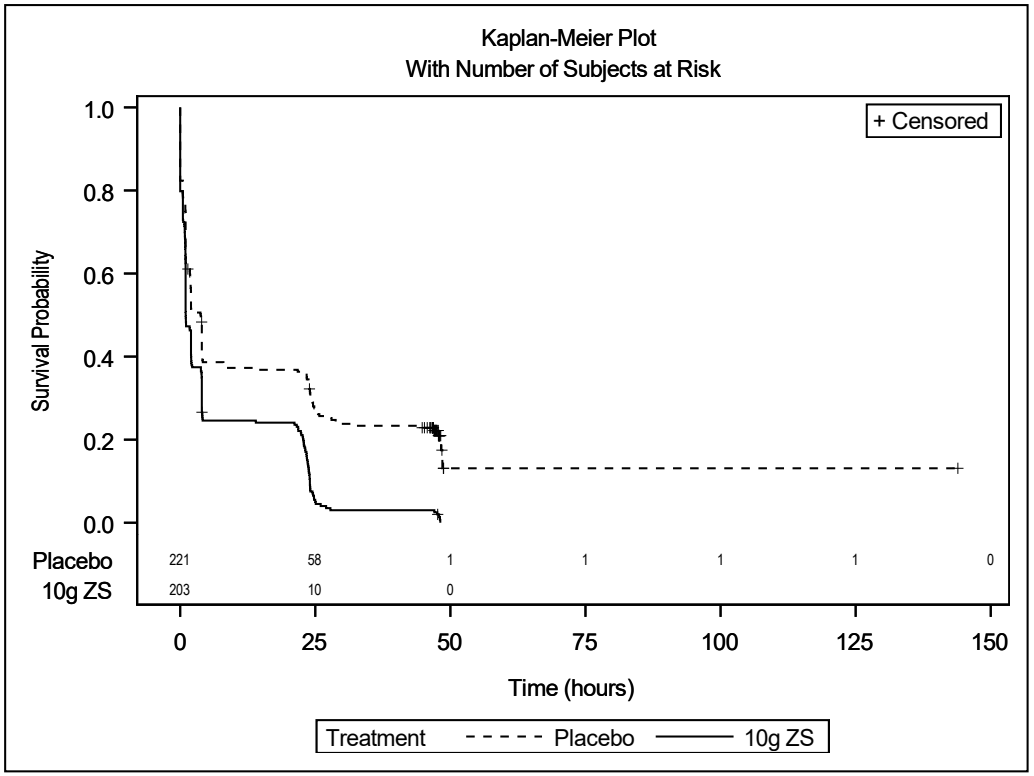
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Figure 3.1.4.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Overall



Plots shown for subgroups where interaction p-value is <=0.05

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Table 3.1.5.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction(%) (95% CI)	ARR p-value	Subgroup interaction test p-value(RR)	Study interaction test p-value(RR)
Overall												
1 hour	221	75 (33.9%)	203	99 (48.8%)	1.89 (1.28, 2.80)	0.0015	1.45 (1.07, 1.96)	0.0154	15.2 (2.9, 27.6)	0.0153		0.2735
2 hours	220	85 (38.6%)	202	105 (52.0%)	1.74 (1.18, 2.58)	0.0054	1.35 (1.01, 1.80)	0.0409	13.8 (1.0, 26.6)	0.0349		0.7753
4 hours	220	111 (50.5%)	203	129 (63.5%)	1.74 (1.17, 2.57)	0.0057	1.27 (0.98, 1.63)	0.0693	13.2 (-1.2, 27.7)	0.0726		0.8277
24 hours	219	107 (48.9%)	200	158 (79.0%)	4.10 (2.65, 6.34)	<.0001	1.63 (1.27, 2.08)	0.0001	31.8 (16.3, 47.3)	<.0001		0.2237
28 hours	218	106 (48.6%)	200	176 (88.0%)	7.79 (4.71, 12.89)	<.0001	1.81 (1.42, 2.31)	<.0001	39.7 (23.6, 55.7)	<.0001		0.5677
48 hours	218	99 (45.4%)	200	175 (87.5%)	9.15 (5.49, 15.24)	<.0001	1.94 (1.52, 2.49)	<.0001	45.6 (29.9, 61.3)	<.0001		0.0422
Baseline S-K												
1 hour											0.3634	
<=5.3 mmol/L	126	65 (51.6%)	125	78 (62.4%)	1.54 (0.93, 2.56)	0.0932	1.20 (0.86, 1.68)	0.2709	10.0 (-9.0, 29.1)	0.3024		
>5.3 - <=5.5 mmol/L	36	9 (25.0%)	42	18 (42.9%)	2.43 (0.90, 6.58)	0.0797	1.76 (0.79, 3.92)	0.1662	14.3 (-25.7, 54.3)	0.4833		
>5.5 mmol/L	59	1 (1.7%)	36	3 (8.3%)	5.06 (0.47, 54.01)	0.1797	4.37 (0.45, 42.23)	0.2030	20.3 (-69.6, 110.2)	0.6578		
2 hours											0.9367	
<=5.3 mmol/L	126	69 (54.8%)	124	85 (68.5%)	1.76 (1.04, 3.00)	0.0358	1.23 (0.89, 1.70)	0.2002	13.3 (-6.0, 32.6)	0.1776		
>5.3 - <=5.5 mmol/L	36	10 (27.8%)	42	14 (33.3%)	1.45 (0.52, 4.06)	0.4741	1.26 (0.56, 2.85)	0.5709	5.9 (-34.3, 46.1)	0.7734		
>5.5 mmol/L	58	6 (10.3%)	36	6 (16.7%)	1.56 (0.45, 5.43)	0.4846	1.45 (0.46, 4.52)	0.5241	3.3 (-11.5, 18.2)	0.6604		
4 hours											0.4612	
<=5.3 mmol/L	126	84 (66.7%)	125	90 (72.0%)	1.24 (0.72, 2.14)	0.4305	1.07 (0.79, 1.44)	0.6637	3.8 (-17.0, 24.5)	0.7216		
>5.3 - <=5.5 mmol/L	36	17 (47.2%)	42	28 (66.7%)	2.22 (0.89, 5.56)	0.0886	1.41 (0.77, 2.57)	0.2674	19.3 (-14.8, 53.5)	0.2673		
>5.5 mmol/L	58	10 (17.2%)	36	11 (30.6%)	2.02 (0.75, 5.44)	0.1660	1.70 (0.72, 4.02)	0.2274	12.1 (-9.1, 33.4)	0.2618		
24 hours											0.0917	
<=5.3 mmol/L	126	83 (65.9%)	123	109 (88.6%)	4.05 (2.07, 7.93)	<.0001	1.35 (1.01, 1.79)	0.0424	22.9 (0.8, 45.0)	0.0420		
>5.3 - <=5.5 mmol/L	36	16 (44.4%)	41	31 (75.6%)	4.00 (1.50, 10.67)	0.0056	1.71 (0.94, 3.13)	0.0810	31.5 (-2.8, 65.8)	0.0722		
>5.5 mmol/L	57	8 (14.0%)	36	18 (50.0%)	6.10 (2.24, 16.62)	0.0004	3.53 (1.53, 8.16)	0.0032	40.7 (3.9, 77.6)	0.0304		
28 hours											0.0653	
<=5.3 mmol/L	126	79 (62.7%)	123	113 (91.9%)	6.63 (3.15, 13.94)	<.0001	1.46 (1.09, 1.95)	0.0102	28.9 (6.9, 50.9)	0.0100		
>5.3 - <=5.5 mmol/L	36	15 (41.7%)	41	37 (90.2%)	18.71 (4.65, 75.21)	<.0001	2.20 (1.21, 4.02)	0.0099	52.1 (14.4, 89.8)	0.0068		
>5.5 mmol/L	56	12 (21.4%)	36	26 (72.2%)	9.41 (3.56, 24.88)	<.0001	3.35 (1.68, 6.66)	0.0006	53.3 (20.6, 86.1)	0.0014		
48 hours											0.0034	
<=5.3 mmol/L	126	77 (61.1%)	123	107 (87.0%)	4.46 (2.34, 8.51)	<.0001	1.44 (1.07, 1.93)	0.0161	26.8 (5.3, 48.3)	0.0148		
>5.3 - <=5.5 mmol/L	36	13 (36.1%)	41	38 (92.7%)	24.20 (5.98, 98.02)	<.0001	2.56 (1.36, 4.81)	0.0035	58.6 (23.6, 93.5)	0.0010		
>5.5 mmol/L	56	9 (16.1%)	36	30 (83.3%)	28.36 (8.77, 91.69)	<.0001	5.26 (2.49, 11.11)	<.0001	71.6 (25.7, 117.6)	0.0023		

OR, RR and ARR derived from logistic regression using model with treatment group and study.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 3.1.5.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction(%) (95% CI)	ARR p-value	Subgroup interaction test p-value(RR)	Study interaction test p-value(RR)
Chronic kidney disease												
1 hour											0.7286	
Yes	128	37 (28.9%)	116	51 (44.0%)	1.95 (1.13, 3.36)	0.0156	1.50 (0.98, 2.30)	0.0588	15.4 (0.4, 30.4)	0.0439		
No	93	38 (40.9%)	87	48 (55.2%)	1.75 (0.97, 3.17)	0.0654	1.34 (0.87, 2.05)	0.1843	14.9 (-5.5, 35.3)	0.1514		
2 hours											0.2360	
Yes	127	36 (28.3%)	115	53 (46.1%)	2.21 (1.27, 3.84)	0.0049	1.59 (1.04, 2.44)	0.0308	17.3 (2.2, 32.3)	0.0244		
No	93	49 (52.7%)	87	52 (59.8%)	1.30 (0.72, 2.36)	0.3825	1.12 (0.76, 1.66)	0.5638	6.6 (-15.4, 28.6)	0.5562		
4 hours											0.2738	
Yes	127	57 (44.9%)	116	75 (64.7%)	2.23 (1.33, 3.76)	0.0024	1.43 (1.01, 2.02)	0.0414	19.4 (0.8, 38.1)	0.0414		
No	93	54 (58.1%)	87	54 (62.1%)	1.21 (0.66, 2.21)	0.5356	1.08 (0.74, 1.58)	0.6956	4.5 (-18.3, 27.3)	0.6995		
24 hours											0.0538	
Yes	127	50 (39.4%)	113	91 (80.5%)	6.44 (3.57, 11.61)	<.0001	2.04 (1.45, 2.88)	<.0001	41.6 (21.7, 61.5)	<.0001		
No	92	57 (62.0%)	87	67 (77.0%)	2.15 (1.11, 4.16)	0.0235	1.26 (0.88, 1.79)	0.2069	16.7 (-8.2, 41.5)	0.1893		
28 hours											0.6075	
Yes	126	57 (45.2%)	113	98 (86.7%)	7.92 (4.13, 15.17)	<.0001	1.91 (1.37, 2.64)	0.0001	41.2 (20.3, 62.1)	0.0001		
No	92	49 (53.3%)	87	78 (89.7%)	7.57 (3.38, 16.97)	<.0001	1.68 (1.17, 2.41)	0.0046	36.8 (11.5, 62.0)	0.0043		
48 hours											0.0592	
Yes	126	47 (37.3%)	113	102 (90.3%)	17.07 (8.13, 35.86)	<.0001	2.42 (1.71, 3.43)	<.0001	55.3 (35.0, 75.6)	<.0001		
No	92	52 (56.5%)	87	73 (83.9%)	4.23 (2.06, 8.67)	<.0001	1.50 (1.05, 2.14)	0.0263	30.0 (4.7, 55.3)	0.0202		
Congestive heart disease												
1 hour											0.8835	
Yes	81	25 (30.9%)	75	33 (44.0%)	1.72 (0.88, 3.35)	0.1109	1.39 (0.83, 2.34)	0.2146	11.5 (-7.8, 30.9)	0.2435		
No	140	50 (35.7%)	128	66 (51.6%)	1.97 (1.20, 3.24)	0.0072	1.46 (1.01, 2.11)	0.0438	18.4 (2.4, 34.4)	0.0239		
2 hours											0.1648	
Yes	81	33 (40.7%)	74	31 (41.9%)	1.01 (0.53, 1.95)	0.9646	1.01 (0.62, 1.65)	0.9735	0.6 (-19.8, 21.1)	0.9531		
No	139	52 (37.4%)	128	74 (57.8%)	2.32 (1.41, 3.81)	0.0009	1.55 (1.08, 2.21)	0.0161	20.6 (4.0, 37.2)	0.0152		
4 hours											0.6894	
Yes	81	37 (45.7%)	75	47 (62.7%)	1.96 (1.02, 3.76)	0.0419	1.35 (0.88, 2.08)	0.1730	16.7 (-6.3, 39.6)	0.1549		
No	139	74 (53.2%)	128	82 (64.1%)	1.59 (0.97, 2.61)	0.0646	1.21 (0.88, 1.66)	0.2329	11.0 (-7.5, 29.5)	0.2441		
24 hours											0.8388	
Yes	81	38 (46.9%)	75	56 (74.7%)	3.35 (1.67, 6.70)	0.0006	1.56 (1.04, 2.36)	0.0335	28.1 (3.8, 52.3)	0.0236		
No	138	69 (50.0%)	125	102 (81.6%)	4.68 (2.64, 8.30)	<.0001	1.65 (1.22, 2.25)	0.0014	34.0 (14.0, 54.0)	0.0008		
28 hours											0.8457	
Yes	81	38 (46.9%)	75	62 (82.7%)	5.41 (2.57, 11.38)	<.0001	1.75 (1.17, 2.63)	0.0065	35.3 (9.9, 60.7)	0.0065		
No	137	68 (49.6%)	125	114 (91.2%)	10.72 (5.28, 21.78)	<.0001	1.84 (1.36, 2.49)	<.0001	42.5 (21.8, 63.2)	<.0001		
48 hours											0.7657	
Yes	81	37 (45.7%)	75	64 (85.3%)	7.22 (3.26, 15.99)	<.0001	1.84 (1.23, 2.76)	0.0032	39.9 (14.6, 65.2)	0.0020		
No	137	62 (45.3%)	125	111 (88.8%)	10.80 (5.49, 21.24)	<.0001	1.99 (1.46, 2.72)	<.0001	49.0 (28.9, 69.1)	<.0001		

OR, RR and ARR derived from logistic regression using model with treatment group and study.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 3.1.5.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction(%) (95% CI)	ARR p-value	Subgroup interaction test p-value(RR)	Study interaction test p-value(RR)
Diabetes mellitus												
1 hour											0.8244	
Yes	131	40 (30.5%)	116	48 (41.4%)	1.65 (0.97, 2.81)	0.0650	1.38 (0.90, 2.10)	0.1402	10.4 (-4.9, 25.6)	0.1833		
No	90	35 (38.9%)	87	51 (58.6%)	2.17 (1.18, 3.99)	0.0125	1.48 (0.96, 2.27)	0.0770	19.9 (-0.3, 40.2)	0.0540		
2 hours											0.6178	
Yes	131	47 (35.9%)	116	52 (44.8%)	1.47 (0.87, 2.47)	0.1518	1.25 (0.84, 1.86)	0.2732	8.7 (-7.0, 24.5)	0.2774		
No	89	38 (42.7%)	86	53 (61.6%)	2.17 (1.18, 3.98)	0.0125	1.44 (0.95, 2.19)	0.0842	19.6 (-1.9, 41.0)	0.0734		
4 hours											0.4206	
Yes	131	56 (42.7%)	116	68 (58.6%)	1.95 (1.16, 3.26)	0.0112	1.38 (0.97, 1.98)	0.0747	15.8 (-2.3, 33.8)	0.0870		
No	89	55 (61.8%)	87	61 (70.1%)	1.42 (0.75, 2.66)	0.2814	1.12 (0.78, 1.62)	0.5318	7.7 (-16.3, 31.7)	0.5306		
24 hours											0.2891	
Yes	130	56 (43.1%)	115	89 (77.4%)	4.64 (2.63, 8.17)	<.0001	1.81 (1.29, 2.54)	0.0006	35.1 (15.2, 55.0)	0.0005		
No	89	51 (57.3%)	85	69 (81.2%)	3.21 (1.59, 6.49)	0.0012	1.39 (0.97, 2.00)	0.0733	26.2 (1.7, 50.7)	0.0364		
28 hours											0.6489	
Yes	129	61 (47.3%)	115	103 (89.6%)	9.79 (4.87, 19.69)	<.0001	1.90 (1.38, 2.61)	<.0001	42.6 (21.3, 63.9)	<.0001		
No	89	45 (50.6%)	85	73 (85.9%)	5.96 (2.84, 12.50)	<.0001	1.70 (1.17, 2.46)	0.0054	35.6 (11.0, 60.2)	0.0046		
48 hours											0.8605	
Yes	129	58 (45.0%)	115	100 (87.0%)	9.31 (4.76, 18.22)	<.0001	1.98 (1.43, 2.74)	<.0001	47.1 (26.0, 68.2)	<.0001		
No	89	41 (46.1%)	85	75 (88.2%)	8.90 (4.03, 19.65)	<.0001	1.89 (1.29, 2.77)	0.0010	43.5 (19.4, 67.6)	0.0004		
RAASi medications												
1 hour											0.1269	
Yes	147	55 (37.4%)	142	66 (46.5%)	1.46 (0.91, 2.34)	0.1179	1.24 (0.87, 1.78)	0.2363	10.4 (-4.6, 25.4)	0.1725		
No	74	20 (27.0%)	61	33 (54.1%)	3.65 (1.71, 7.80)	0.0008	2.11 (1.20, 3.72)	0.0099	27.6 (5.9, 49.4)	0.0127		
2 hours											0.8383	
Yes	146	57 (39.0%)	141	73 (51.8%)	1.68 (1.05, 2.69)	0.0309	1.32 (0.94, 1.87)	0.1124	12.7 (-2.8, 28.3)	0.1081		
No	74	28 (37.8%)	61	32 (52.5%)	1.83 (0.89, 3.77)	0.1026	1.37 (0.81, 2.30)	0.2372	15.0 (-7.5, 37.5)	0.1921		
4 hours											0.7917	
Yes	146	72 (49.3%)	142	91 (64.1%)	1.84 (1.14, 2.95)	0.0118	1.30 (0.95, 1.77)	0.0976	14.8 (-2.7, 32.2)	0.0966		
No	74	39 (52.7%)	61	38 (62.3%)	1.54 (0.76, 3.12)	0.2333	1.20 (0.76, 1.89)	0.4367	10.7 (-15.2, 36.6)	0.4186		
24 hours											0.6326	
Yes	145	68 (46.9%)	139	111 (79.9%)	4.65 (2.72, 7.95)	<.0001	1.70 (1.26, 2.30)	0.0006	34.7 (16.3, 53.2)	0.0002		
No	74	39 (52.7%)	61	47 (77.0%)	3.03 (1.41, 6.50)	0.0044	1.46 (0.95, 2.26)	0.0832	24.5 (-3.5, 52.6)	0.0869		
28 hours											0.6889	
Yes	145	67 (46.2%)	139	121 (87.1%)	7.82 (4.32, 14.15)	<.0001	1.88 (1.40, 2.54)	<.0001	41.4 (22.2, 60.6)	<.0001		
No	73	39 (53.4%)	61	55 (90.2%)	8.25 (3.12, 21.80)	<.0001	1.70 (1.12, 2.58)	0.0124	38.1 (8.7, 67.5)	0.0112		
48 hours											0.9062	
Yes	145	65 (44.8%)	139	120 (86.3%)	8.15 (4.49, 14.77)	<.0001	1.93 (1.43, 2.61)	<.0001	44.6 (25.8, 63.4)	<.0001		
No	73	34 (46.6%)	61	55 (90.2%)	13.22 (4.81, 36.36)	<.0001	2.03 (1.31, 3.13)	0.0015	48.8 (20.0, 77.6)	0.0009		

OR, RR and ARR derived from logistic regression using model with treatment group and study.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 3.1.5.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction(%) (95% CI)	ARR p-value	Subgroup interaction test p-value(RR)	Study interaction test p-value(RR)
Baseline eGFR												
1 hour											0.8112	
<15 ml/min/1.73m**2	26	5 (19.2%)	19	6 (31.6%)	1.90 (0.48, 7.58)	0.3615	1.61 (0.49, 5.29)	0.4319	10.3 (-21.3, 41.9)	0.5229		
15- <30 ml/min/1.73m**2	56	10 (17.9%)	56	16 (28.6%)	1.84 (0.75, 4.53)	0.1833	1.60 (0.72, 3.52)	0.2459	9.3 (-22.2, 40.8)	0.5619		
30- <60 ml/min/1.73m**2	100	37 (37.0%)	83	47 (56.6%)	2.26 (1.24, 4.10)	0.0076	1.54 (1.00, 2.37)	0.0504	19.1 (-1.0, 39.3)	0.0626		
>=60 ml/min/1.73m**2	39	23 (59.0%)	45	30 (66.7%)	1.25 (0.51, 3.07)	0.6245	1.09 (0.62, 1.90)	0.7622	6.0 (-28.7, 40.7)	0.7337		
2 hours											0.7838	
<15 ml/min/1.73m**2	26	6 (23.1%)	19	7 (36.8%)	1.94 (0.49, 7.67)	0.3470	1.52 (0.51, 4.53)	0.4528	1.5 (-30.8, 33.9)	0.9258		
15- <30 ml/min/1.73m**2	55	10 (18.2%)	56	19 (33.9%)	2.26 (0.92, 5.56)	0.0747	1.80 (0.83, 3.87)	0.1350	12.2 (-19.0, 43.4)	0.4422		
30- <60 ml/min/1.73m**2	100	45 (45.0%)	82	45 (54.9%)	1.50 (0.83, 2.72)	0.1800	1.22 (0.81, 1.84)	0.3461	11.8 (-8.8, 32.3)	0.2621		
>=60 ml/min/1.73m**2	39	24 (61.5%)	45	34 (75.6%)	1.78 (0.69, 4.59)	0.2343	1.20 (0.70, 2.05)	0.5016	12.4 (-23.3, 48.2)	0.4951		
4 hours											0.6749	
<15 ml/min/1.73m**2	26	9 (34.6%)	19	13 (68.4%)	4.16 (1.15, 15.09)	0.0303	1.94 (0.83, 4.54)	0.1271	33.0 (-10.1, 76.0)	0.1336		
15- <30 ml/min/1.73m**2	55	22 (40.0%)	56	28 (50.0%)	1.54 (0.72, 3.31)	0.2681	1.26 (0.72, 2.20)	0.4177	10.7 (-14.1, 35.6)	0.3973		
30- <60 ml/min/1.73m**2	100	56 (56.0%)	83	59 (71.1%)	1.95 (1.05, 3.62)	0.0348	1.27 (0.88, 1.83)	0.1970	15.0 (-8.3, 38.4)	0.2077		
>=60 ml/min/1.73m**2	39	24 (61.5%)	45	29 (64.4%)	1.01 (0.41, 2.49)	0.9746	1.01 (0.58, 1.75)	0.9843	-0.3 (-35.1, 34.6)	0.9884		
24 hours											0.4469	
<15 ml/min/1.73m**2	26	10 (38.5%)	18	15 (83.3%)	8.33 (1.88, 36.89)	0.0053	2.19 (0.98, 4.88)	0.0560	47.3 (-1.3, 95.8)	0.0566		
15- <30 ml/min/1.73m**2	54	19 (35.2%)	56	39 (69.6%)	4.29 (1.91, 9.62)	0.0004	1.97 (1.14, 3.41)	0.0159	34.9 (7.4, 62.4)	0.0130		
30- <60 ml/min/1.73m**2	100	50 (50.0%)	81	66 (81.5%)	4.60 (2.30, 9.21)	<.0001	1.64 (1.13, 2.37)	0.0085	32.5 (8.6, 56.5)	0.0077		
>=60 ml/min/1.73m**2	39	28 (71.8%)	45	38 (84.4%)	1.98 (0.68, 5.79)	0.2129	1.16 (0.71, 1.91)	0.5552	11.6 (-26.7, 49.9)	0.5511		
28 hours											0.4194	
<15 ml/min/1.73m**2	26	9 (34.6%)	18	17 (94.4%)	31.90 (3.62, 281.37)	0.0018	2.71 (1.20, 6.08)	0.0160	59.3 (8.8, 109.8)	0.0213		
15- <30 ml/min/1.73m**2	54	21 (38.9%)	56	44 (78.6%)	5.87 (2.51, 13.72)	<.0001	2.02 (1.20, 3.39)	0.0084	40.9 (11.7, 70.0)	0.0060		
30- <60 ml/min/1.73m**2	99	49 (49.5%)	81	74 (91.4%)	10.78 (4.51, 25.74)	<.0001	1.84 (1.28, 2.64)	0.0009	41.6 (16.6, 66.7)	0.0011		
>=60 ml/min/1.73m**2	39	27 (69.2%)	45	41 (91.1%)	4.27 (1.24, 14.72)	0.0215	1.31 (0.80, 2.14)	0.2868	21.4 (-17.4, 60.2)	0.2800		
48 hours											0.0187	
<15 ml/min/1.73m**2	26	7 (26.9%)	18	18 (100.0%)	n/a	n/a	3.71 (1.55, 8.91)	0.0033	73.0 (22.6, 123.4)	0.0045		
15- <30 ml/min/1.73m**2	54	17 (31.5%)	56	53 (94.6%)	48.97 (12.05, 199.05)	<.0001	3.04 (1.76, 5.26)	<.0001	66.2 (37.1, 95.3)	<.0001		
30- <60 ml/min/1.73m**2	99	47 (47.5%)	81	69 (85.2%)	7.19 (3.35, 15.42)	<.0001	1.81 (1.25, 2.62)	0.0017	42.3 (18.5, 66.1)	0.0005		
>=60 ml/min/1.73m**2	39	28 (71.8%)	45	35 (77.8%)	1.26 (0.46, 3.43)	0.6472	1.06 (0.64, 1.76)	0.8164	4.5 (-33.0, 41.9)	0.8148		

OR, RR and ARR derived from logistic regression using model with treatment group and study.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 3.1.5.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction(%) (95% CI)	ARR p-value	Subgroup interaction test p-value(RR)	Study interaction test p-value(RR)
Sex												
1 hour											0.5345	
Male	144	42 (29.2%)	117	51 (43.6%)	1.95 (1.16, 3.29)	0.0118	1.53 (1.01, 2.31)	0.0437	15.2 (0.3, 30.1)	0.0463		
Female	77	33 (42.9%)	86	48 (55.8%)	1.59 (0.85, 2.97)	0.1505	1.26 (0.81, 1.97)	0.3109	12.3 (-9.3, 33.9)	0.2636		
2 hours											0.7615	
Male	143	52 (36.4%)	117	58 (49.6%)	1.79 (1.08, 2.97)	0.0248	1.39 (0.95, 2.03)	0.0894	14.4 (-1.8, 30.5)	0.0814		
Female	77	33 (42.9%)	85	47 (55.3%)	1.61 (0.86, 3.04)	0.1399	1.27 (0.81, 1.99)	0.2988	11.8 (-9.5, 33.1)	0.2774		
4 hours											0.7111	
Male	143	67 (46.9%)	117	70 (59.8%)	1.69 (1.03, 2.79)	0.0390	1.28 (0.91, 1.80)	0.1555	12.9 (-5.2, 30.9)	0.1625		
Female	77	44 (57.1%)	86	59 (68.6%)	1.50 (0.78, 2.88)	0.2268	1.16 (0.78, 1.72)	0.4688	11.0 (-13.2, 35.1)	0.3741		
24 hours											0.4920	
Male	142	73 (51.4%)	115	88 (76.5%)	3.40 (1.95, 5.93)	<.0001	1.54 (1.12, 2.10)	0.0077	27.6 (7.5, 47.7)	0.0072		
Female	77	34 (44.2%)	85	70 (82.4%)	5.82 (2.82, 12.00)	<.0001	1.85 (1.22, 2.79)	0.0035	40.4 (16.1, 64.6)	0.0011		
28 hours											0.5706	
Male	141	64 (45.4%)	115	99 (86.1%)	7.38 (3.93, 13.86)	<.0001	1.89 (1.37, 2.60)	<.0001	40.5 (19.8, 61.1)	0.0001		
Female	77	42 (54.5%)	85	77 (90.6%)	7.71 (3.26, 18.22)	<.0001	1.64 (1.12, 2.40)	0.0105	35.9 (9.8, 62.1)	0.0071		
48 hours											0.4611	
Male	141	61 (43.3%)	115	101 (87.8%)	10.58 (5.41, 20.68)	<.0001	2.09 (1.51, 2.88)	<.0001	48.6 (27.9, 69.3)	<.0001		
Female	77	38 (49.4%)	85	74 (87.1%)	7.17 (3.19, 16.13)	<.0001	1.73 (1.17, 2.56)	0.0065	39.2 (14.7, 63.6)	0.0017		
Age (years)												
1 hour											0.5128	
<65 years	76	23 (30.3%)	66	33 (50.0%)	2.36 (1.16, 4.80)	0.0174	1.65 (0.96, 2.83)	0.0681	18.8 (-2.0, 39.7)	0.0766		
>=65 years	145	52 (35.9%)	137	66 (48.2%)	1.68 (1.04, 2.71)	0.0348	1.35 (0.94, 1.94)	0.1092	14.0 (-1.2, 29.1)	0.0718		
2 hours											0.3733	
<65 years	76	26 (34.2%)	66	37 (56.1%)	2.57 (1.27, 5.18)	0.0084	1.65 (0.99, 2.74)	0.0529	21.7 (-0.4, 43.8)	0.0540		
>=65 years	144	59 (41.0%)	136	68 (50.0%)	1.46 (0.91, 2.35)	0.1181	1.23 (0.87, 1.74)	0.2508	9.4 (-6.4, 25.2)	0.2428		
4 hours											0.6468	
<65 years	76	31 (40.8%)	66	37 (56.1%)	1.98 (1.00, 3.93)	0.0495	1.41 (0.87, 2.28)	0.1596	17.6 (-6.4, 41.6)	0.1496		
>=65 years	144	80 (55.6%)	137	92 (67.2%)	1.66 (1.02, 2.69)	0.0424	1.21 (0.90, 1.64)	0.2065	11.9 (-6.5, 30.2)	0.2044		
24 hours											0.7330	
<65 years	76	36 (47.4%)	64	52 (81.3%)	4.98 (2.25, 11.02)	<.0001	1.70 (1.11, 2.62)	0.0151	33.9 (7.0, 60.8)	0.0135		
>=65 years	143	71 (49.7%)	136	106 (77.9%)	3.68 (2.18, 6.23)	<.0001	1.58 (1.17, 2.13)	0.0030	30.5 (11.6, 49.4)	0.0015		
28 hours											0.9500	
<65 years	75	36 (48.0%)	64	55 (85.9%)	6.22 (2.67, 14.47)	<.0001	1.76 (1.15, 2.69)	0.0093	36.6 (8.8, 64.4)	0.0100		
>=65 years	143	70 (49.0%)	136	121 (89.0%)	8.51 (4.53, 15.98)	<.0001	1.82 (1.36, 2.44)	<.0001	40.7 (21.1, 60.3)	<.0001		
48 hours											0.7119	
<65 years	75	37 (49.3%)	64	57 (89.1%)	8.42 (3.35, 21.13)	<.0001	1.80 (1.19, 2.74)	0.0056	39.4 (11.3, 67.6)	0.0061		
>=65 years	143	62 (43.4%)	136	118 (86.8%)	9.36 (5.06, 17.29)	<.0001	2.01 (1.48, 2.74)	<.0001	48.4 (29.6, 67.2)	<.0001		

OR, RR and ARR derived from logistic regression using model with treatment group and study.
For subgroup interaction analysis, the subgroup variable (if not already present)and an interaction term for subgroup*treatment group were added.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 3.2.1.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test RR p-value
Overall	221	21 (9.5%)	203	29 (14.3%)	1.55 (0.84 , 2.88)	0.1622	1.47 (0.85 , 2.53)	0.1684	4.99 (-1.19 , 11.17)	0.1134		0.2140
Baseline S-K											0.9429	
<=5.3 mmol/L	126	11 (8.7%)	125	16 (12.8%)	1.53 (0.69 , 3.42)	0.2990	1.46 (0.71 , 3.00)	0.2991	4.51 (-3.21 , 12.22)	0.2526		
>5.3 - <=5.5 mmol/L	36	2 (5.6%)	42	5 (11.9%)	1.66 (0.35 , 7.82)	0.5238	1.55 (0.39 , 6.16)	0.5341	6.19 (-6.42 , 18.80)	0.3359		
>5.5 mmol/L	59	8 (13.6%)	36	8 (22.2%)	1.83 (0.58 , 5.81)	0.3039	1.78 (0.75 , 4.23)	0.1921	8.90 (-6.74 , 24.54)	0.2647		
Chronic kidney disease											0.4146	
Yes	128	14 (10.9%)	116	17 (14.7%)	1.27 (0.56 , 2.84)	0.5654	1.22 (0.60 , 2.47)	0.5812	3.47 (-4.90 , 11.84)	0.4164		
No	93	7 (7.5%)	87	12 (13.8%)	2.13 (0.79 , 5.73)	0.1357	1.95 (0.81 , 4.71)	0.1362	7.71 (-2.30 , 17.72)	0.1310		
Congestive heart disease											0.1872	
Yes	81	13 (16.0%)	75	13 (17.3%)	1.03 (0.43 , 2.47)	0.9442	1.04 (0.51 , 2.16)	0.9060	0.73 (-10.99 , 12.45)	0.9027		
No	140	8 (5.7%)	128	16 (12.5%)	2.37 (0.97 , 5.80)	0.0596	2.19 (0.96 , 4.97)	0.0624	6.94 (0.00 , 13.88)	0.0499		
Diabetes mellitus											0.5225	
Yes	131	15 (11.5%)	116	17 (14.7%)	1.32 (0.59 , 2.94)	0.4953	1.31 (0.67 , 2.58)	0.4289	4.16 (-4.29 , 12.60)	0.3348		
No	90	6 (6.7%)	87	12 (13.8%)	2.06 (0.75 , 5.69)	0.1621	1.90 (0.76 , 4.76)	0.1685	7.02 (-1.86 , 15.90)	0.1213		
RAASi medications											0.1058	
Yes	147	11 (7.5%)	142	22 (15.5%)	2.23 (1.02 , 4.88)	0.0445	2.00 (1.01 , 3.97)	0.0468	7.82 (0.60 , 15.04)	0.0338		
No	74	10 (13.5%)	61	7 (11.5%)	0.76 (0.27 , 2.16)	0.6129	0.79 (0.32 , 1.93)	0.6062	-2.90 (-15.31 , 9.51)	0.6469		
Baseline eGFR											0.3340	
<15 ml/min/1.73m**2	26	1 (3.8%)	19	3 (15.8%)	3.21 (0.38 , 27.26)	0.2850	2.81 (0.39 , 20.01)	0.3024	11.87 (-6.16 , 29.91)	0.1969		
15- <30 ml/min/1.73m**2	56	10 (17.9%)	56	8 (14.3%)	0.78 (0.28 , 2.18)	0.6419	0.82 (0.35 , 1.91)	0.6415	-3.27 (-17.01 , 10.47)	0.6409		
30- <60 ml/min/1.73m**2	100	8 (8.0%)	83	11 (13.3%)	1.78 (0.62 , 5.11)	0.2836	1.71 (0.68 , 4.30)	0.2582	5.40 (-3.58 , 14.38)	0.2384		
>=60 ml/min/1.73m**2	39	2 (5.1%)	45	7 (15.6%)	3.71 (0.72 , 19.10)	0.1174	3.24 (0.72 , 14.66)	0.1262	11.81 (-1.72 , 25.34)	0.0871		
Sex											0.7635	
Male	144	14 (9.7%)	117	17 (14.5%)	1.54 (0.70 , 3.38)	0.2829	1.44 (0.73 , 2.85)	0.2961	5.56 (-2.47 , 13.59)	0.1748		
Female	77	7 (9.1%)	86	12 (14.0%)	1.26 (0.45 , 3.55)	0.6640	1.20 (0.47 , 3.07)	0.6961	3.89 (-5.78 , 13.57)	0.4303		
Age (years)											0.6207	
<65 years	76	8 (10.5%)	66	11 (16.7%)	1.87 (0.69 , 5.04)	0.2169	1.68 (0.72 , 3.89)	0.2265	7.43 (-4.40 , 19.26)	0.2182		
>=65 years	145	13 (9.0%)	137	18 (13.1%)	1.34 (0.59 , 3.05)	0.4836	1.27 (0.60 , 2.66)	0.5348	4.29 (-3.14 , 11.73)	0.2578		

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods

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Table 3.2.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any serious adverse event (SAE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test RR p-value
Overall	221	1 (0.5%)	203	0 (0.0%)	0.37 (0.01 , 9.05)	0.5391	0.37 (0.02 , 8.96)	0.5395	-0.63 (-1.87 , 0.60)	0.3158		

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods

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Table 3.2.1.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any AE leading to discontinuation of study medication (DAE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test RR p-value
Overall	221	1 (0.5%)	203	1 (0.5%)	1.11 (0.07 , 17.84)	0.9436	1.10 (0.07 , 17.50)	0.9436	0.07 (-1.78 , 1.91)	0.9437		

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods

t_zsiss_ae_dae.pdf generated by zsiss_ac_ae_soc_pt.sas at 10:05:32 on 4 March 2021

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Table 3.2.1.4 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any AE graded as severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test RR p-value
Overall	221	0 (0.0%)	203	1 (0.5%)	3.34 (0.13 , 82.57)	0.4617	3.31 (0.14 , 80.67)	0.4622	0.70 (-0.67 , 2.07)	0.3156		

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods

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Table 3.2.1.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any AE graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test RR p-value
Overall	221	21 (9.5%)	203	28 (13.8%)	1.49 (0.80 , 2.77)	0.2133	1.41 (0.81 , 2.45)	0.2195	4.50 (-1.63 , 10.62)	0.1506		0.1834
Baseline S-K											0.9040	
<=5.3 mmol/L	126	11 (8.7%)	125	15 (12.0%)	1.42 (0.63 , 3.22)	0.3971	1.37 (0.66 , 2.85)	0.3957	3.70 (-3.90 , 11.29)	0.3405		
>5.3 - <=5.5 mmol/L	36	2 (5.6%)	42	5 (11.9%)	1.66 (0.35 , 7.82)	0.5238	1.55 (0.39 , 6.16)	0.5341	6.19 (-6.42 , 18.80)	0.3359		
>5.5 mmol/L	59	8 (13.6%)	36	8 (22.2%)	1.83 (0.58 , 5.81)	0.3039	1.78 (0.75 , 4.23)	0.1921	8.90 (-6.74 , 24.54)	0.2647		
Chronic kidney disease											0.3569	
Yes	128	14 (10.9%)	116	16 (13.8%)	1.17 (0.51 , 2.67)	0.7118	1.14 (0.55 , 2.36)	0.7222	2.59 (-5.66 , 10.84)	0.5385		
No	93	7 (7.5%)	87	12 (13.8%)	2.13 (0.79 , 5.73)	0.1357	1.95 (0.81 , 4.71)	0.1362	7.71 (-2.30 , 17.72)	0.1310		
Congestive heart disease											0.2362	
Yes	81	13 (16.0%)	75	13 (17.3%)	1.03 (0.43 , 2.47)	0.9442	1.04 (0.51 , 2.16)	0.9060	0.73 (-10.99 , 12.45)	0.9027		
No	140	8 (5.7%)	128	15 (11.7%)	2.19 (0.88 , 5.42)	0.0912	2.04 (0.88 , 4.70)	0.0946	6.15 (-0.66 , 12.96)	0.0766		
Diabetes mellitus											0.4702	
Yes	131	15 (11.5%)	116	16 (13.8%)	1.23 (0.54 , 2.78)	0.6254	1.25 (0.62 , 2.50)	0.5346	3.26 (-5.07 , 11.58)	0.4429		
No	90	6 (6.7%)	87	12 (13.8%)	2.06 (0.75 , 5.69)	0.1621	1.90 (0.76 , 4.76)	0.1685	7.02 (-1.86 , 15.90)	0.1213		
RAASi medications											0.1271	
Yes	147	11 (7.5%)	142	21 (14.8%)	2.10 (0.95 , 4.63)	0.0659	1.91 (0.95 , 3.81)	0.0677	7.11 (-0.02 , 14.24)	0.0505		
No	74	10 (13.5%)	61	7 (11.5%)	0.76 (0.27 , 2.16)	0.6129	0.79 (0.32 , 1.93)	0.6062	-2.90 (-15.31 , 9.51)	0.6469		
Baseline eGFR											0.3959	
<15 ml/min/1.73m**2	26	1 (3.8%)	19	2 (10.5%)	1.98 (0.20 , 19.51)	0.5571	1.85 (0.22 , 15.49)	0.5723	6.39 (-9.37 , 22.16)	0.4267		
15- <30 ml/min/1.73m**2	56	10 (17.9%)	56	8 (14.3%)	0.78 (0.28 , 2.18)	0.6419	0.82 (0.35 , 1.91)	0.6415	-3.27 (-17.01 , 10.47)	0.6409		
30- <60 ml/min/1.73m**2	100	8 (8.0%)	83	11 (13.3%)	1.78 (0.62 , 5.11)	0.2836	1.71 (0.68 , 4.30)	0.2582	5.40 (-3.58 , 14.38)	0.2384		
>=60 ml/min/1.73m**2	39	2 (5.1%)	45	7 (15.6%)	3.71 (0.72 , 19.10)	0.1174	3.24 (0.72 , 14.66)	0.1262	11.81 (-1.72 , 25.34)	0.0871		
Sex											0.8496	
Male	144	14 (9.7%)	117	16 (13.7%)	1.42 (0.64 , 3.16)	0.3863	1.35 (0.67 , 2.71)	0.4005	4.69 (-3.22 , 12.60)	0.2454		
Female	77	7 (9.1%)	86	12 (14.0%)	1.26 (0.45 , 3.55)	0.6640	1.20 (0.47 , 3.07)	0.6961	3.89 (-5.78 , 13.57)	0.4303		
Age (years)											0.7402	
<65 years	76	8 (10.5%)	66	10 (15.2%)	1.67 (0.61 , 4.57)	0.3212	1.53 (0.65 , 3.62)	0.3289	5.80 (-5.73 , 17.33)	0.3244		
>=65 years	145	13 (9.0%)	137	18 (13.1%)	1.34 (0.59 , 3.05)	0.4836	1.27 (0.60 , 2.66)	0.5348	4.29 (-3.14 , 11.73)	0.2578		

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods

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Table 3.2.1.6 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any AE resulting in death, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test RR p-value
Overall	221	0 (0.0%)	203	0 (0.0%)								

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods
t_zsiss_ae_death.pdf generated by zsiss_ac_ae_soc_pt.sas at 10:05:37 on 4 March 2021

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Table 3.2.1.7 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Adverse events leading to discontinuation (DAE) by SOC and PT, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)	
Subgroup / Category / SOC / PT	N	n (%)	N	n (%)
Overall				
Any AE	221	1 (0.5%)	203	1 (0.5%)
Gastrointestinal disorders	221	0 (0.0%)	203	1 (0.5%)
Diarrhoea	221	0 (0.0%)	203	1 (0.5%)
Vomiting	221	0 (0.0%)	203	1 (0.5%)
Investigations	221	1 (0.5%)	203	0 (0.0%)
Blood potassium increased	221	1 (0.5%)	203	0 (0.0%)
Baseline S-K				
<=5.3 mmol/L				
Any AE	126	0 (0.0%)	125	1 (0.8%)
Gastrointestinal disorders	126	0 (0.0%)	125	1 (0.8%)
Diarrhoea	126	0 (0.0%)	125	1 (0.8%)
Vomiting	126	0 (0.0%)	125	1 (0.8%)
>5.3 - <=5.5 mmol/L				
Any AE	36	0 (0.0%)	42	0 (0.0%)
>5.5 mmol/L				
Any AE	59	1 (1.7%)	36	0 (0.0%)
Investigations	59	1 (1.7%)	36	0 (0.0%)
Blood potassium increased	59	1 (1.7%)	36	0 (0.0%)
Chronic kidney disease				
Yes				
Any AE	128	1 (0.8%)	116	1 (0.9%)
Gastrointestinal disorders	128	0 (0.0%)	116	1 (0.9%)
Diarrhoea	128	0 (0.0%)	116	1 (0.9%)
Vomiting	128	0 (0.0%)	116	1 (0.9%)
Investigations	128	1 (0.8%)	116	0 (0.0%)
Blood potassium increased	128	1 (0.8%)	116	0 (0.0%)
No				
Any AE	93	0 (0.0%)	87	0 (0.0%)
Congestive heart disease				
Yes				
Any AE	81	1 (1.2%)	75	0 (0.0%)
Investigations	81	1 (1.2%)	75	0 (0.0%)
Blood potassium increased	81	1 (1.2%)	75	0 (0.0%)
No				
Any AE	140	0 (0.0%)	128	1 (0.8%)
Gastrointestinal disorders	140	0 (0.0%)	128	1 (0.8%)
Diarrhoea	140	0 (0.0%)	128	1 (0.8%)
Vomiting	140	0 (0.0%)	128	1 (0.8%)

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Table 3.2.1.7 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Adverse events leading to discontinuation (DAE) by SOC and PT, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)	
Subgroup / Category / SOC / PT	N	n (%)	N	n (%)
Diabetes mellitus				
Yes				
Any AE	131	1 (0.8%)	116	1 (0.9%)
Gastrointestinal disorders	131	0 (0.0%)	116	1 (0.9%)
Diarrhoea	131	0 (0.0%)	116	1 (0.9%)
Vomiting	131	0 (0.0%)	116	1 (0.9%)
Investigations	131	1 (0.8%)	116	0 (0.0%)
Blood potassium increased	131	1 (0.8%)	116	0 (0.0%)
No				
Any AE	90	0 (0.0%)	87	0 (0.0%)
RAASi medications				
Yes				
Any AE	147	0 (0.0%)	142	1 (0.7%)
Gastrointestinal disorders	147	0 (0.0%)	142	1 (0.7%)
Diarrhoea	147	0 (0.0%)	142	1 (0.7%)
Vomiting	147	0 (0.0%)	142	1 (0.7%)
No				
Any AE	74	1 (1.4%)	61	0 (0.0%)
Investigations	74	1 (1.4%)	61	0 (0.0%)
Blood potassium increased	74	1 (1.4%)	61	0 (0.0%)
Baseline eGFR				
<15 ml/min/1.73m**2				
Any AE	26	0 (0.0%)	19	1 (5.3%)
Gastrointestinal disorders	26	0 (0.0%)	19	1 (5.3%)
Diarrhoea	26	0 (0.0%)	19	1 (5.3%)
Vomiting	26	0 (0.0%)	19	1 (5.3%)
15- <30 ml/min/1.73m**2				
Any AE	56	1 (1.8%)	56	0 (0.0%)
Investigations	56	1 (1.8%)	56	0 (0.0%)
Blood potassium increased	56	1 (1.8%)	56	0 (0.0%)
30- <60 ml/min/1.73m**2				
Any AE	100	0 (0.0%)	83	0 (0.0%)
>=60 ml/min/1.73m**2				
Any AE	39	0 (0.0%)	45	0 (0.0%)
Sex				
Male				
Any AE	144	0 (0.0%)	117	1 (0.9%)
Gastrointestinal disorders	144	0 (0.0%)	117	1 (0.9%)
Diarrhoea	144	0 (0.0%)	117	1 (0.9%)
Vomiting	144	0 (0.0%)	117	1 (0.9%)
Female				
Any AE	77	1 (1.3%)	86	0 (0.0%)
Investigations	77	1 (1.3%)	86	0 (0.0%)
Blood potassium increased	77	1 (1.3%)	86	0 (0.0%)

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Table 3.2.1.7 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Adverse events leading to discontinuation (DAE) by SOC and PT, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)	
Subgroup / Category / SOC / PT	**N**	**n (%)**	**N**	**n (%)**
Age (years)				
<65 years				
Any AE	76	1 (1.3%)	66	1 (1.5%)
Gastrointestinal disorders	76	0 (0.0%)	66	1 (1.5%)
Diarrhoea	76	0 (0.0%)	66	1 (1.5%)
Vomiting	76	0 (0.0%)	66	1 (1.5%)
Investigations	76	1 (1.3%)	66	0 (0.0%)
Blood potassium increased	76	1 (1.3%)	66	0 (0.0%)

t_zsiss_ae_dae_socpt.pdf generated by zsiss_ac_ae_soc_pt.sas at 10:05:49 on 4 March 2021

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Table 3.2.1.7 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Adverse events leading to discontinuation (DAE) by SOC and PT, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)	
Subgroup / Category / SOC / PT	**N**	**n (%)**	**N**	**n (%)**
>=65 years				
Any AE	145	0 (0.0%)	137	0 (0.0%)

t_zsiss_ae_dae_socpt.pdf generated by zsiss_ac_ae_soc_pt.sas at 10:05:49 on 4 March 2021

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Table 3.2.1.8 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Adverse events (AE) by SOC and PT occurring in at least 10% of subjects in any treatment group, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test p-value
Overall												
Any AE	221	21 (9.5%)	203	29 (14.3%)	1.55 (0.84 , 2.88)	0.1622	1.47 (0.85 , 2.53)	0.1684	4.99 (-1.19 , 11.17)	0.1134		0.2140
Gastrointestinal disorders: All	221	10 (4.5%)	203	9 (4.4%)	1.02 (0.39 , 2.68)	0.9643	1.04 (0.42 , 2.56)	0.9376	0.18 (-4.52 , 4.88)	0.9408		0.1953

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods

t_zsiss_ae_any_socpt.pdf generated by zsiss_ac_ae_soc_pt.sas at 10:05:43 on 4 March 2021

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Table 3.2.1.9 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serious adverse events (SAE) by SOC and PT occurring in at least 5% of subjects in any treatment group, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test p-value
Overall												
Any AE	221	1 (0.5%)	203	0 (0.0%)	0.37 (0.01 , 9.05)	0.5391	0.37 (0.02 , 8.96)	0.5395	-0.63 (-1.87 , 0.60)	0.3158		

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 5% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods

t_zsiss_ae_sae_socpt.pdf generated by zsiss_ac_ae_soc_pt.sas at 10:05:45 on 4 March 2021

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Table 3.2.1.10 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: AEs graded as severe by SOC and PT occurring in at least 5% of subjects in any treatment group, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test p-value
Overall												
Any AE	221	0 (0.0%)	203	1 (0.5%)	3.34 (0.13 , 82.57)	0.4617	3.31 (0.14 , 80.67)	0.4622	0.70 (-0.67 , 2.07)	0.3156		

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods

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Table 3.2.1.11 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: AEs graded as non-severe by SOC and PT occurring in at least 10% of subjects in any treatment group, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test p-value
Overall												
Any AE	221	21 (9.5%)	203	28 (13.8%)	1.49 (0.80 , 2.77)	0.2133	1.41 (0.81 , 2.45)	0.2195	4.50 (-1.63 , 10.62)	0.1506		0.1834
Gastrointestinal disorders: All	221	10 (4.5%)	203	8 (3.9%)	0.91 (0.33 , 2.50)	0.8550	0.94 (0.36 , 2.42)	0.8907	-0.42 (-4.98 , 4.15)	0.8583		0.1381

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods

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04/03/2021

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Table 3.2.2.1 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: AEs of special interest: urinary tract infection—subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test RR p-value
Overall	221	0 (0.0%)	203	1 (0.5%)	3.89 (0.15 , 99.97)	0.4117	3.72 (0.16 , 87.42)	0.4147	4.17 (-3.83 , 12.16)	0.3070		

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods

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04/03/2021

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Table 3.2.2.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: AEs of special interest: urinary tract infection—subjects experiencing any serious adverse event (SAE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test RR p-value
Overall	221	0 (0.0%)	203	0 (0.0%)								

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods

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Table 3.2.2.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: AEs of special interest: urinary tract infection—subjects experiencing any AE graded as severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test RR p-value
Overall	221	0 (0.0%)	203	0 (0.0%)								

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods

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Table 3.2.2.4 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: AEs of special interest: urinary tract infection—subjects experiencing any AE graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=221)		10g ZS (N=203)									
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test RR p-value	Study interaction test RR p-value
Overall	221	0 (0.0%)	203	1 (0.5%)	3.89 (0.15 , 99.97)	0.4117	3.72 (0.16 , 87.42)	0.4147	4.17 (-3.83 , 12.16)	0.3070		

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
Risk estimates are stratified by subgroup and study and results are combined across studies using inverse-variance methods

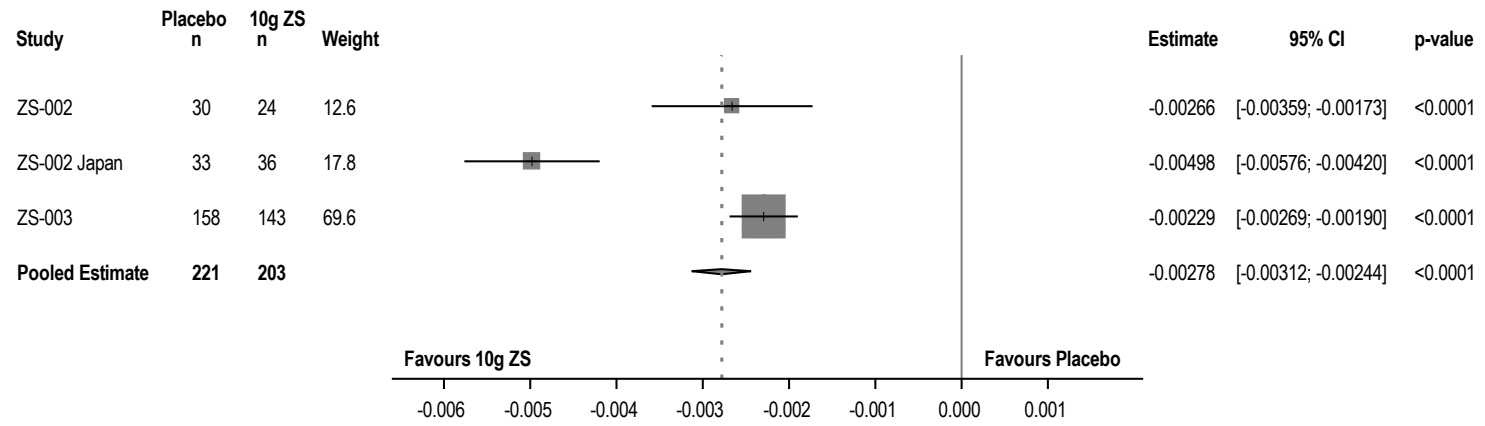
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Overall



Study interaction p-value <0.0001

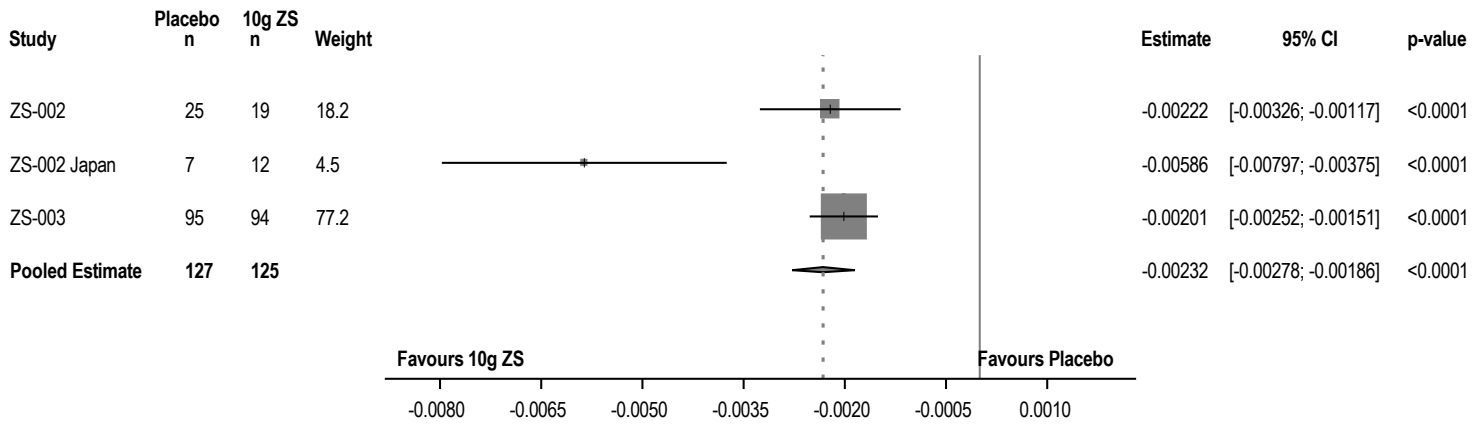
Significant heterogeneity between the studies; validity of pooled estimate is questionable.

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline S-K value: <=5.3 mmol/L



Study interaction p-value 0.0010

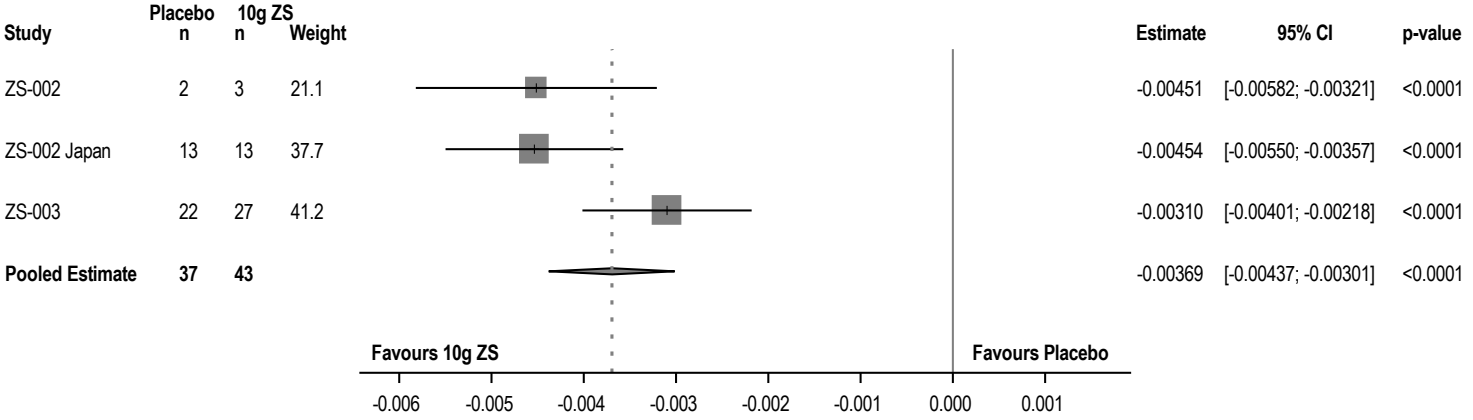
Significant heterogeneity between the studies; validity of pooled estimate is questionable.

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline S-K value: 5.4-5.5 mmol/L



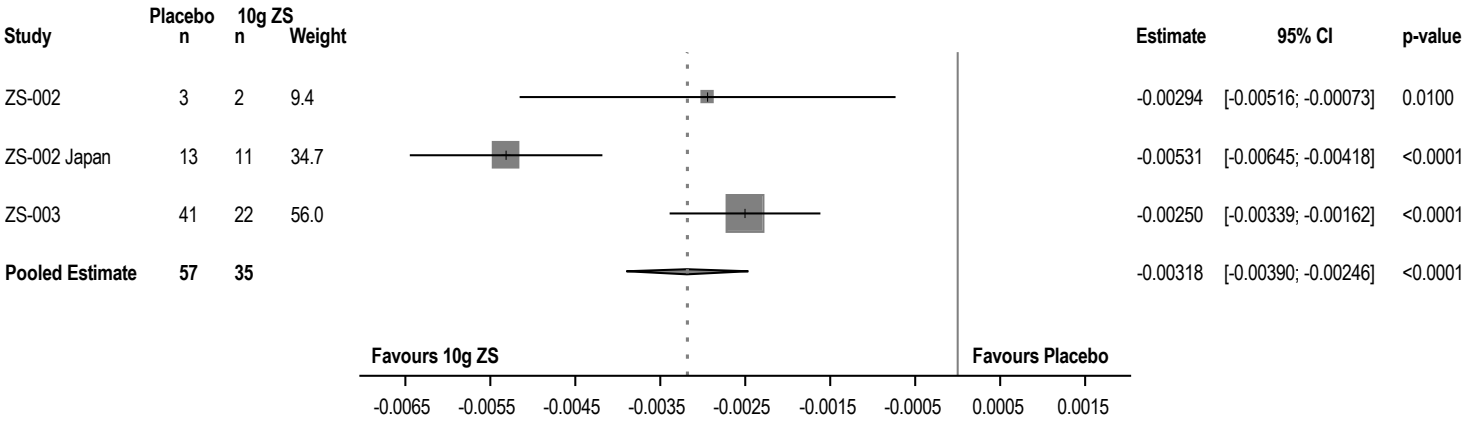
Study interaction p-value 0.2399

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline S-K value: >5.5 mmol/L



Study interaction p-value 0.0470

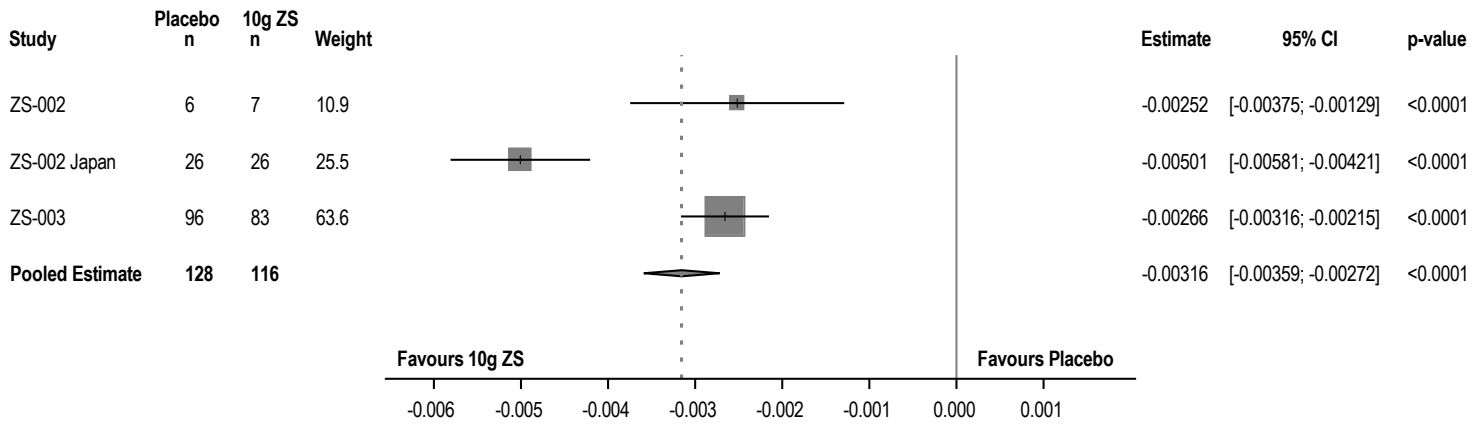
Significant heterogeneity between the studies; validity of pooled estimate is questionable.

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: Yes



Study interaction p-value <0.0001

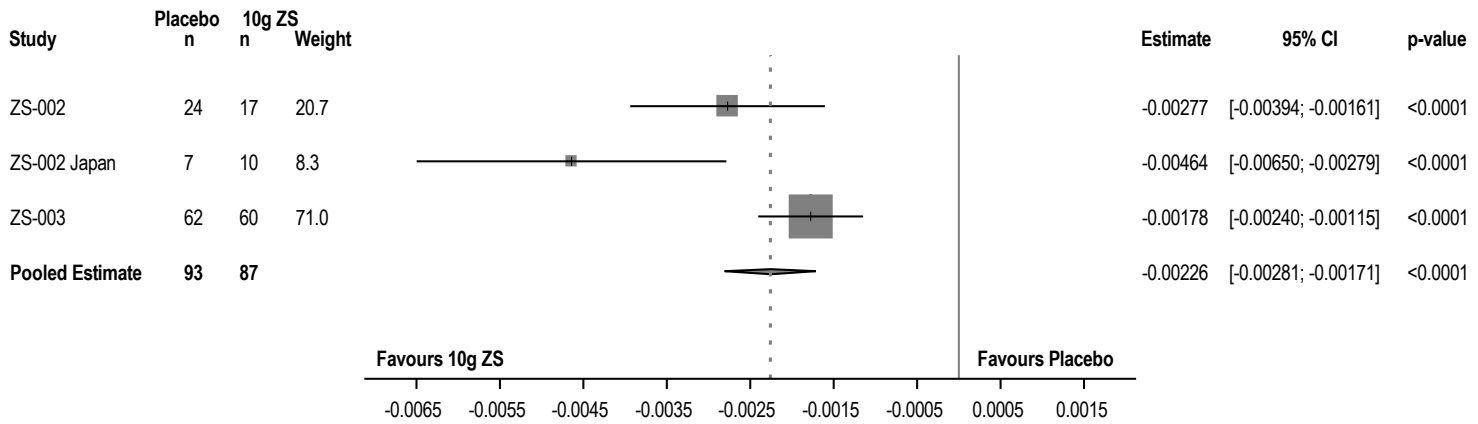
Significant heterogeneity between the studies; validity of pooled estimate is questionable.

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: No



Study interaction p-value 0.0130

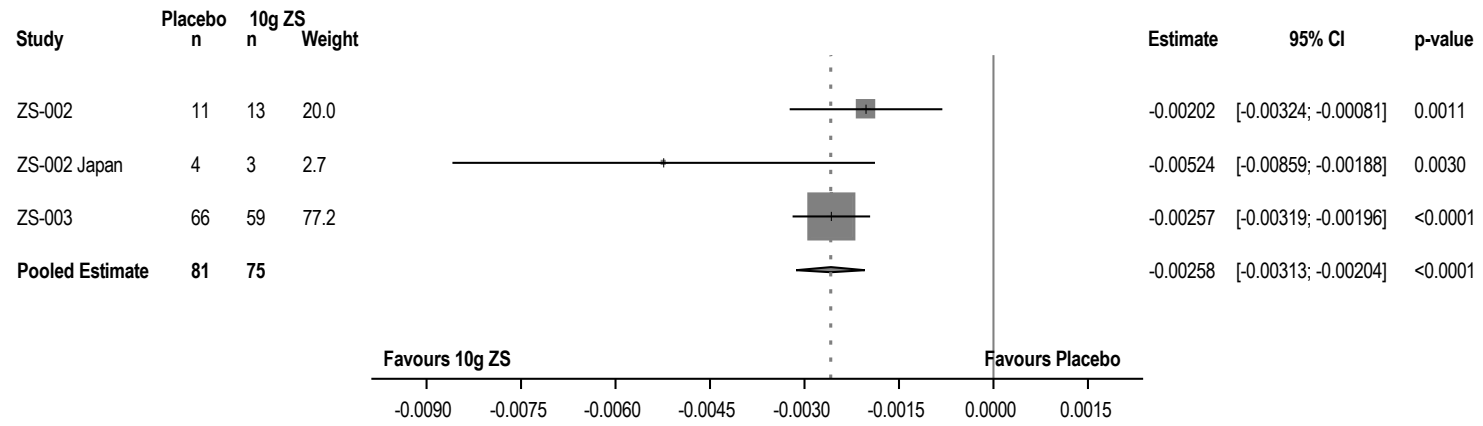
Significant heterogeneity between the studies; validity of pooled estimate is questionable.

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Congestive Heart Disease: Yes



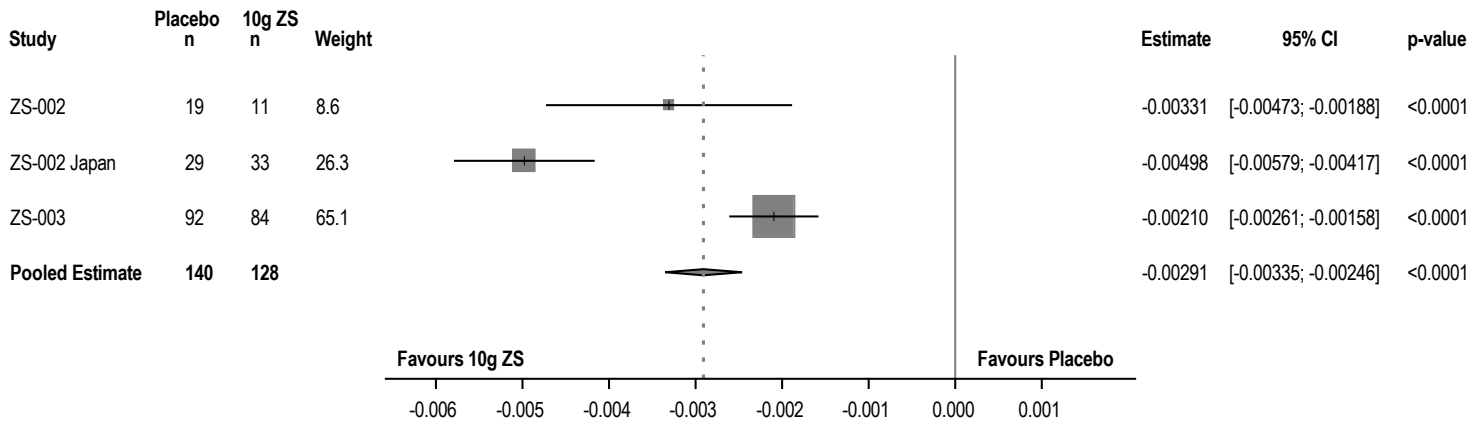
Study interaction p-value 0.3259

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Congestive Heart Disease: No



Study interaction p-value <0.0001

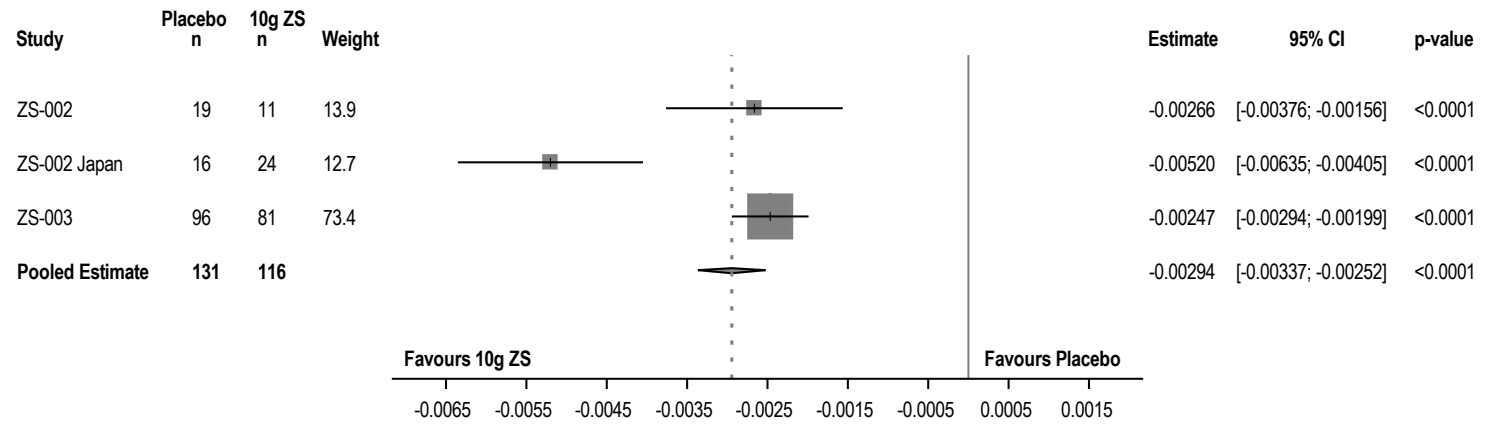
Significant heterogeneity between the studies; validity of pooled estimate is questionable.

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Diabetes mellitus: Yes



Study interaction p-value 0.0001

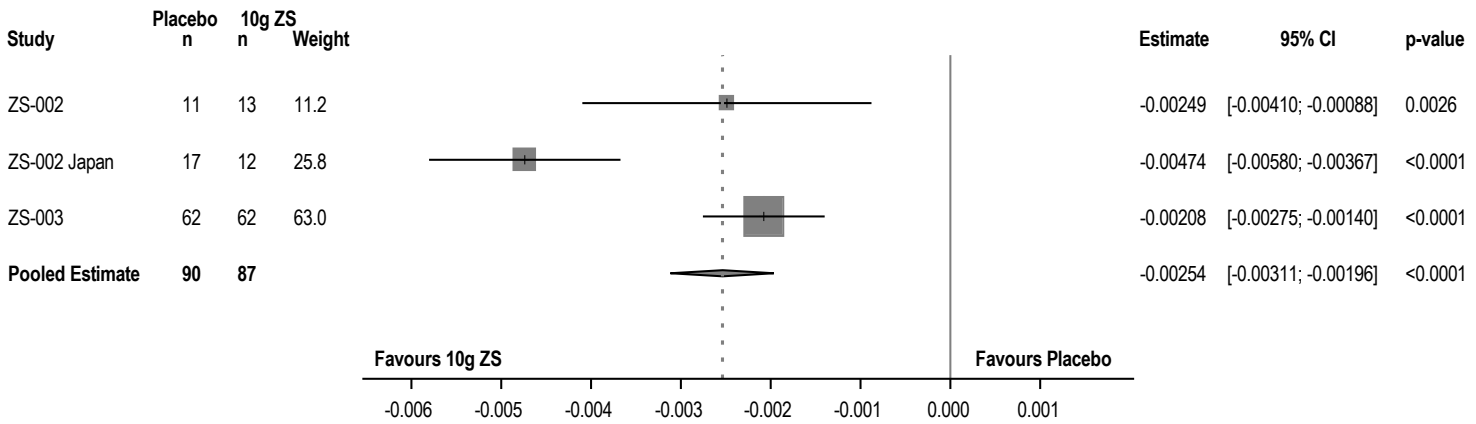
Significant heterogeneity between the studies; validity of pooled estimate is questionable.

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
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The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Diabetes mellitus: No



Study interaction p-value 0.0040

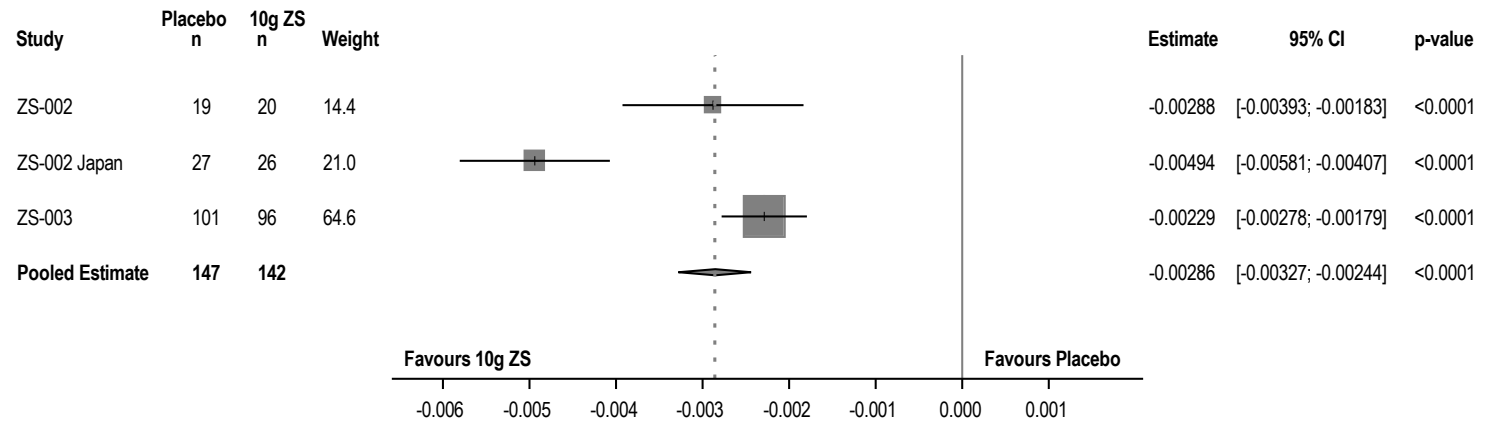
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

RAASi Medications: Yes



Study interaction p-value <0.0001

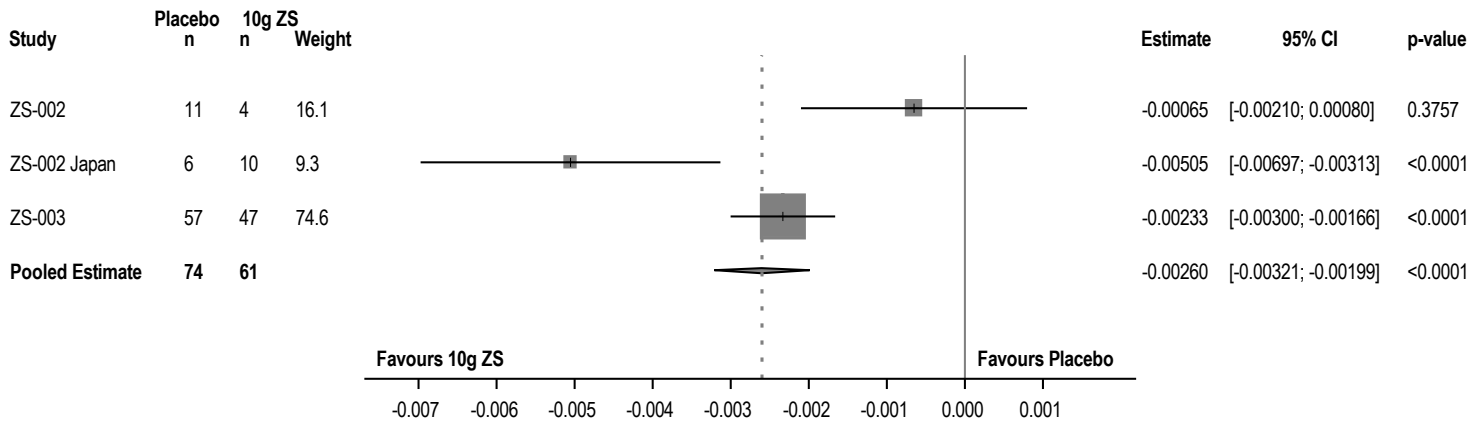
Significant heterogeneity between the studies; validity of pooled estimate is questionable.

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The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
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The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

RAASi Medications: No



Study interaction p-value 0.0005

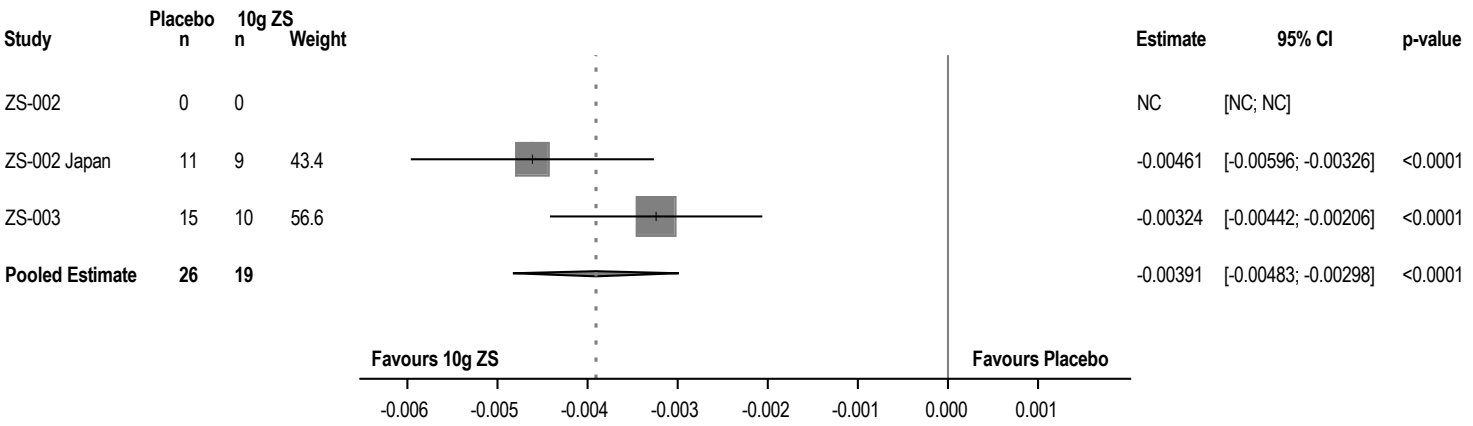
Significant heterogeneity between the studies; validity of pooled estimate is questionable.

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline eGFR: <15



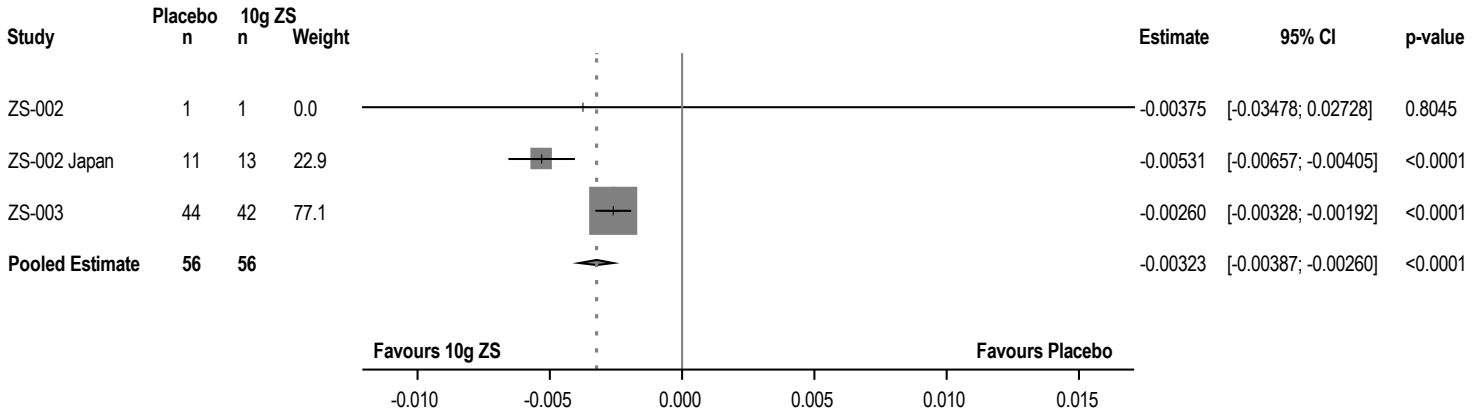
Study interaction p-value 0.1569

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline eGFR: 15-29+



Study interaction p-value 0.0004

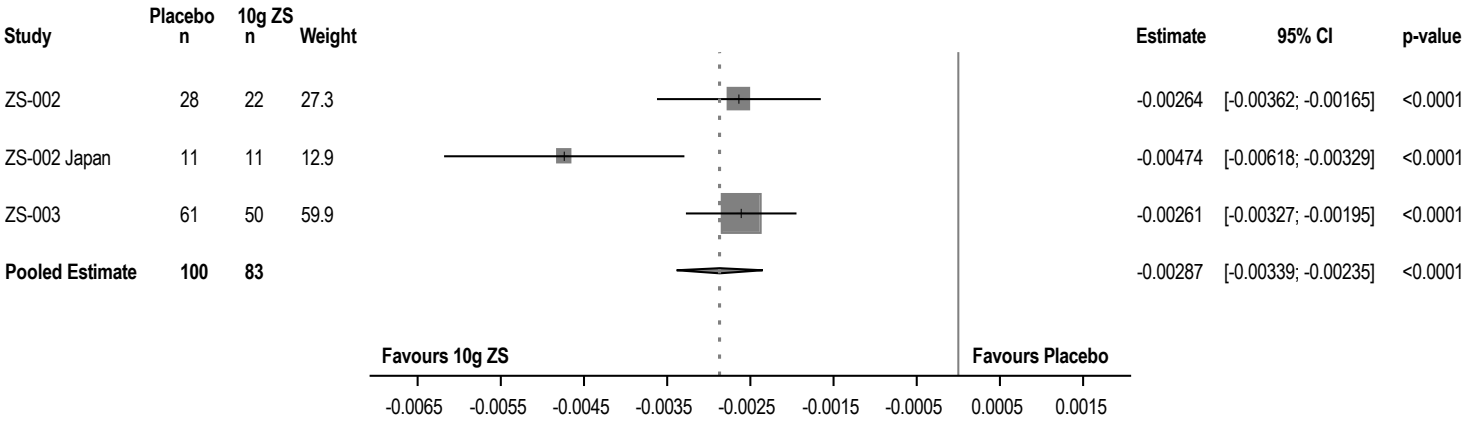
Significant heterogeneity between the studies; validity of pooled estimate is questionable.

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
Confidence limits for ZS-002 extend beyond the bounds of the x-axis; this is done so as not to visually squash the intervals for the other studies.
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline eGFR: 30-59+



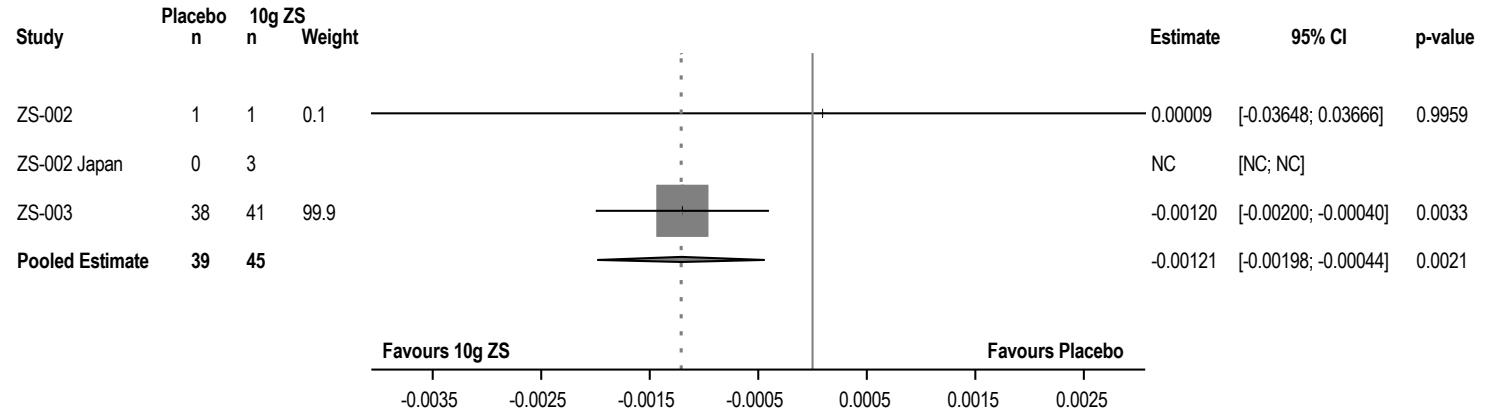
Study interaction p-value 0.1460

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline eGFR: >=60



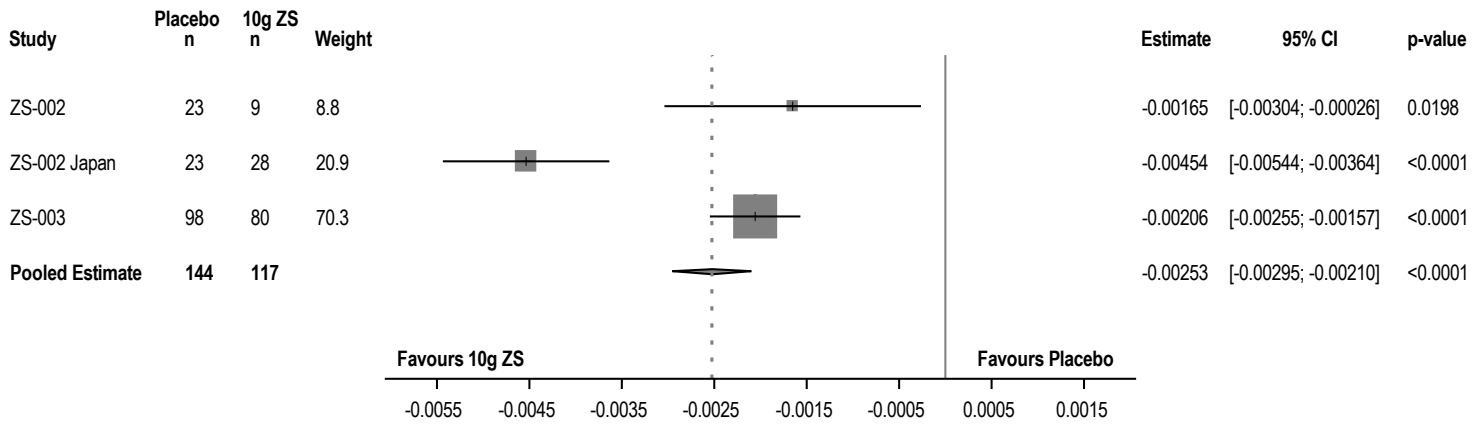
Study interaction p-value 0.8796

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
Confidence limits for ZS-002 extend beyond the bounds of the x-axis; this is done so as not to visually squash the intervals for the other studies.
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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Sex: Male



Study interaction p-value <0.0001

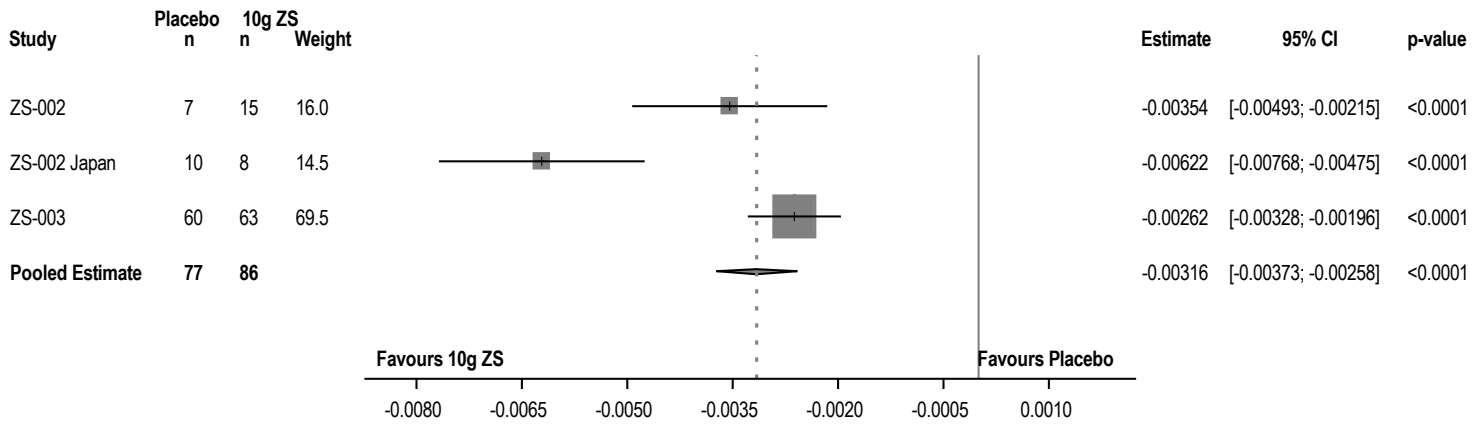
Significant heterogeneity between the studies; validity of pooled estimate is questionable.

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
f_forest.pdf generated by f_forest.sas at 18FEB2021:10:31:56

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Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Sex: Female



Study interaction p-value 0.0008

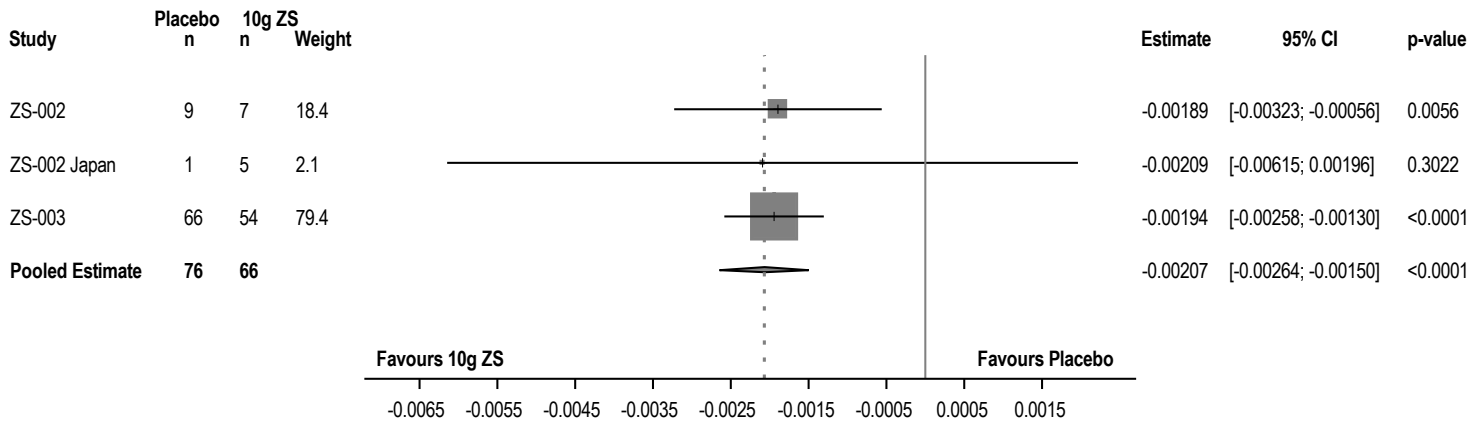
Significant heterogeneity between the studies; validity of pooled estimate is questionable.

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
f_forest.pdf generated by f_forest.sas at 18FEB2021:10:31:56

LOKELMA

Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Age: <65 years



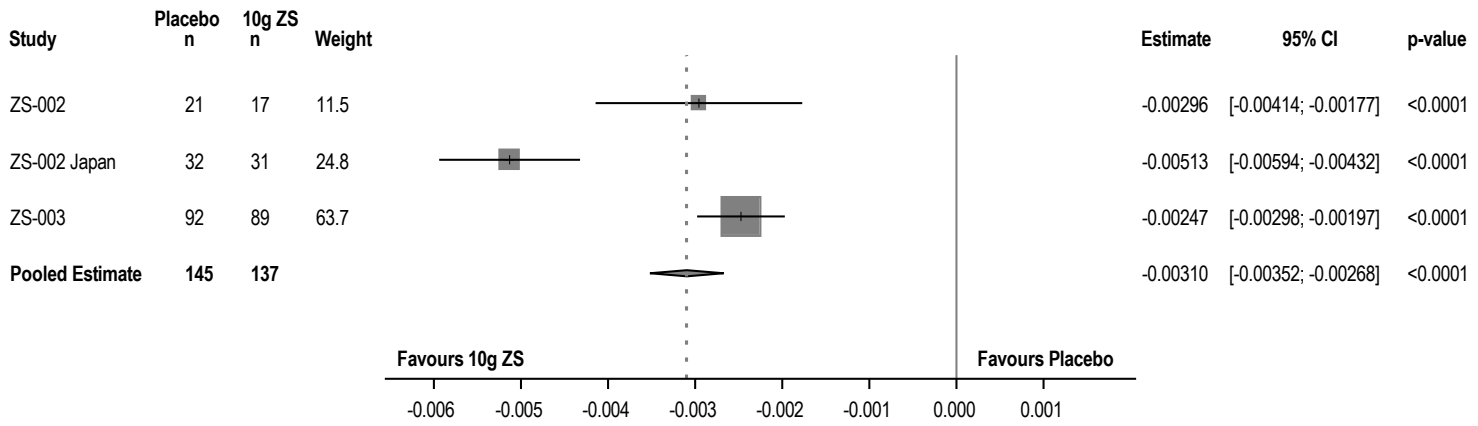
Study interaction p-value 0.1866

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
f_forest.pdf generated by f_forest.sas at 18FEB2021:10:31:56

LOKELMA

Figure 3.1.1.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) exponential rate of change to 48 hours post baseline, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Age: >=65 years



Study interaction p-value <0.0001

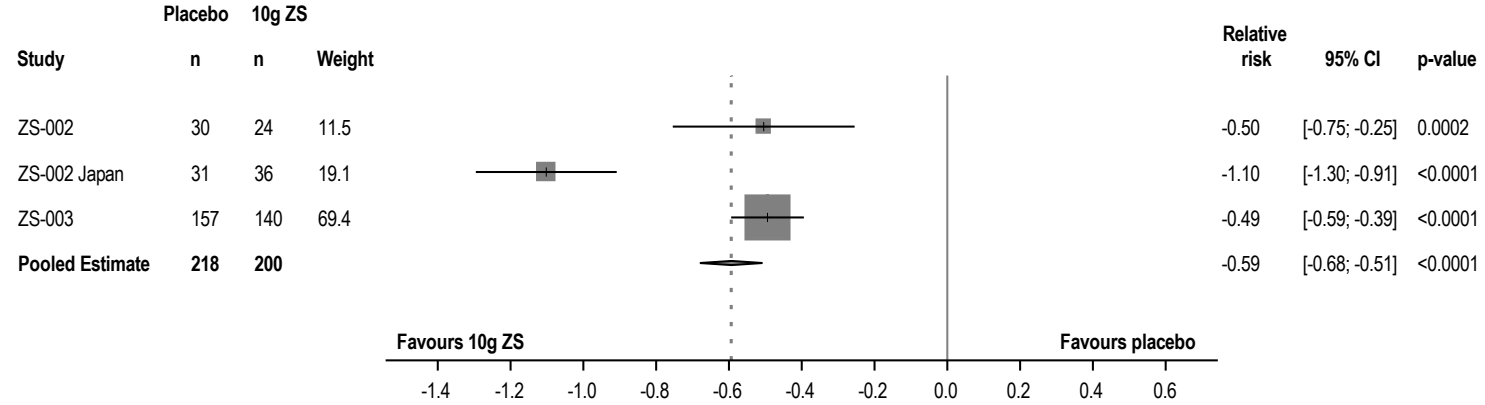
Significant heterogeneity between the studies; validity of pooled estimate is questionable.

Exponential rate of change estimated using a mixed effects longitudinal model with log(S-K) as the dependent variable.
The model for individual studies includes: fixed effects for time and time*treatment, random effects for intercept and time with an unstructured covariance matrix.
The model for the pooled estimate additional includes study as a fixed effect.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated from the pooled mixed effects longitudinal model with study*time*treatment as an additional fixed effect.
CI = Confidence Intervals, NC = Not calculated
f_forest.pdf generated by f_forest.sas at 18FEB2021:10:31:56

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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Overall



Study interaction p-value 0.0145

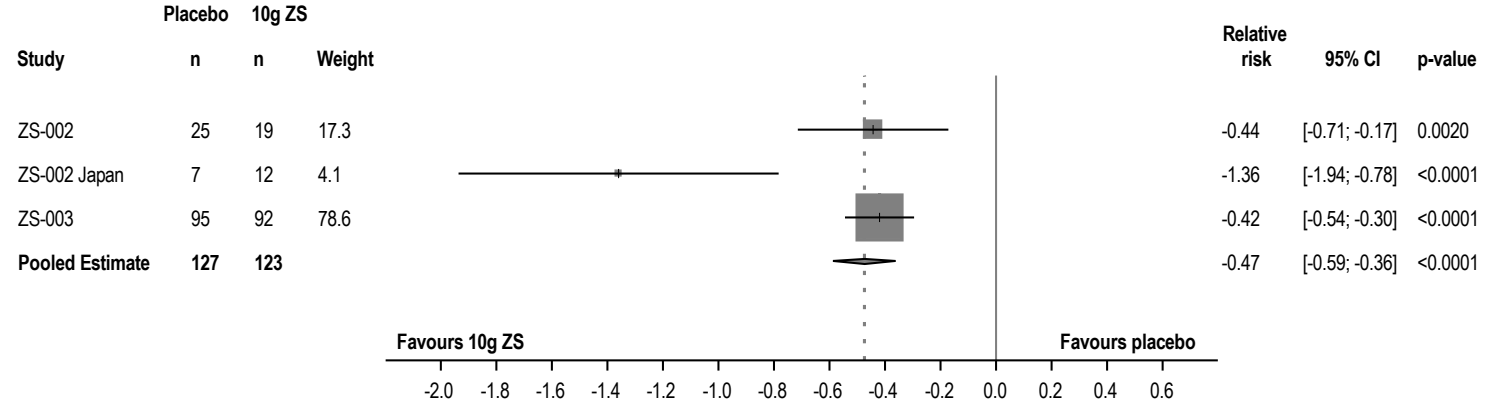
Significant heterogeneity between the studies; validity of pooled relative risk is questionable.

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline S-K value: <=5.3 mmol/L



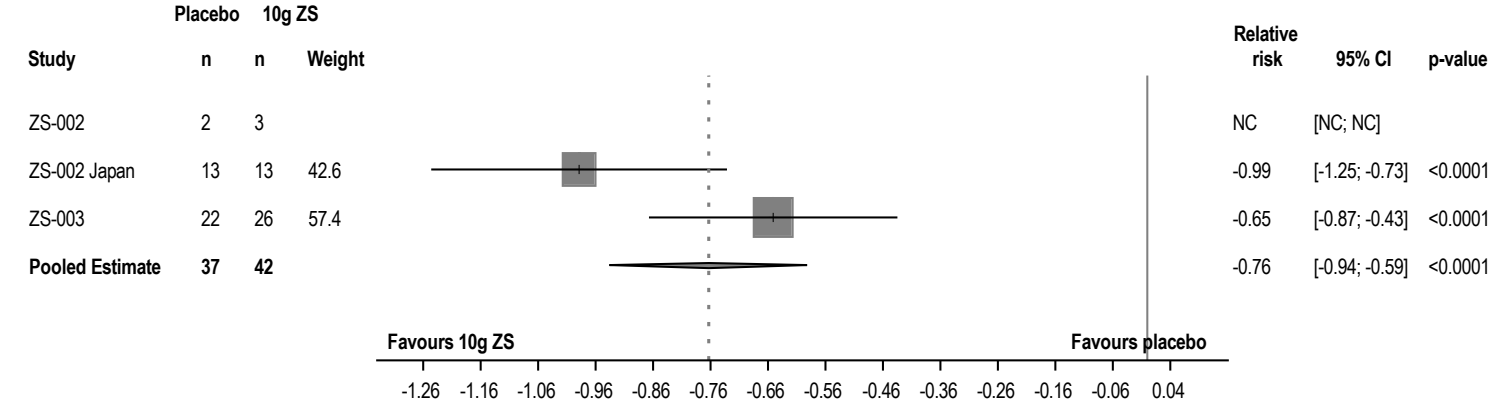
Study interaction p-value 0.3467

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
f_forest.pdf generated by f_forest.sas at 19FEB2021:18:16:02

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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline S-K value: 5.4-5.5 mmol/L



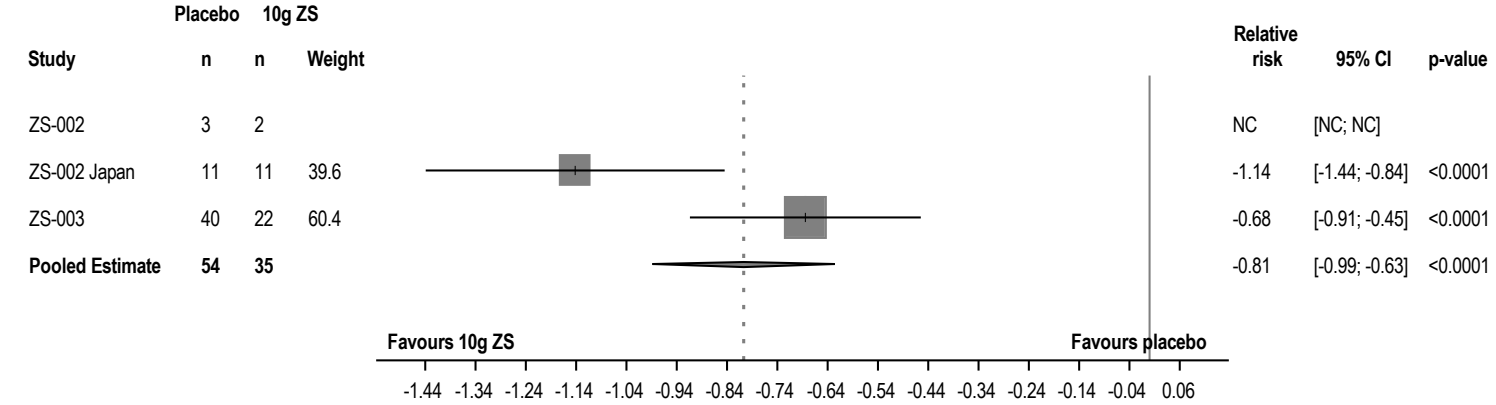
Study interaction p-value 0.8550

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
f_forest.pdf generated by f_forest.sas at 19FEB2021:18:16:02

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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline S-K value: >5.5 mmol/L



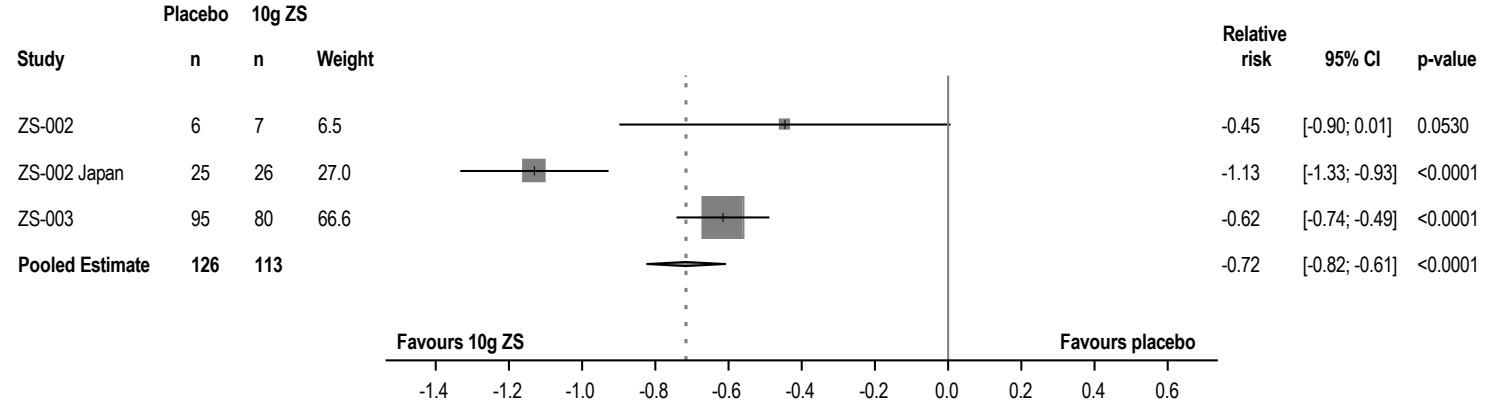
Study interaction p-value 0.0552

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
f_forest.pdf generated by f_forest.sas at 19FEB2021:18:16:02

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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: Yes



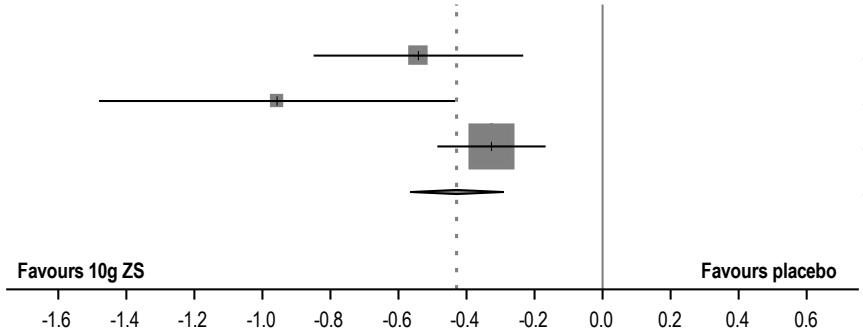
Study interaction p-value 0.1745

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
f_forest.pdf generated by f_forest.sas at 19FEB2021:18:16:02

LOKELMA

Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: No



Study	Placebo n	10g ZS n	Weight	Relative risk	95% CI	p-value
ZS-002	24	17	20.1	-0.54	[-0.85; -0.23]	0.0010
ZS-002 Japan	6	10	7.9	-0.96	[-1.48; -0.43]	0.0017
ZS-003	62	60	72.0	-0.33	[-0.49; -0.17]	<0.0001
Pooled Estimate	**92**	**87**		-0.43	[-0.57; -0.29]	<0.0001

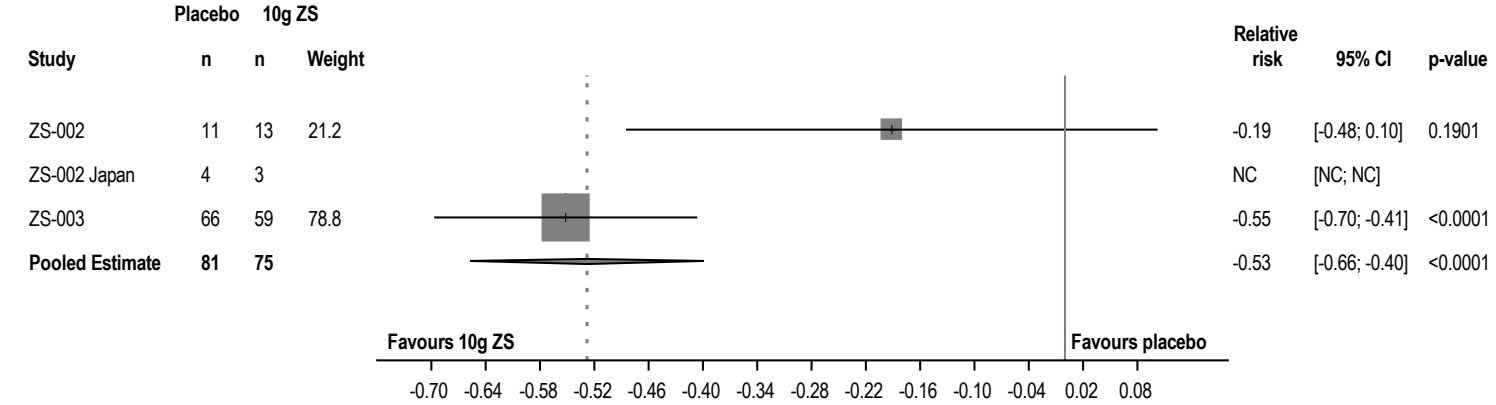
Study interaction p-value 0.0822

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
f_forest.pdf generated by f_forest.sas at 19FEB2021:18:16:02

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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Congestive Heart Disease: Yes



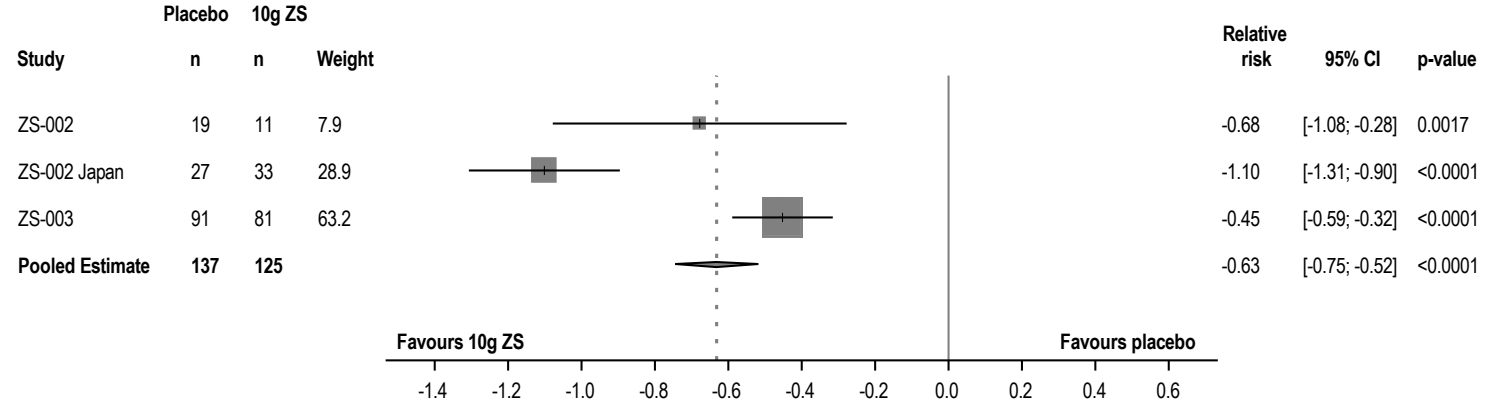
Study interaction p-value 0.1179

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
f_forest.pdf generated by f_forest.sas at 19FEB2021:18:16:02

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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Congestive Heart Disease: No



Study interaction p-value 0.0398

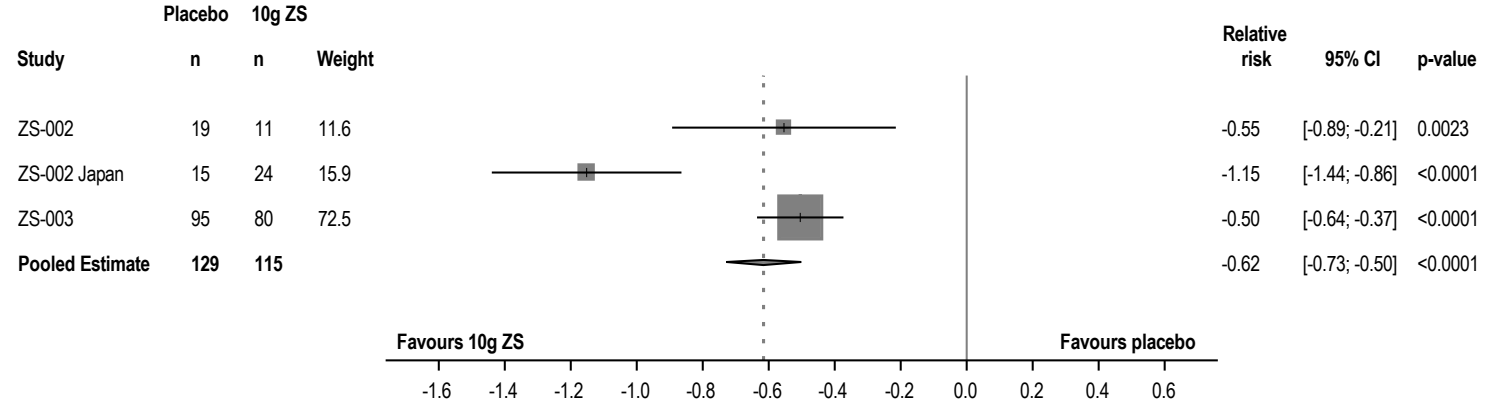
Significant heterogeneity between the studies; validity of pooled relative risk is questionable.

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
f_forest.pdf generated by f_forest.sas at 19FEB2021:18:16:02

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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Diabetes mellitus: Yes



Study interaction p-value 0.0045

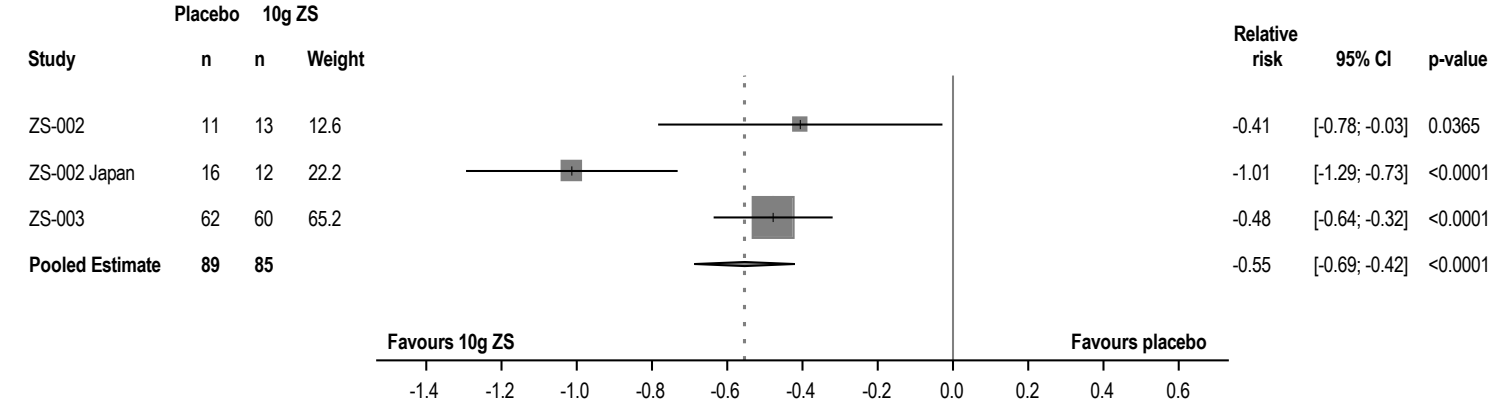
Significant heterogeneity between the studies; validity of pooled relative risk is questionable.

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
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Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
f_forest.pdf generated by f_forest.sas at 19FEB2021:18:16:02

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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Diabetes mellitus: No



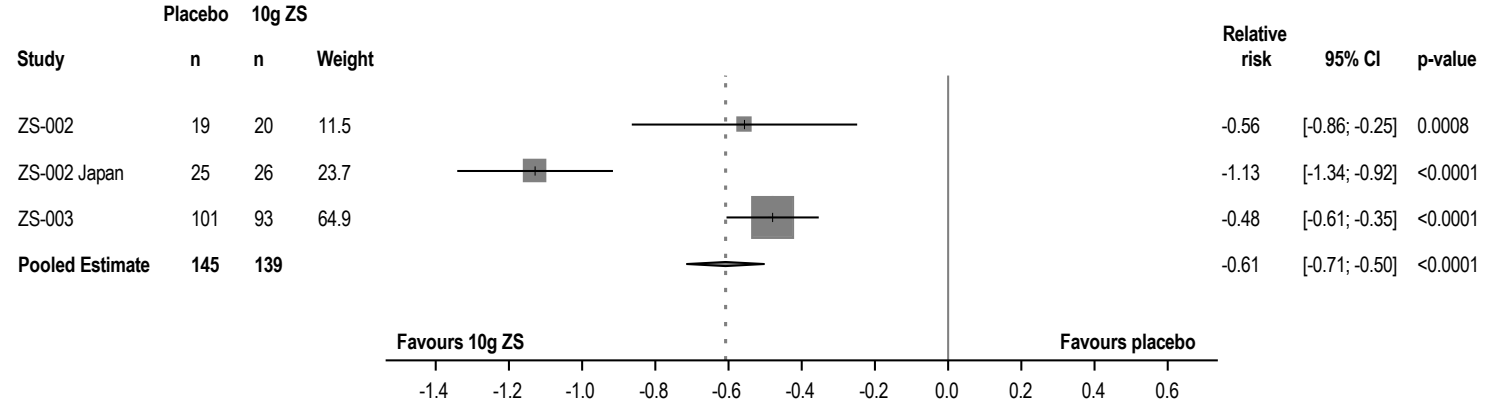
Study interaction p-value 0.3462

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
f_forest.pdf generated by f_forest.sas at 19FEB2021:18:16:02

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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

RAASi Medications: Yes



Study interaction p-value 0.0052

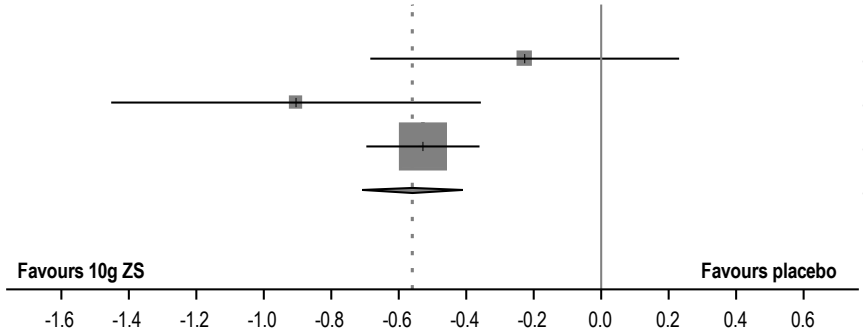
Significant heterogeneity between the studies; validity of pooled relative risk is questionable.

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

RAASi Medications: No



Study	Placebo n	10g ZS n	Weight	Relative risk	95% CI	p-value
ZS-002	11	4	12.4	-0.23	[-0.68; 0.23]	0.3057
ZS-002 Japan	6	10	8.6	-0.90	[-1.45; -0.36]	0.0033
ZS-003	56	47	78.9	-0.53	[-0.70; -0.36]	<0.0001
Pooled Estimate	**73**	**61**		-0.56	[-0.71; -0.41]	<0.0001

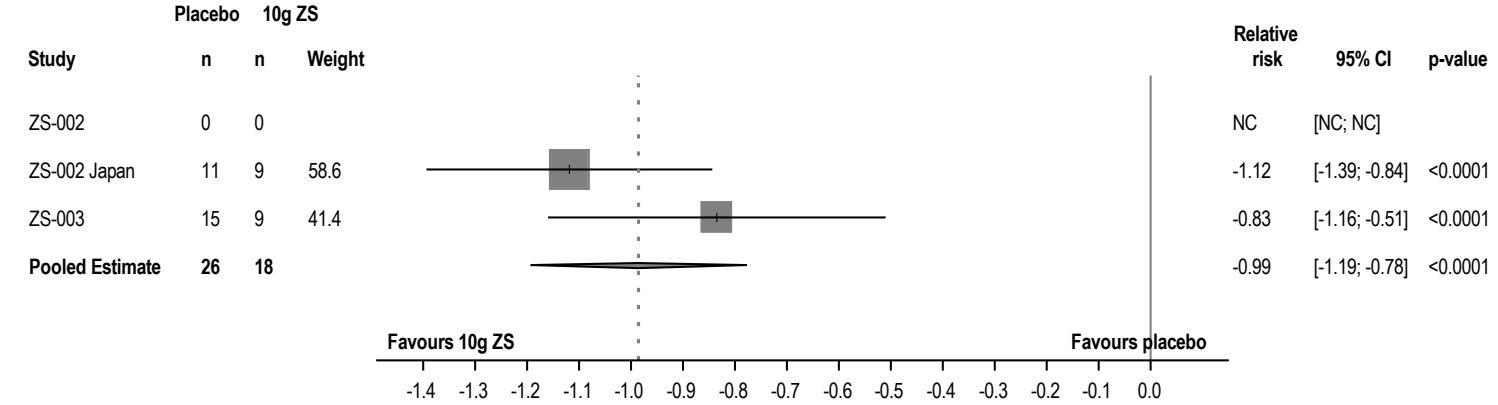
Study interaction p-value 0.0699

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline eGFR: <15



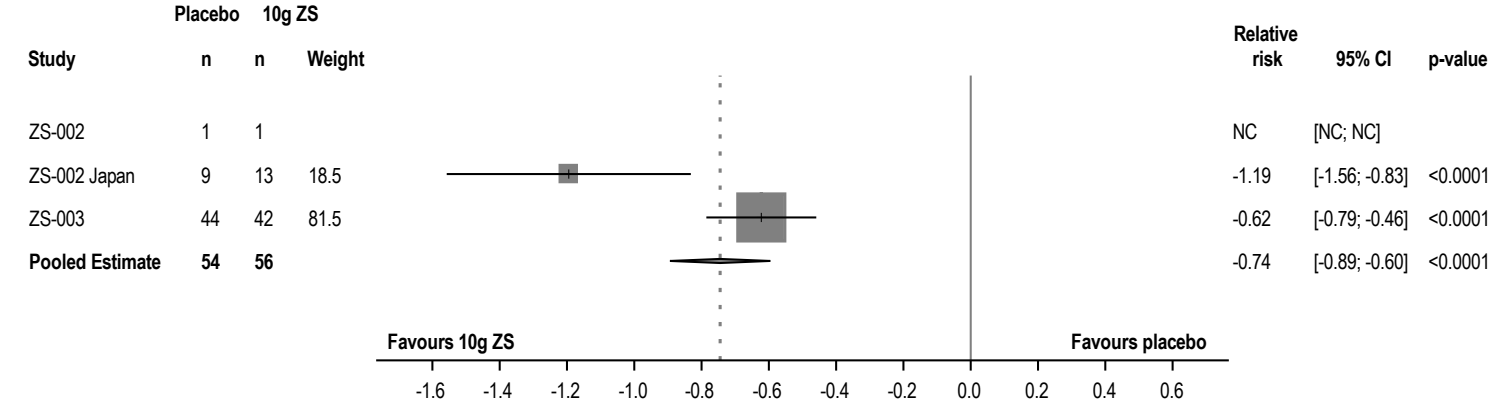
Study interaction p-value 0.6110

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline eGFR: 15-29+



Study interaction p-value 0.0139

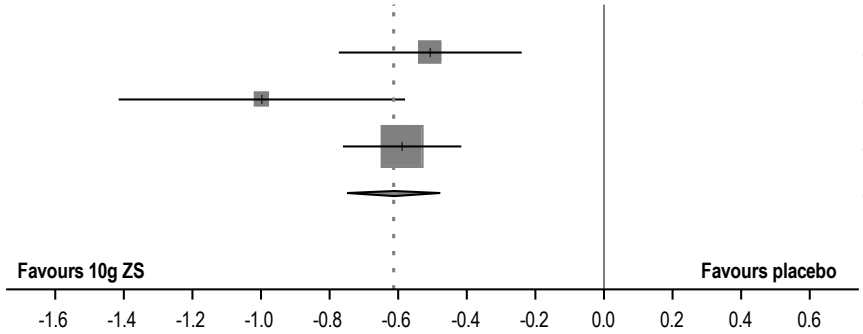
Significant heterogeneity between the studies; validity of pooled relative risk is questionable.

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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Normalization defined as S-K levels between 3.5-5.0 mmol
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline eGFR: 30-59+



Study	Placebo n	10g ZS n	Weight	Relative risk	95% CI	p-value
ZS-002	28	22	26.6	-0.51	[-0.77; -0.24]	0.0004
ZS-002 Japan	11	11	11.7	-1.00	[-1.42; -0.58]	<0.0001
ZS-003	60	48	61.8	-0.59	[-0.76; -0.42]	<0.0001
Pooled Estimate	**99**	**81**		-0.61	[-0.75; -0.48]	<0.0001

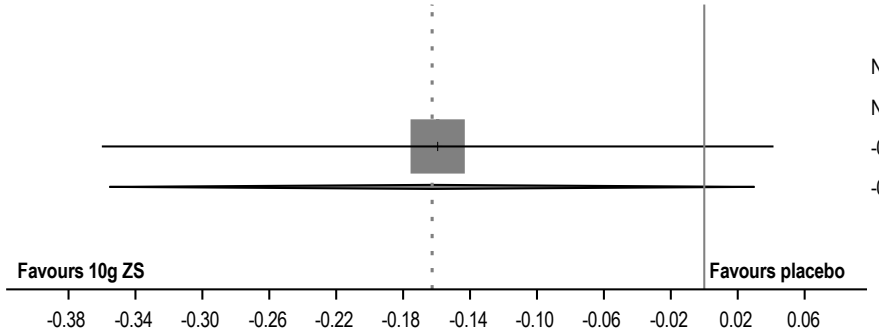
Study interaction p-value 0.3278

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Acute Baseline eGFR: >=60



Study	Placebo n	10g ZS n	Weight	Relative risk	95% CI	p-value
ZS-002	1	1		NC	[NC; NC]	
ZS-002 Japan	0	3		NC	[NC; NC]	
ZS-003	38	41	100.0	-0.16	[-0.36; 0.04]	0.1180
Pooled Estimate	**39**	**45**		-0.16	[-0.36; 0.03]	0.0972

Study interaction p-value .

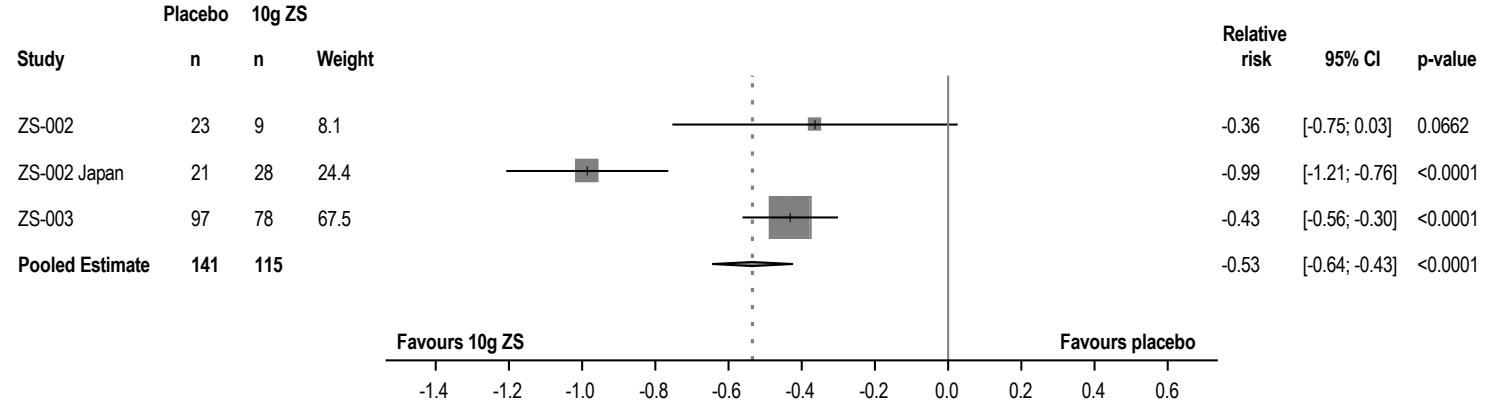
Significant heterogeneity between the studies; validity of pooled relative risk is questionable.

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
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The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Sex: Male



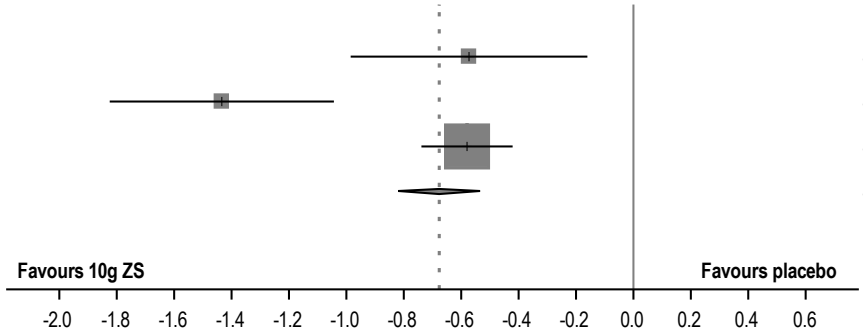
Study interaction p-value 0.1063

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Sex: Female



Study	Placebo n	10g ZS n	Weight	Relative risk	95% CI	p-value
ZS-002	7	15	12.2	-0.57	[-0.99; -0.16]	0.0090
ZS-002 Japan	10	8	14.0	-1.43	[-1.82; -1.04]	<0.0001
ZS-003	60	62	73.8	-0.58	[-0.74; -0.42]	<0.0001
Pooled Estimate	**77**	**85**		-0.68	[-0.82; -0.53]	<0.0001

Study interaction p-value 0.0360

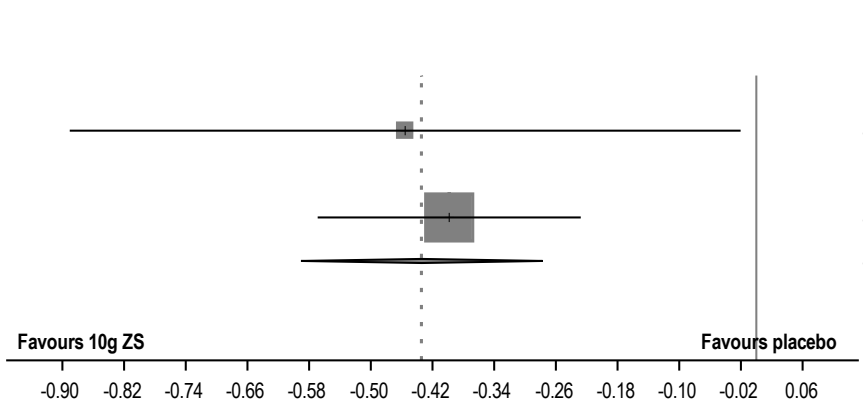
Significant heterogeneity between the studies; validity of pooled relative risk is questionable.

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Age: <65 years



Study	Placebo n	10g ZS n	Weight	Relative risk	95% CI	p-value
ZS-002	9	7	15.3	-0.46	[-0.89; -0.02]	0.0414
ZS-002 Japan	1	5		NC	[NC; NC]	
ZS-003	65	52	84.7	-0.40	[-0.57; -0.23]	<0.0001
Pooled Estimate	**75**	**64**		-0.43	[-0.59; -0.28]	<0.0001

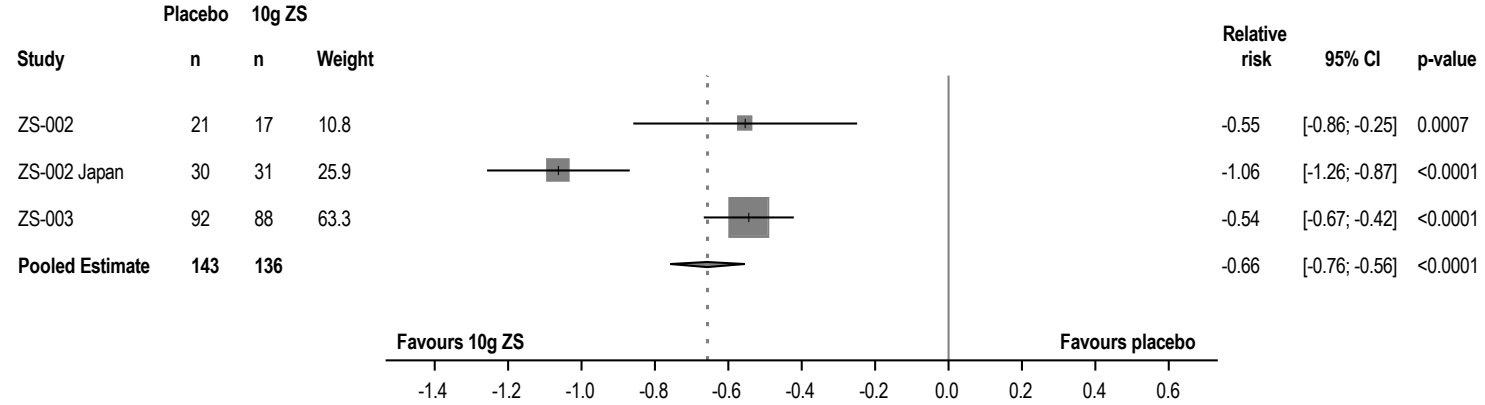
Study interaction p-value 0.9272

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.2.5 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Serum potassium (mmol/L) over time up to 48 hours (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Age: >= 65 years



Study interaction p-value 0.0123

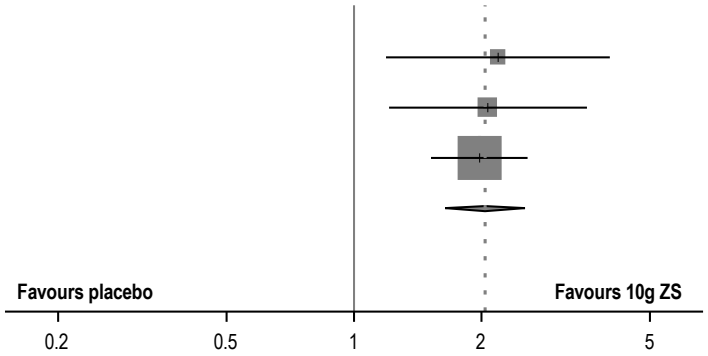
Significant heterogeneity between the studies; validity of pooled relative risk is questionable.

Absolute treatment differences for individual studies are estimated using a mixed methods repeated measures (MMRM) model including baseline S-K, treatment, timepoint and treatment*timepoint. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of absolute treatment difference is estimated using an MMRM model including baseline S-K, treatment, timepoint, study and treatment*timepoint.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of absolute treatment difference.
The study*treatment interaction p-value is presented as an indicator of the inter-study heterogeneity and is estimated using an MMRM model including baseline S-K, treatment, timepoint, study, treatment*timepoint and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
The single-study estimates shown in Sections 1, 2 and 8 are derived from models that include all available timepoints, however those shown in the first three lines of the forest plots are derived from models that include only the timepoints included in the unified model used for the pooled analysis.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Overall



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Hazard ratio	95% CI	p-value
ZS-002	22	30	23	24	12.9	2.19	[1.19; 4.02]	0.0118
ZS-002 Japan	22	33	36	36	16.5	2.07	[1.21; 3.55]	0.0081
ZS-003	106	158	131	143	70.6	1.98	[1.52; 2.57]	<0.0001
Pooled Estimate	**150**	**221**	**190**	**203**		2.04	[1.64; 2.54]	<0.0001

Study interaction p-value 0.6981

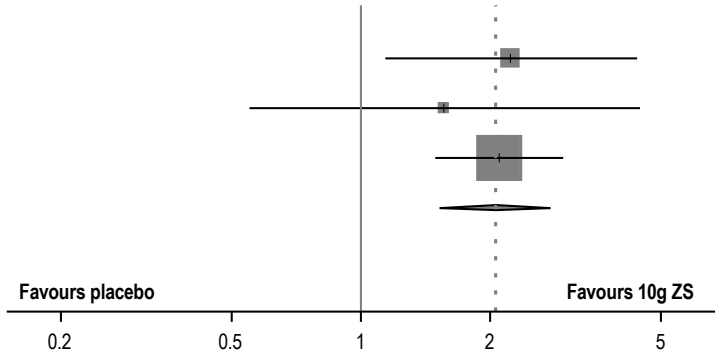
Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of log(hazard ratio).
The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a Cox proportional hazards regression model including treatment, study and study*treatment.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline S-K: <=5.3 mmol/L

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	18	25	18	19	19.0	2.23	[1.14; 4.40]	0.0199
ZS-002 Japan	5	6	12	12	7.9	1.56	[0.55; 4.47]	0.4048
ZS-003	57	95	82	94	73.1	2.10	[1.49; 2.96]	<0.0001
Pooled Estimate	**80**	**126**	**112**	**125**		2.06	[1.53; 2.76]	<0.0001



Study interaction p-value 0.9301

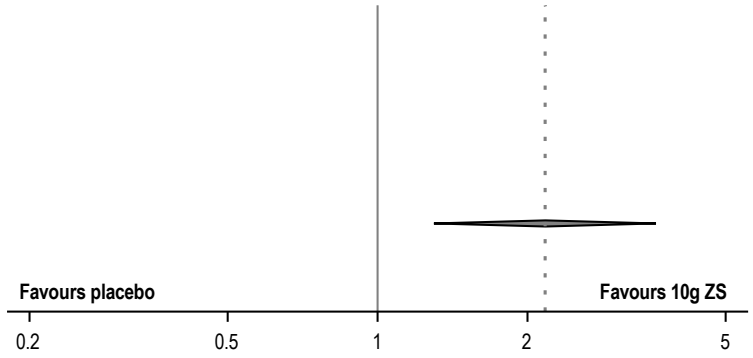
Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of log(hazard ratio).
The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a Cox proportional hazards regression model including treatment, study and study*treatment.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline S-K: >5.3 - <=5.5 mmol/L

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	1	2	3	3		NC	[NC; NC]	
ZS-002 Japan	8	12	12	12		NC	[NC; NC]	
ZS-003	17	22	27	27		NC	[NC; NC]	
Pooled Estimate	**26**	**36**	**42**	**42**		2.17	[1.30; 3.63]	0.0032



Study interaction p-value 0.9166

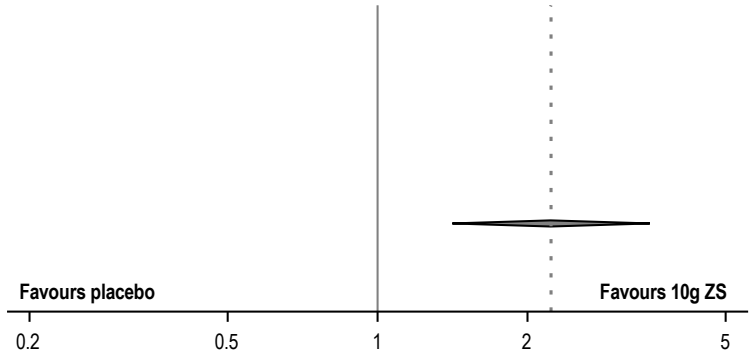
Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline S-K: >5.5 mmol/L

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	3	3	2	2		NC	[NC; NC]	
ZS-002 Japan	9	15	12	12		NC	[NC; NC]	
ZS-003	32	41	22	22		NC	[NC; NC]	
Pooled Estimate	**44**	**59**	**36**	**36**		2.23	[1.41; 3.52]	0.0006



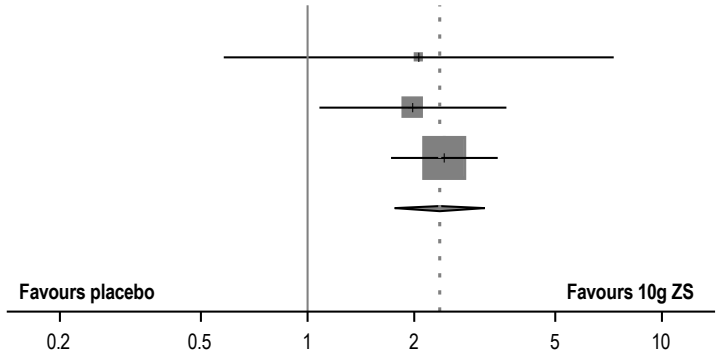
Study interaction p-value 0.4659

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a Cox proportional hazards regression model including treatment, study and study*treatment.
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: Yes



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Hazard ratio	95% CI	p-value
ZS-002	5	6	7	7	5.4	2.06	[0.58; 7.31]	0.2630
ZS-002 Japan	18	26	26	26	23.3	1.98	[1.08; 3.64]	0.0270
ZS-003	60	96	77	83	71.3	2.43	[1.72; 3.44]	<0.0001
Pooled Estimate	**83**	**128**	**110**	**116**		2.36	[1.76; 3.16]	<0.0001

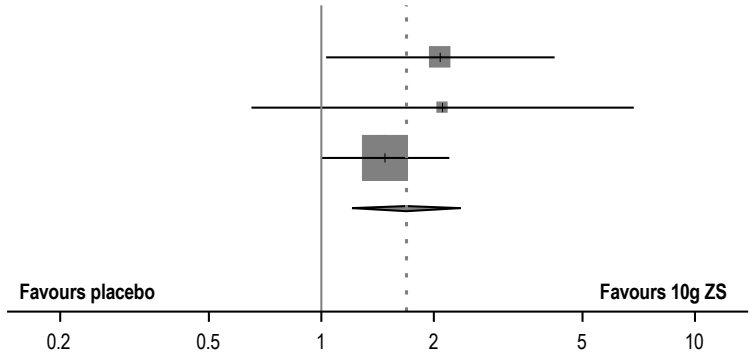
Study interaction p-value 0.9666

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of log(hazard ratio).
The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a Cox proportional hazards regression model including treatment, study and study*treatment.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Hazard ratio	95% CI	p-value
ZS-002	17	24	16	17	22.1	2.08	[1.03; 4.21]	0.0407
ZS-002 Japan	4	7	10	10	7.9	2.11	[0.65; 6.86]	0.2121
ZS-003	46	62	54	60	70.0	1.48	[1.00; 2.20]	0.0526
Pooled Estimate	**67**	**93**	**80**	**87**		1.69	[1.21; 2.35]	0.0020

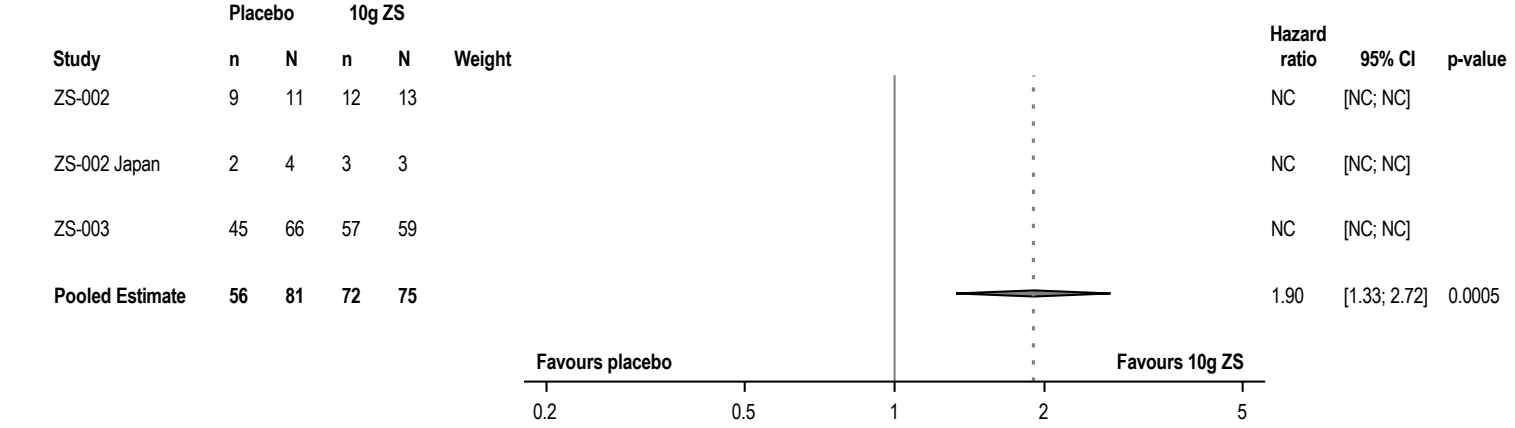
Study interaction p-value 0.4887

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of log(hazard ratio).
The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a Cox proportional hazards regression model including treatment, study and study*treatment.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Congestive heart disease: Yes



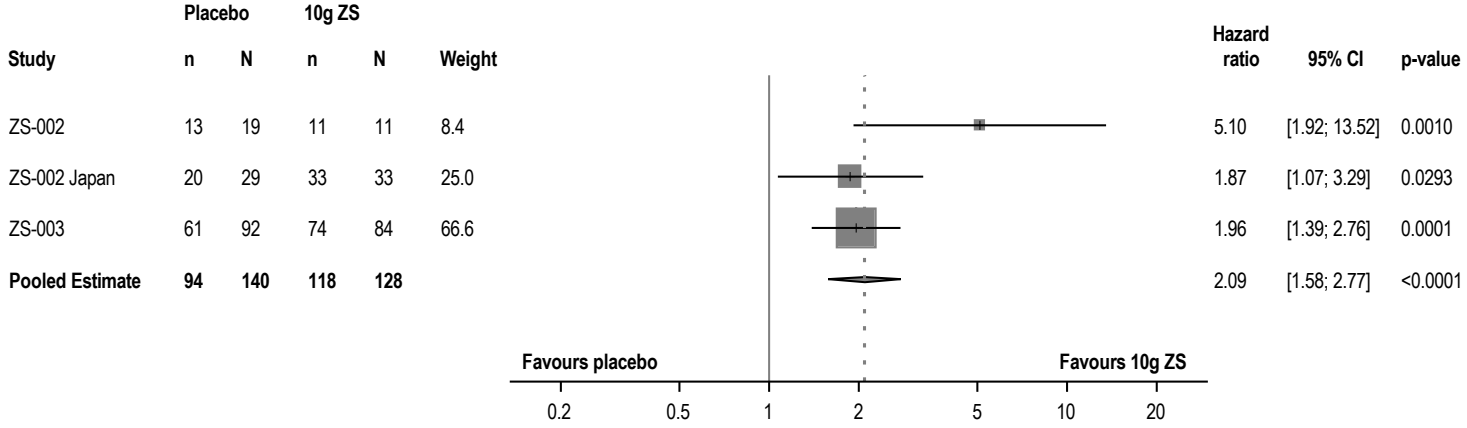
Study interaction p-value 0.3456

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of log(hazard ratio).
The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a Cox proportional hazards regression model including treatment, study and study*treatment.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Congestive heart disease: No



Study interaction p-value 0.4258

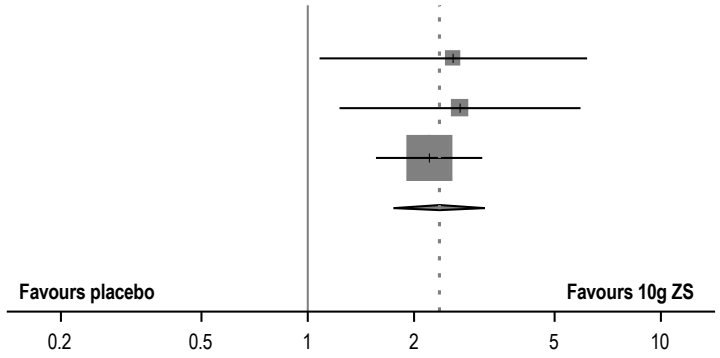
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Diabetes mellitus: Yes

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	13	19	11	11	11.7	2.58	[1.08; 6.18]	0.0338
ZS-002 Japan	9	16	24	24	14.5	2.70	[1.23; 5.92]	0.0133
ZS-003	61	96	74	81	73.9	2.21	[1.56; 3.12]	<0.0001
Pooled Estimate	**83**	**131**	**109**	**116**		2.36	[1.75; 3.18]	<0.0001



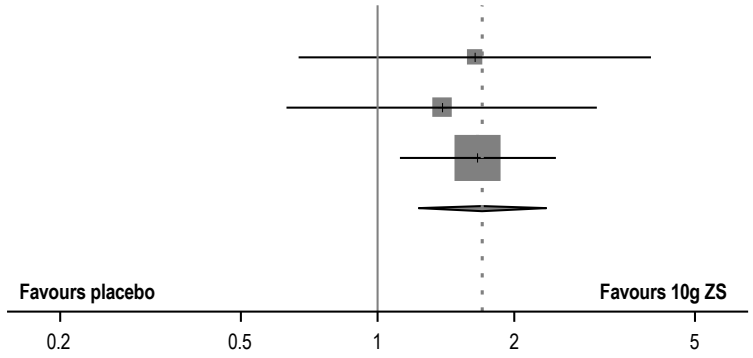
Study interaction p-value 0.4432

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of log(hazard ratio).
The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a Cox proportional hazards regression model including treatment, study and study*treatment.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Diabetes mellitus: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Hazard ratio	95% CI	p-value
ZS-002	9	11	12	13	13.7	1.64	[0.67; 4.00]	0.2751
ZS-002 Japan	13	17	12	12	17.4	1.39	[0.63; 3.04]	0.4166
ZS-003	45	62	57	62	68.9	1.66	[1.12; 2.47]	0.0116
Pooled Estimate	**67**	**90**	**81**	**87**		1.70	[1.23; 2.36]	0.0015

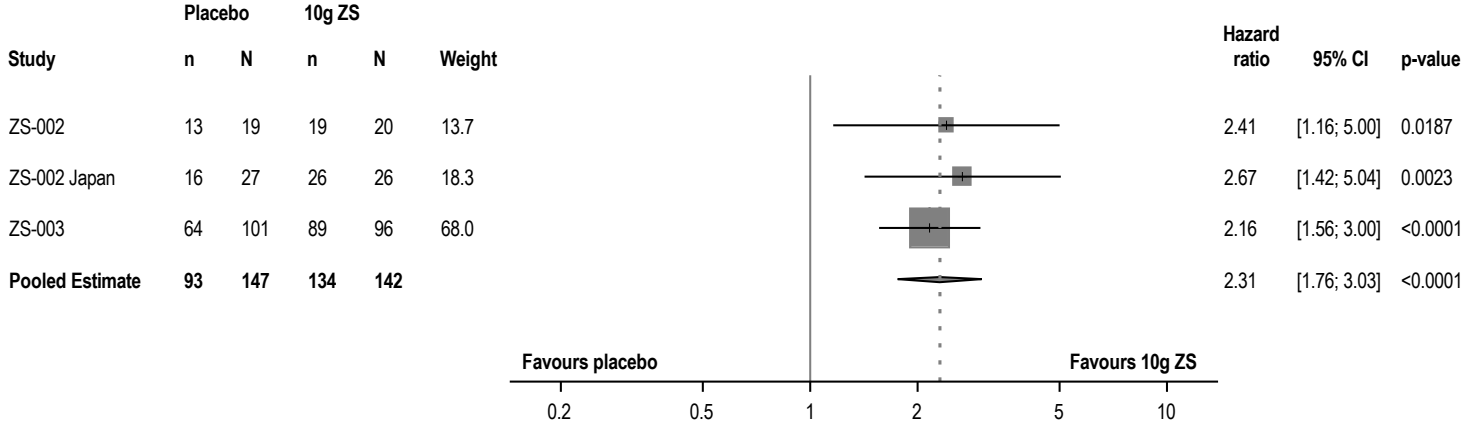
Study interaction p-value 0.9997

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of log(hazard ratio).
The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a Cox proportional hazards regression model including treatment, study and study*treatment.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

RAASi medications: Yes



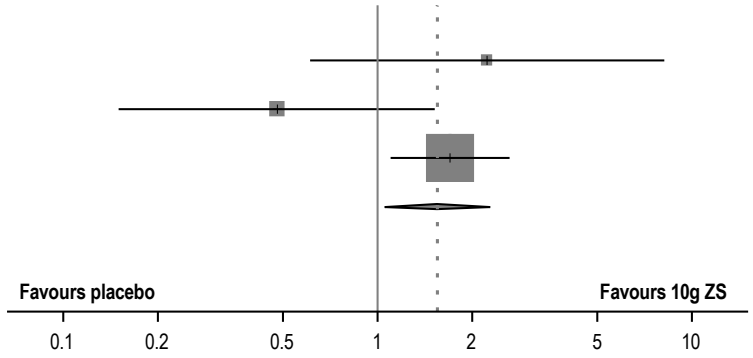
Study interaction p-value 0.5185

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

RAASi medications: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Hazard ratio	95% CI	p-value
ZS-002	9	11	4	4	8.9	2.23	[0.61; 8.17]	0.2263
ZS-002 Japan	6	6	10	10	11.3	0.48	[0.15; 1.52]	0.2139
ZS-003	42	57	42	47	79.8	1.70	[1.10; 2.63]	0.0160
Pooled Estimate	**57**	**74**	**56**	**61**		1.55	[1.05; 2.29]	0.0272

Study interaction p-value 0.1423

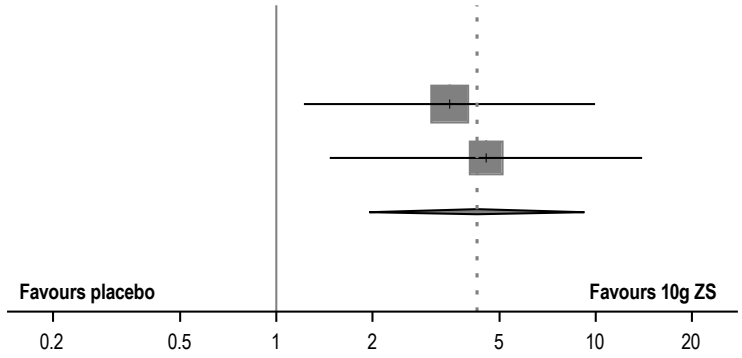
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: <15 ml/min/1.73m2**

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	0	0	0	0		NC	[NC; NC]	
ZS-002 Japan	7	11	9	9	53.6	3.49	[1.22; 9.95]	0.0193
ZS-003	8	15	9	10	46.4	4.54	[1.47; 13.97]	0.0084
Pooled Estimate	**15**	**26**	**18**	**19**		4.25	[1.95; 9.24]	0.0003



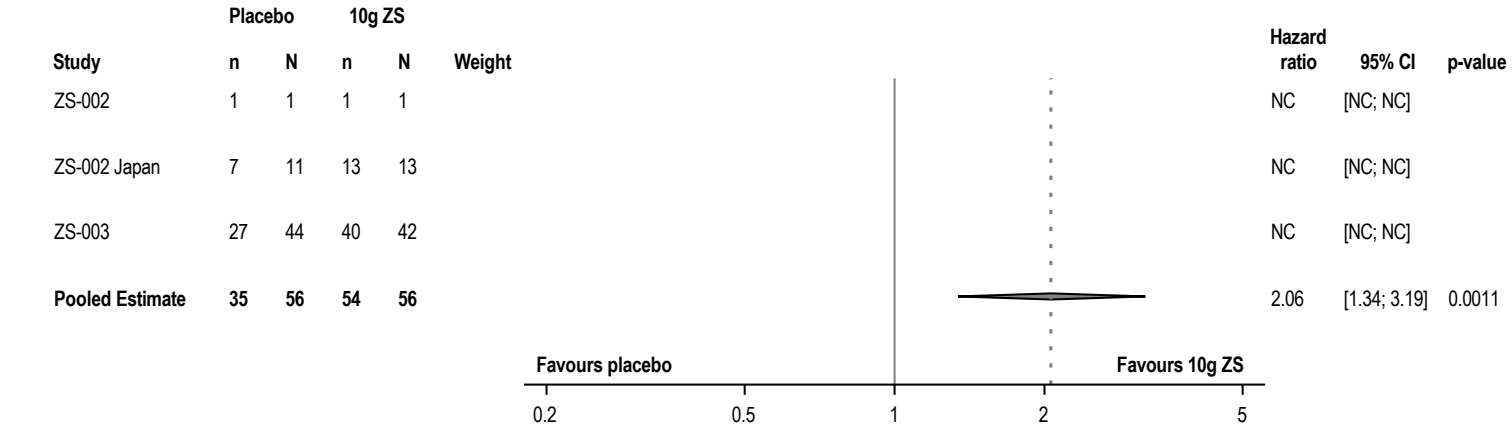
Study interaction p-value 1.0000

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
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The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a Cox proportional hazards regression model including treatment, study and study*treatment.
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: 15- <30 ml/min/1.73m2**



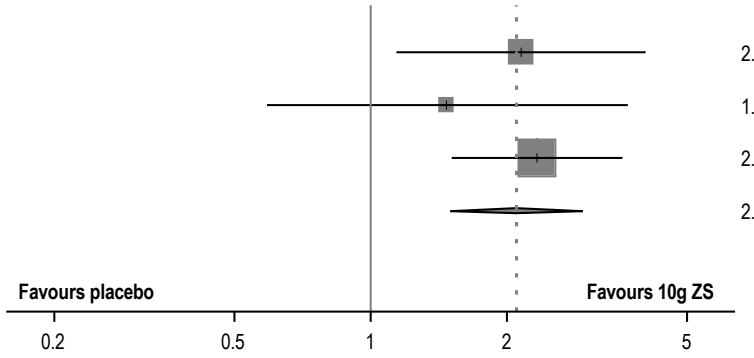
Study interaction p-value 0.7740

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of log(hazard ratio).
The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a Cox proportional hazards regression model including treatment, study and study*treatment.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: 30- <60 ml/min/1.73m2**



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Hazard ratio	95% CI	p-value
ZS-002	20	28	21	22	27.8	2.15	[1.14; 4.05]	0.0178
ZS-002 Japan	8	11	11	11	13.1	1.47	[0.59; 3.70]	0.4106
ZS-003	41	61	46	50	59.1	2.33	[1.51; 3.60]	0.0001
Pooled Estimate	**69**	**100**	**78**	**83**		2.10	[1.50; 2.94]	<0.0001

Study interaction p-value 0.8976

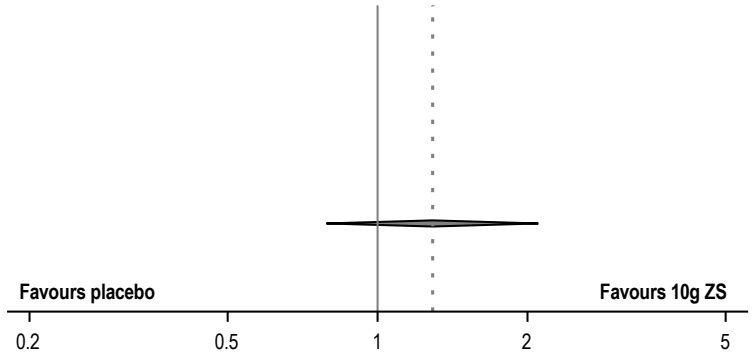
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: >=60 ml/min/1.73m2**

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	1	1	1	1		NC	[NC; NC]	
ZS-002 Japan	0	0	3	3		NC	[NC; NC]	
ZS-003	30	38	36	41		NC	[NC; NC]	
Pooled Estimate	**31**	**39**	**40**	**45**		1.29	[0.79; 2.10]	0.3103



Study interaction p-value 0.9840

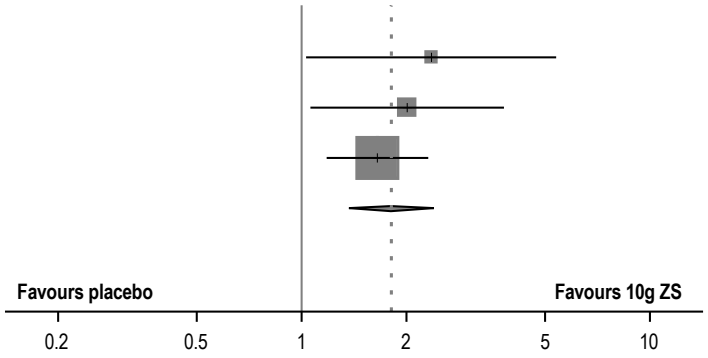
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Sex: Male

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	18	23	9	9	11.5	2.36	[1.03; 5.38]	0.0420
ZS-002 Japan	15	23	28	28	19.3	2.01	[1.06; 3.81]	0.0316
ZS-003	68	98	71	80	69.2	1.65	[1.18; 2.31]	0.0036
Pooled Estimate	**101**	**144**	**108**	**117**		1.81	[1.37; 2.39]	<0.0001



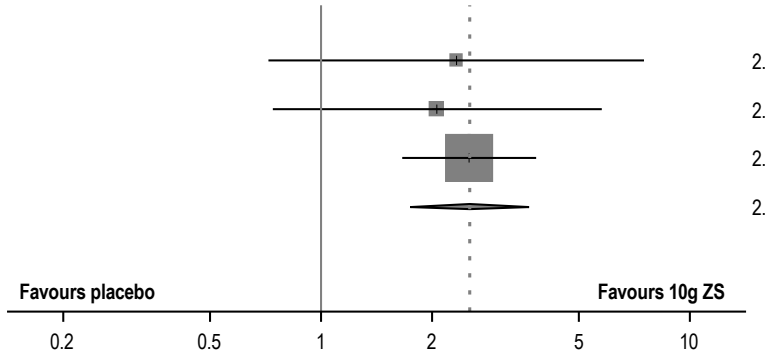
Study interaction p-value 0.4183

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of log(hazard ratio).
The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a Cox proportional hazards regression model including treatment, study and study*treatment.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Sex: Female



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Hazard ratio	95% CI	p-value
ZS-002	4	7	14	15	9.9	2.33	[0.72; 7.51]	0.1559
ZS-002 Japan	7	10	8	8	12.8	2.06	[0.74; 5.77]	0.1679
ZS-003	38	60	60	63	77.2	2.52	[1.66; 3.83]	<0.0001
Pooled Estimate	**49**	**77**	**82**	**86**		2.53	[1.75; 3.67]	<0.0001

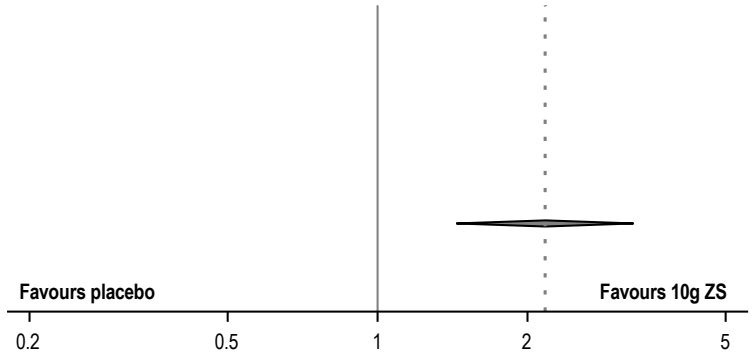
Study interaction p-value 0.9267

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of log(hazard ratio).
The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a Cox proportional hazards regression model including treatment, study and study*treatment.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Age (years): <65 years



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Hazard ratio	95% CI	p-value
ZS-002	6	9	7	7		NC	[NC; NC]	
ZS-002 Japan	1	1	5	5		NC	[NC; NC]	
ZS-003	39	66	45	54		NC	[NC; NC]	
Pooled Estimate	**46**	**76**	**57**	**66**		2.17	[1.44; 3.26]	0.0002

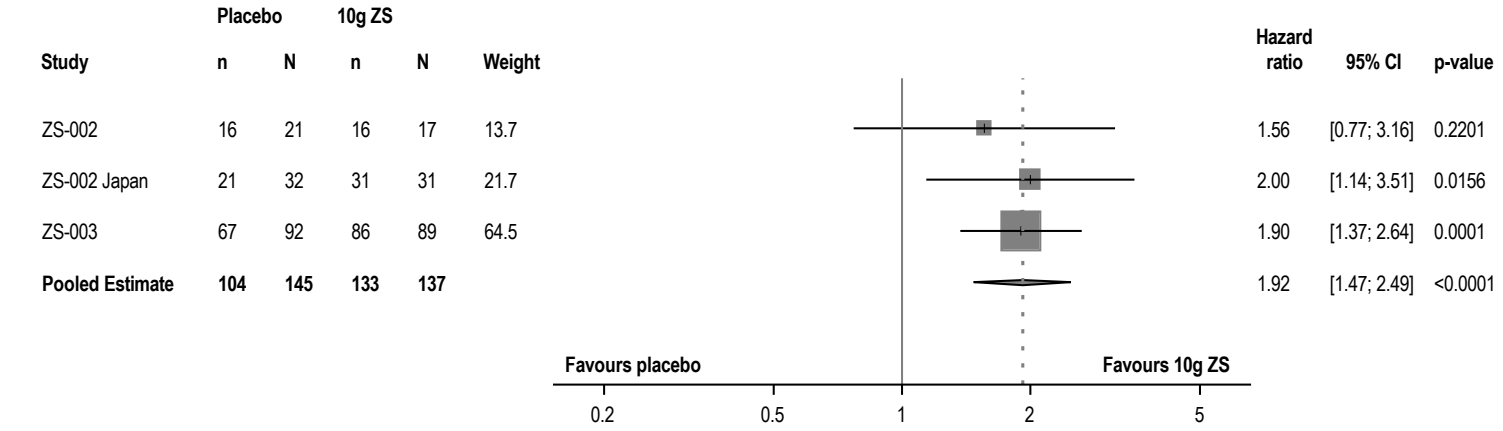
Study interaction p-value 0.2859

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
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The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a Cox proportional hazards regression model including treatment, study and study*treatment.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.3.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to first decrease of 0.5 mmol/L from baseline in serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Age (years): >=65 years



Study interaction p-value 0.7041

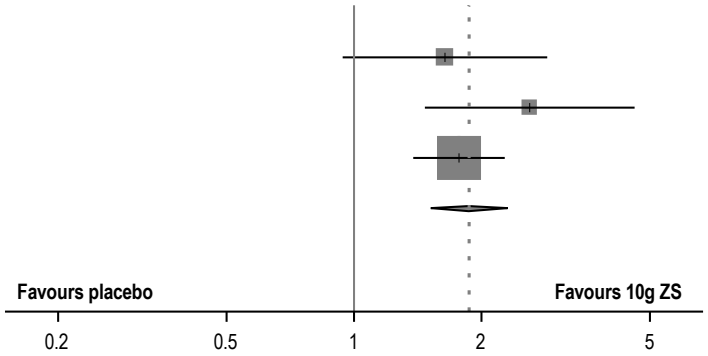
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Overall

Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Hazard ratio	95% CI	p-value
ZS-002	29	30	24	24	14.2	1.64	[0.94; 2.86]	0.0821
ZS-002 Japan	19	33	36	36	13.7	2.60	[1.47; 4.60]	0.0010
ZS-003	125	158	141	143	72.1	1.77	[1.38; 2.27]	<0.0001
Pooled Estimate	**173**	**221**	**201**	**203**		1.87	[1.52; 2.31]	<0.0001



Study interaction p-value 0.3321

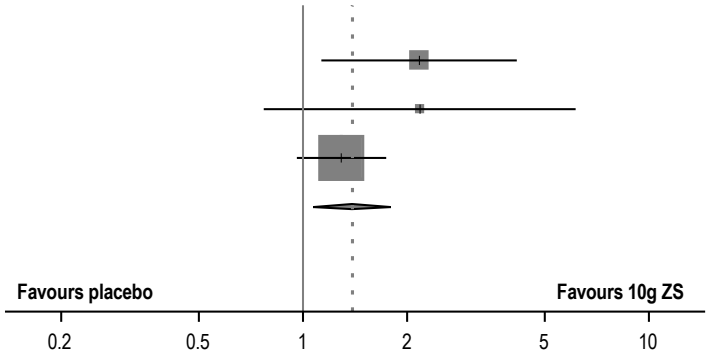
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline S-K: <=5.3 mmol/L

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	24	25	19	19	16.3	2.17	[1.13; 4.15]	0.0194
ZS-002 Japan	6	6	12	12	6.4	2.18	[0.77; 6.14]	0.1398
ZS-003	87	95	93	94	77.3	1.29	[0.96; 1.74]	0.0953
Pooled Estimate	**117**	**126**	**124**	**125**		1.39	[1.07; 1.80]	0.0143



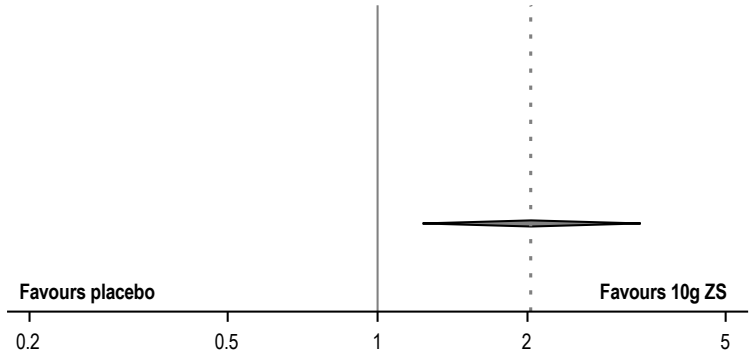
Study interaction p-value 0.4745

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline S-K: >5.3 - <=5.5 mmol/L



	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	2	2	3	3		NC	[NC; NC]	
ZS-002 Japan	9	12	12	12		NC	[NC; NC]	
ZS-003	17	22	27	27		NC	[NC; NC]	
Pooled Estimate	**28**	**36**	**42**	**42**		2.03	[1.23; 3.37]	0.0060

Study interaction p-value 0.7861

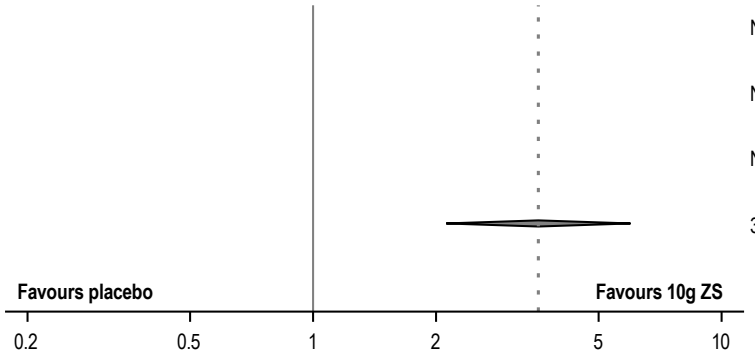
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline S-K: >5.5 mmol/L

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	3	3	2	2		NC	[NC; NC]	
ZS-002 Japan	4	15	12	12		NC	[NC; NC]	
ZS-003	21	41	21	22		NC	[NC; NC]	
Pooled Estimate	**28**	**59**	**35**	**36**		3.56	[2.12; 5.98]	<0.0001



Study interaction p-value 0.1208

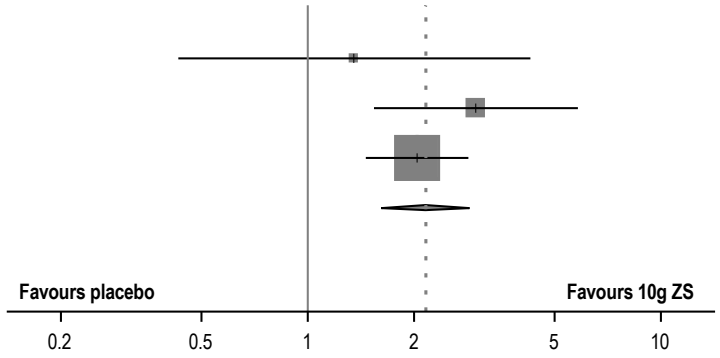
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: Yes

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	6	6	7	7	6.3	1.35	[0.43; 4.27]	0.6046
ZS-002 Japan	14	26	26	26	18.8	2.99	[1.54; 5.82]	0.0012
ZS-003	70	96	81	83	74.9	2.04	[1.46; 2.85]	<0.0001
Pooled Estimate	**90**	**128**	**114**	**116**		2.16	[1.62; 2.87]	<0.0001



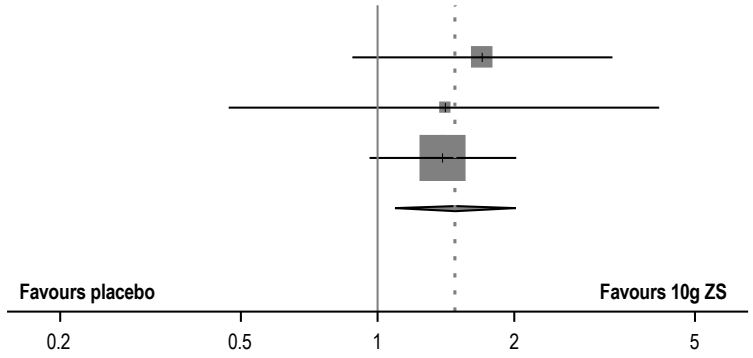
Study interaction p-value 0.2128

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Hazard ratio	95% CI	p-value
ZS-002	23	24	17	17	22.1	1.70	[0.88; 3.29]	0.1144
ZS-002 Japan	5	7	10	10	8.1	1.41	[0.47; 4.17]	0.5378
ZS-003	55	62	60	60	69.8	1.39	[0.96; 2.02]	0.0793
Pooled Estimate	**83**	**93**	**87**	**87**		1.48	[1.09; 2.02]	0.0131

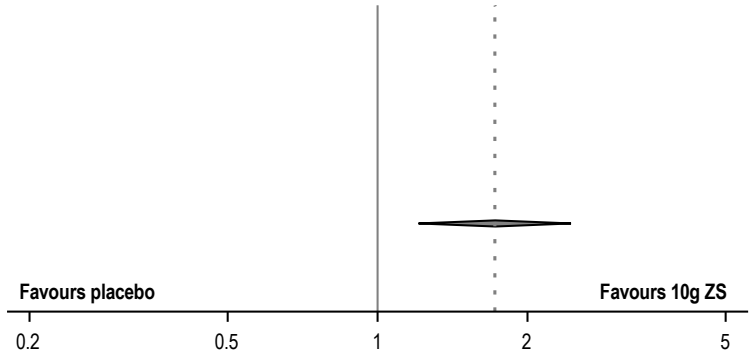
Study interaction p-value 0.8325

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Congestive heart disease: Yes



	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	11	11	13	13		NC	[NC; NC]	
ZS-002 Japan	3	4	3	3		NC	[NC; NC]	
ZS-003	46	66	59	59		NC	[NC; NC]	
Pooled Estimate	**60**	**81**	**75**	**75**		1.72	[1.21; 2.45]	0.0025

Study interaction p-value 0.0776

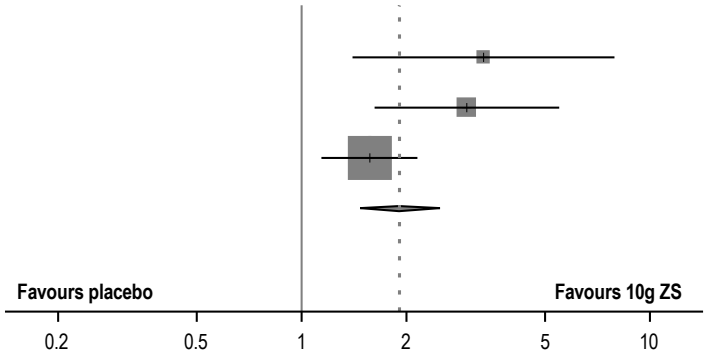
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Congestive heart disease: No

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	18	19	11	11	9.6	3.33	[1.40; 7.91]	0.0063
ZS-002 Japan	16	29	33	33	19.1	2.98	[1.62; 5.49]	0.0005
ZS-003	79	92	82	84	71.3	1.57	[1.14; 2.15]	0.0054
Pooled Estimate	**113**	**140**	**126**	**128**		1.91	[1.47; 2.50]	<0.0001



Study interaction p-value 0.0787

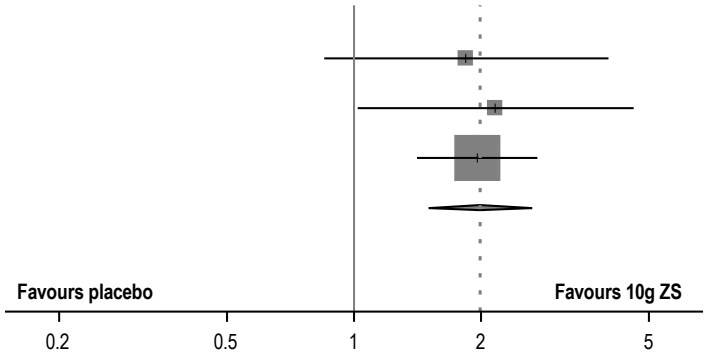
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Diabetes mellitus: Yes

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	18	19	11	11	13.1	1.84	[0.85; 4.01]	0.1232
ZS-002 Japan	10	16	24	24	13.9	2.16	[1.02; 4.60]	0.0446
ZS-003	73	96	80	81	72.9	1.96	[1.41; 2.72]	<0.0001
Pooled Estimate	**101**	**131**	**115**	**116**		1.99	[1.50; 2.64]	<0.0001



Study interaction p-value 0.8766

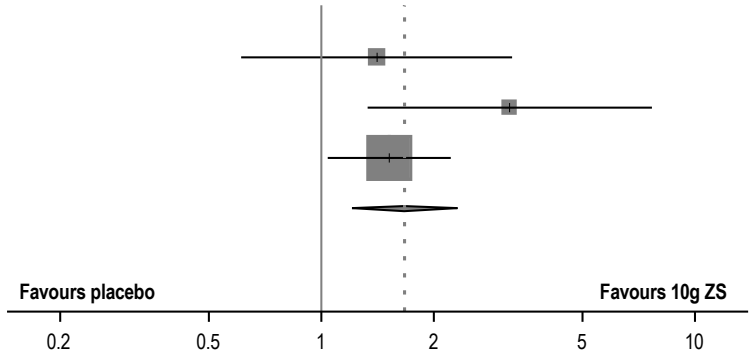
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Diabetes mellitus: No

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	11	11	13	13	14.8	1.41	[0.61; 3.24]	0.4190
ZS-002 Japan	9	17	12	12	13.3	3.19	[1.33; 7.67]	0.0095
ZS-003	52	62	61	62	71.9	1.52	[1.04; 2.22]	0.0290
Pooled Estimate	**72**	**90**	**86**	**87**		1.67	[1.21; 2.31]	0.0017



Study interaction p-value 0.2969

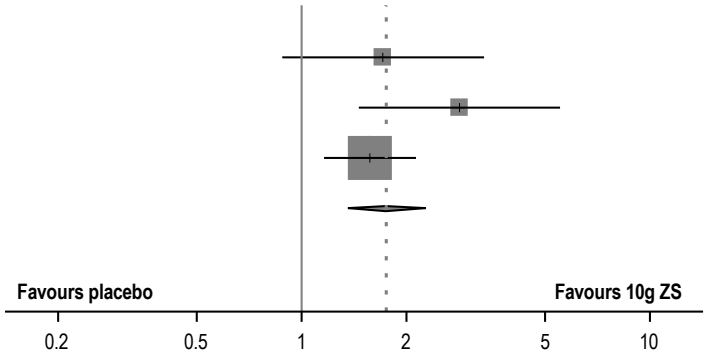
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

RAASi medications: Yes

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	18	19	20	20	14.7	1.71	[0.88; 3.34]	0.1166
ZS-002 Japan	14	27	26	26	14.9	2.84	[1.46; 5.52]	0.0022
ZS-003	78	101	94	96	70.4	1.57	[1.16; 2.13]	0.0039
Pooled Estimate	**110**	**147**	**140**	**142**		1.75	[1.36; 2.27]	<0.0001



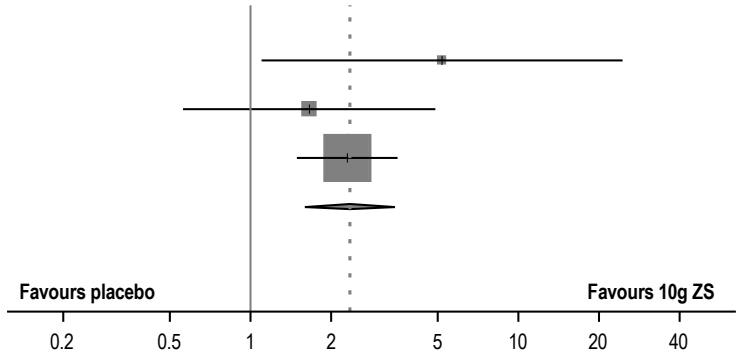
Study interaction p-value 0.2320

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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

RAASi medications: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Hazard ratio	95% CI	p-value
ZS-002	11	11	4	4	6.2	5.19	[1.10; 24.49]	0.0375
ZS-002 Japan	5	6	10	10	12.9	1.66	[0.56; 4.90]	0.3559
ZS-003	47	57	47	47	80.9	2.30	[1.49; 3.54]	0.0002
Pooled Estimate	**63**	**74**	**61**	**61**		2.35	[1.60; 3.45]	<0.0001

Study interaction p-value 0.8516

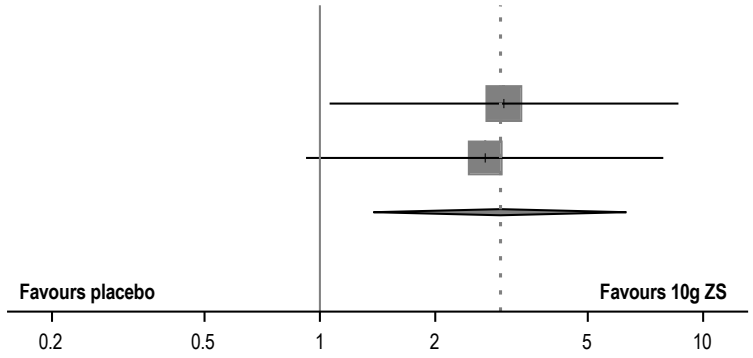
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: <15 ml/min/1.73m2**

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	0	0	0	0		NC	[NC; NC]	
ZS-002 Japan	6	11	9	9	51.1	3.02	[1.06; 8.62]	0.0383
ZS-003	9	15	9	10	48.9	2.70	[0.92; 7.87]	0.0693
Pooled Estimate	**15**	**26**	**18**	**19**		2.96	[1.38; 6.32]	0.0051



Study interaction p-value 0.3832

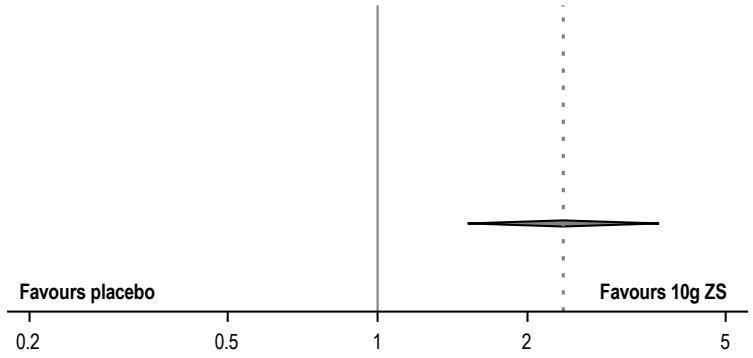
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: 15- <30 ml/min/1.73m2**

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	1	1	1	1		NC	[NC; NC]	
ZS-002 Japan	4	11	13	13		NC	[NC; NC]	
ZS-003	28	44	41	42		NC	[NC; NC]	
Pooled Estimate	**33**	**56**	**55**	**56**		2.36	[1.52; 3.67]	0.0001



Study interaction p-value 0.2491

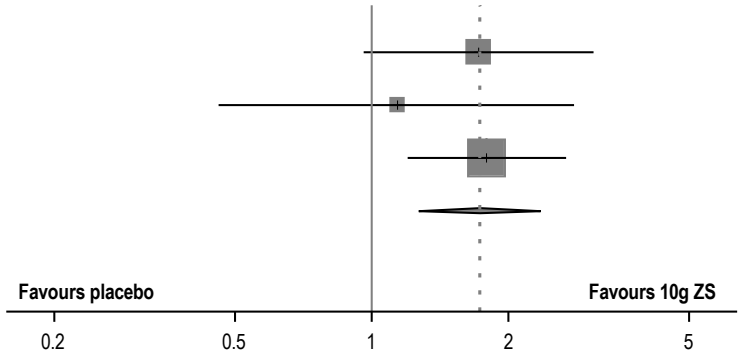
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: 30- <60 ml/min/1.73m2**

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	27	28	22	22	28.6	1.72	[0.96; 3.08]	0.0676
ZS-002 Japan	9	11	11	11	12.0	1.14	[0.46; 2.79]	0.7752
ZS-003	50	61	50	50	59.3	1.79	[1.20; 2.68]	0.0047
Pooled Estimate	**86**	**100**	**83**	**83**		1.73	[1.27; 2.36]	0.0006



Study interaction p-value 0.7663

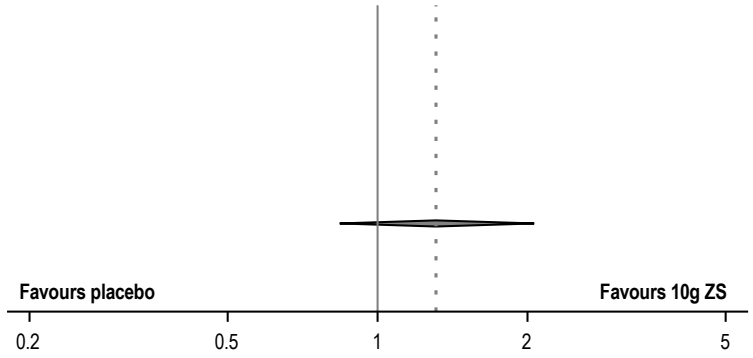
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: >=60 ml/min/1.73m2**

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	1	1	1	1		NC	[NC; NC]	
ZS-002 Japan	0	0	3	3		NC	[NC; NC]	
ZS-003	38	38	41	41		NC	[NC; NC]	
Pooled Estimate	**39**	**39**	**45**	**45**		1.31	[0.84; 2.06]	0.2318



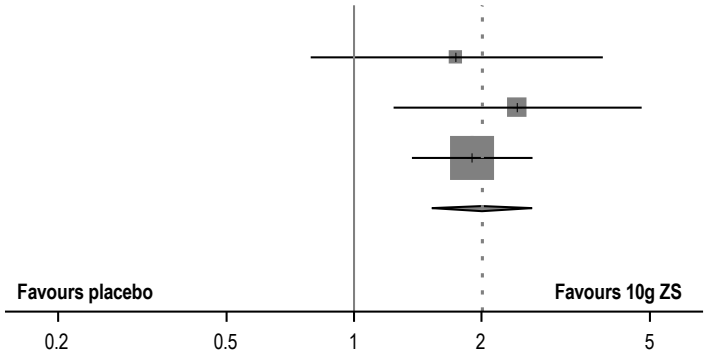
Study interaction p-value 0.8450

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Sex: Male



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Hazard ratio	95% CI	p-value
ZS-002	22	23	9	9	12.0	1.74	[0.79; 3.87]	0.1714
ZS-002 Japan	13	23	28	28	16.8	2.43	[1.24; 4.78]	0.0096
ZS-003	73	98	78	80	71.1	1.90	[1.37; 2.64]	0.0001
Pooled Estimate	**108**	**144**	**115**	**117**		2.01	[1.53; 2.64]	<0.0001

Study interaction p-value 0.6495

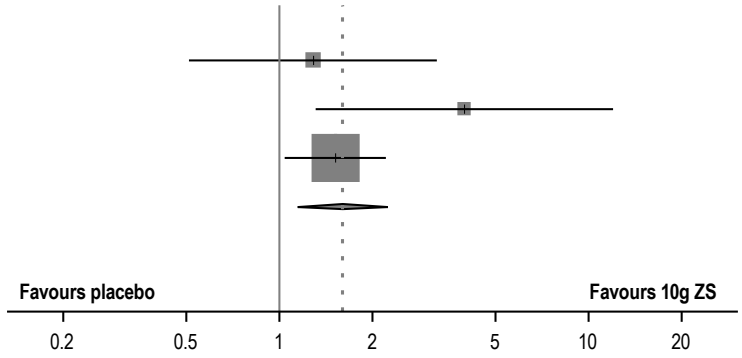
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Sex: Female

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	7	7	15	15	13.1	1.29	[0.51; 3.23]	0.5901
ZS-002 Japan	6	10	8	8	9.0	3.97	[1.31; 12.00]	0.0146
ZS-003	52	60	63	63	77.9	1.52	[1.04; 2.21]	0.0299
Pooled Estimate	**65**	**77**	**86**	**86**		1.60	[1.15; 2.24]	0.0056



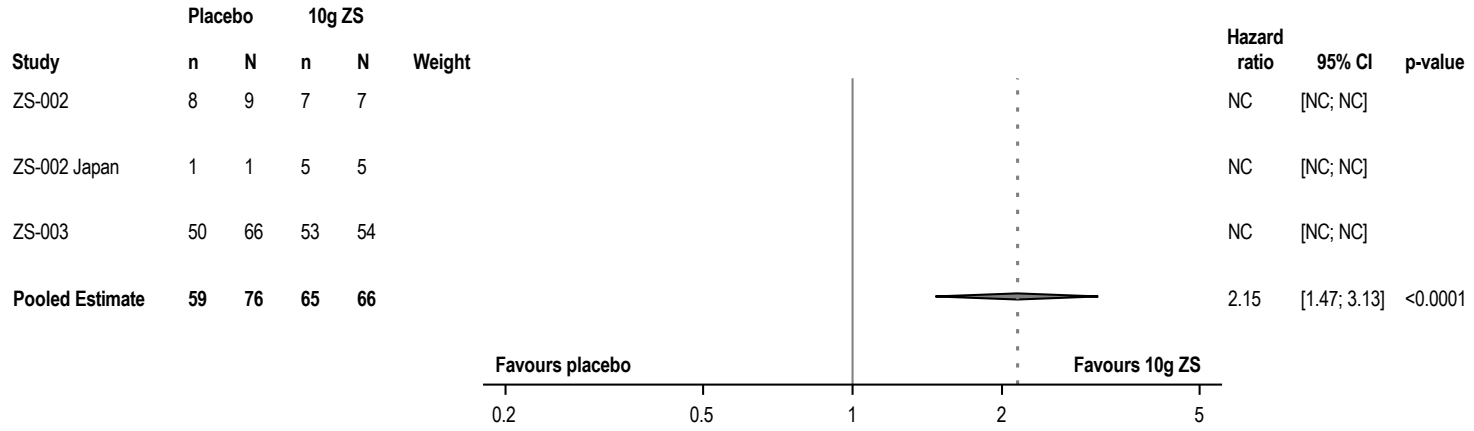
Study interaction p-value 0.2950

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Age (years): <65 years



Study interaction p-value 0.5168

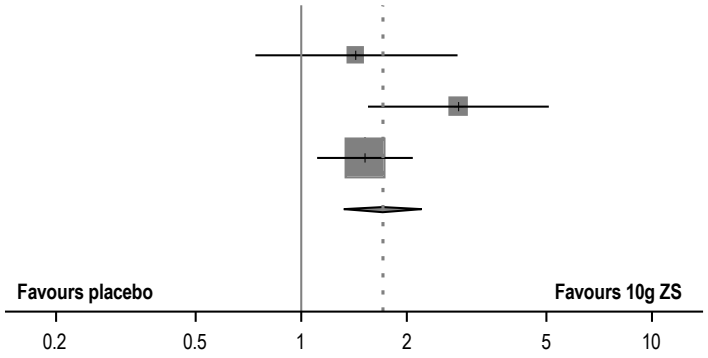
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Figure 3.1.4.3 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Time to normalisation of serum potassium, ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Age (years): >=65 years

	Placebo		10g ZS			Hazard		
Study	**n**	**N**	**n**	**N**	**Weight**	**ratio**	**95% CI**	**p-value**
ZS-002	21	21	17	17	14.8	1.43	[0.74; 2.79]	0.2880
ZS-002 Japan	18	32	31	31	18.7	2.81	[1.55; 5.08]	0.0006
ZS-003	75	92	88	89	66.5	1.52	[1.11; 2.08]	0.0091
Pooled Estimate	**114**	**145**	**136**	**137**		1.71	[1.32; 2.21]	<0.0001



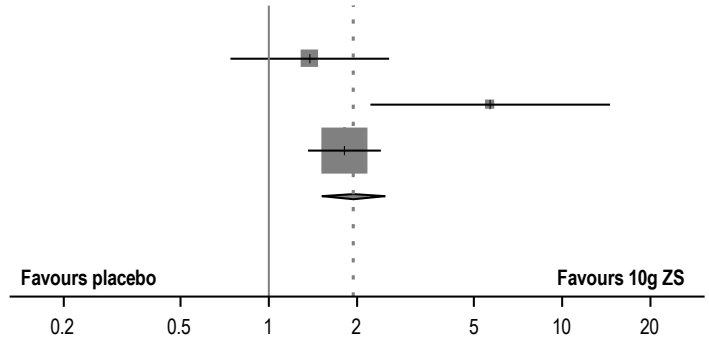
Study interaction p-value 0.1306

Hazard ratios for individual studies are estimated using a Cox proportional hazards regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of hazard ratio is estimated using a Cox proportional hazards regression model including treatment and study.
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Overall



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	19	30	21	24	16.5	1.38	[0.74; 2.57]	0.3073
ZS-002 Japan	5	31	33	36	7.2	5.68	[2.22; 14.56]	0.0003
ZS-003	75	157	121	140	76.4	1.81	[1.36; 2.41]	<0.0001
Pooled Estimate	**99**	**218**	**175**	**200**		1.94	[1.52; 2.49]	<0.0001

Study interaction p-value 0.0422

Significant heterogeneity between the studies; validity of pooled relative risk is questionable.

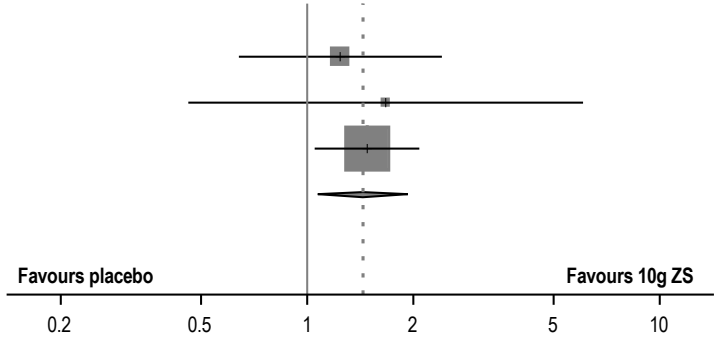
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Normalization defined as S-K levels between 3.5-5.0 mmol
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline S-K: <=5.3 mmol/L

	Placebo		10g ZS					
Study	**n**	**N**	**n**	**N**	**Weight**	**Relative risk**	**95% CI**	**p-value**
ZS-002	18	25	17	19	19.9	1.24	[0.64; 2.41]	0.5206
ZS-002 Japan	3	6	10	12	5.2	1.67	[0.46; 6.06]	0.4377
ZS-003	56	95	80	92	74.9	1.48	[1.05; 2.08]	0.0257
Pooled Estimate	**77**	**126**	**107**	**123**		1.44	[1.07; 1.93]	0.0161



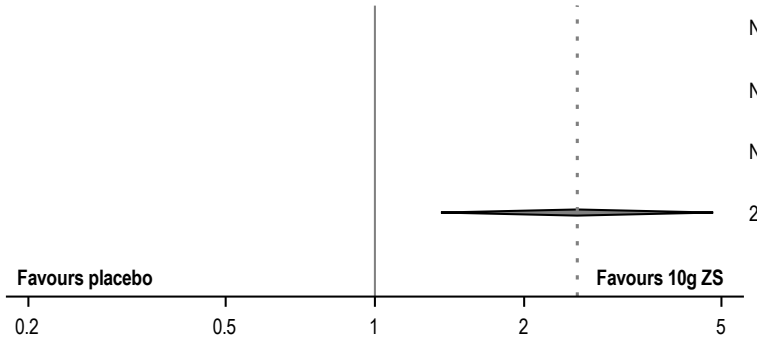
Study interaction p-value 0.8791

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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline S-K: >5.3 - <=5.5 mmol/L



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	1	2	2	3		NC	[NC; NC]	
ZS-002 Japan	2	12	12	12		NC	[NC; NC]	
ZS-003	10	22	24	26		NC	[NC; NC]	
Pooled Estimate	**13**	**36**	**38**	**41**		2.56	[1.36; 4.81]	0.0035

Study interaction p-value 0.3933

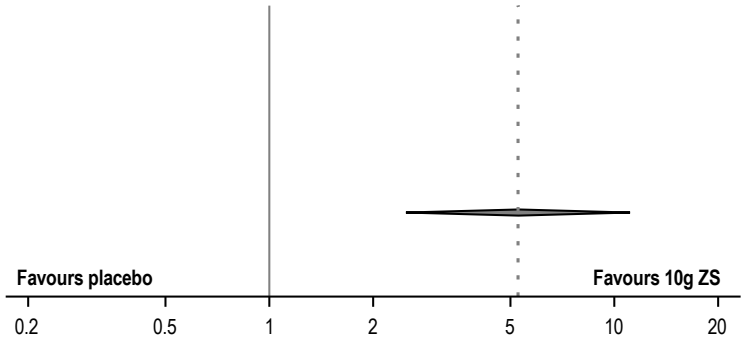
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline S-K: >5.5 mmol/L

	Placebo		10g ZS			Relative		
Study	**n**	**N**	**n**	**N**	**Weight**	**risk**	**95% CI**	**p-value**
ZS-002	0	3	2	2		NC	[NC; NC]	
ZS-002 Japan	0	13	11	12		NC	[NC; NC]	
ZS-003	9	40	17	22		NC	[NC; NC]	
Pooled Estimate	**9**	**56**	**30**	**36**		5.26	[2.49; 11.11]	<0.0001



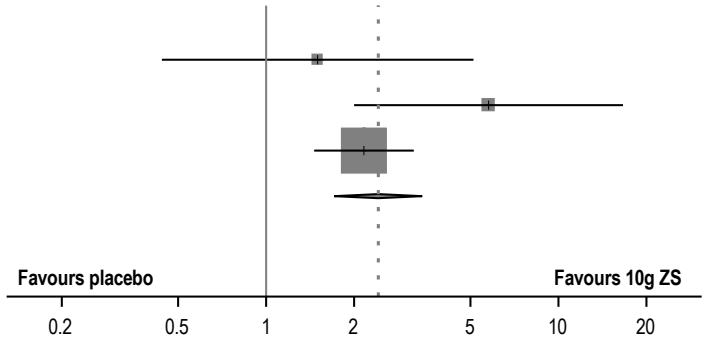
Study interaction p-value NC

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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: Yes



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	4	6	7	7	8.2	1.50	[0.44; 5.12]	0.5177
ZS-002 Japan	4	25	24	26	11.0	5.77	[2.00; 16.63]	0.0012
ZS-003	39	95	71	80	80.8	2.16	[1.46; 3.20]	0.0001
Pooled Estimate	**47**	**126**	**102**	**113**		2.42	[1.71; 3.43]	<0.0001

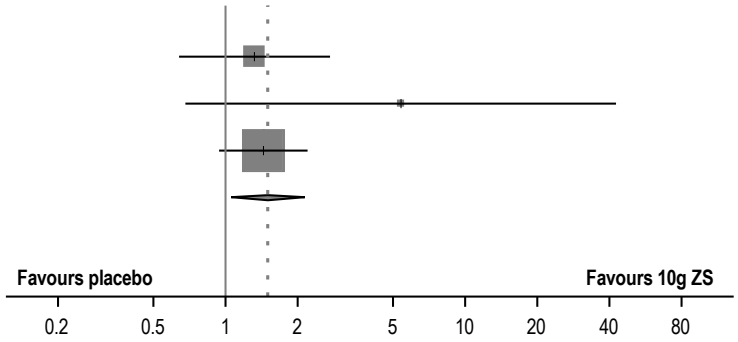
Study interaction p-value 0.1779

Relative risks for individual studies are estimated using a logistic regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Chronic kidney disease: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	15	24	14	17	24.9	1.32	[0.64; 2.73]	0.4579
ZS-002 Japan	1	6	9	10	3.1	5.40	[0.68; 42.62]	0.1096
ZS-003	36	62	50	60	72.0	1.44	[0.94; 2.20]	0.0984
Pooled Estimate	**52**	**92**	**73**	**87**		1.50	[1.05; 2.14]	0.0263

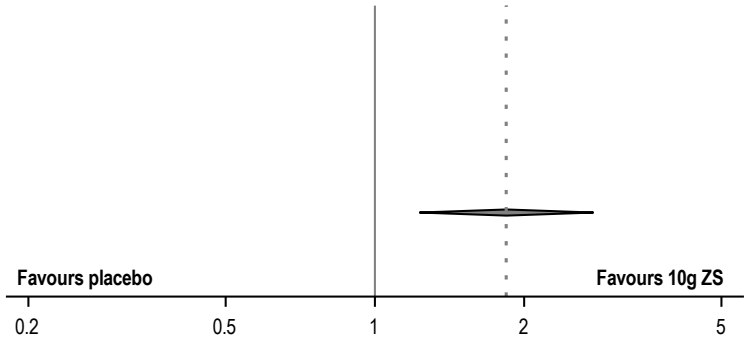
Study interaction p-value 0.4444

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Normalization defined as S-K levels between 3.5-5.0 mmol
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Congestive heart disease: Yes



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	9	11	12	13		NC	[NC; NC]	
ZS-002 Japan	1	4	2	3		NC	[NC; NC]	
ZS-003	27	66	50	59		NC	[NC; NC]	
Pooled Estimate	**37**	**81**	**64**	**75**		1.84	[1.23; 2.76]	0.0032

Study interaction p-value 0.4568

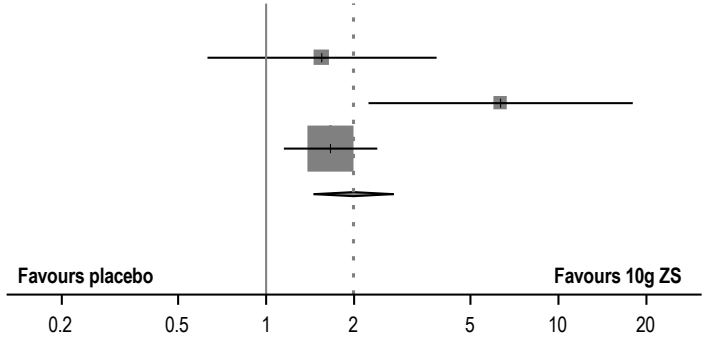
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The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a logistic regression model including treatment, study and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Congestive heart disease: No

	Placebo		10g ZS					
Study	**n**	**N**	**n**	**N**	**Weight**	**Relative risk**	**95% CI**	**p-value**
ZS-002	10	19	9	11	12.8	1.55	[0.63; 3.83]	0.3370
ZS-002 Japan	4	27	31	33	9.6	6.34	[2.24; 17.96]	0.0005
ZS-003	48	91	71	81	77.6	1.66	[1.15; 2.40]	0.0066
Pooled Estimate	**62**	**137**	**111**	**125**		1.99	[1.46; 2.72]	<0.0001



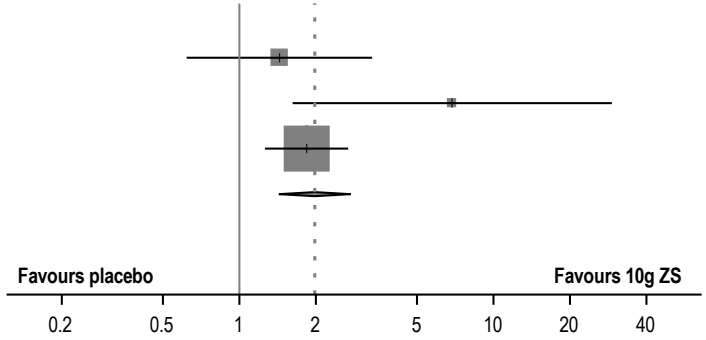
Study interaction p-value 0.0538

Relative risks for individual studies are estimated using a logistic regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of relative risk is estimated using a logistic regression model including treatment and study.
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Normalization defined as S-K levels between 3.5-5.0 mmol
CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Diabetes mellitus: Yes



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	12	19	10	11	16.0	1.44	[0.62; 3.33]	0.3950
ZS-002 Japan	2	15	22	24	5.4	6.87	[1.62; 29.24]	0.0090
ZS-003	44	95	68	80	78.6	1.84	[1.26; 2.68]	0.0017
Pooled Estimate	**58**	**129**	**100**	**115**		1.98	[1.43; 2.74]	<0.0001

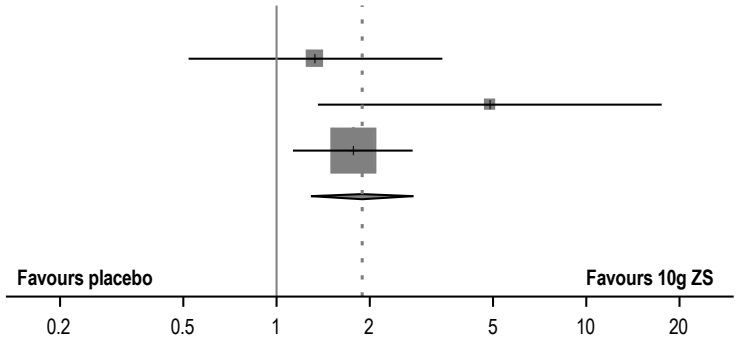
Study interaction p-value 0.1751

Relative risks for individual studies are estimated using a logistic regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Diabetes mellitus: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	7	11	11	13	16.3	1.33	[0.52; 3.43]	0.5556
ZS-002 Japan	3	16	11	12	9.0	4.89	[1.36; 17.52]	0.0148
ZS-003	31	62	53	60	74.7	1.77	[1.13; 2.75]	0.0118
Pooled Estimate	**41**	**89**	**75**	**85**		1.89	[1.29; 2.77]	0.0010

Study interaction p-value 0.2549

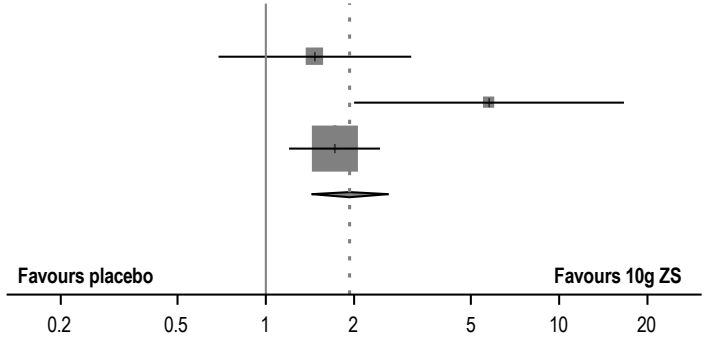
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

RAASi medications: Yes

	Placebo		10g ZS					
Study	**n**	**N**	**n**	**N**	**Weight**	**Relative risk**	**95% CI**	**p-value**
ZS-002	11	19	17	20	16.4	1.47	[0.69; 3.13]	0.3210
ZS-002 Japan	4	25	24	26	8.4	5.77	[2.00; 16.63]	0.0012
ZS-003	50	101	79	93	75.2	1.72	[1.20; 2.45]	0.0028
Pooled Estimate	**65**	**145**	**120**	**139**		1.93	[1.43; 2.61]	<0.0001



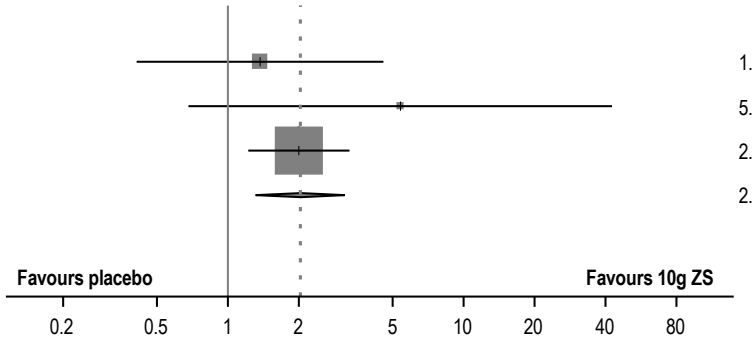
Study interaction p-value 0.0835

Relative risks for individual studies are estimated using a logistic regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

RAASi medications: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	8	11	4	4	13.9	1.37	[0.41; 4.57]	0.6030
ZS-002 Japan	1	6	9	10	4.7	5.40	[0.68; 42.62]	0.1096
ZS-003	25	56	42	47	81.5	2.00	[1.22; 3.28]	0.0060
Pooled Estimate	**34**	**73**	**55**	**61**		2.03	[1.31; 3.13]	0.0015

Study interaction p-value 0.5321

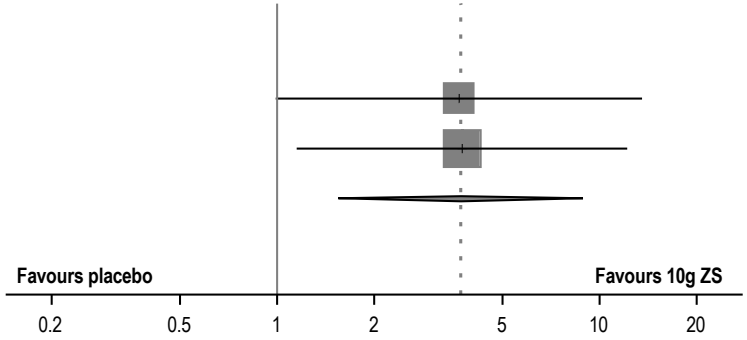
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: <15 ml/min/1.73m2**

	Placebo		10g ZS			Relative		
Study	**n**	**N**	**n**	**N**	**Weight**	**risk**	**95% CI**	**p-value**
ZS-002	0	0	0	0		NC	[NC; NC]	
ZS-002 Japan	3	11	9	9	44.8	3.67	[0.99; 13.54]	0.0513
ZS-003	4	15	9	9	55.2	3.75	[1.15; 12.18]	0.0278
Pooled Estimate	**7**	**26**	**18**	**18**		3.71	[1.55; 8.91]	0.0033



Study interaction p-value 0.9800

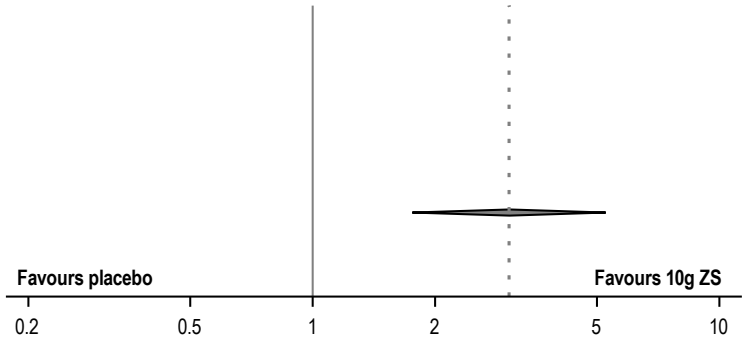
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CI = Confidence Intervals, NC = Not calculated
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: 15- <30 ml/min/1.73m2**

	Placebo		10g ZS			Relative		
Study	**n**	**N**	**n**	**N**	**Weight**	**risk**	**95% CI**	**p-value**
ZS-002	1	1	1	1		NC	[NC; NC]	
ZS-002 Japan	1	9	12	13		NC	[NC; NC]	
ZS-003	15	44	40	42		NC	[NC; NC]	
Pooled Estimate	**17**	**54**	**53**	**56**		3.04	[1.76; 5.26]	<0.0001



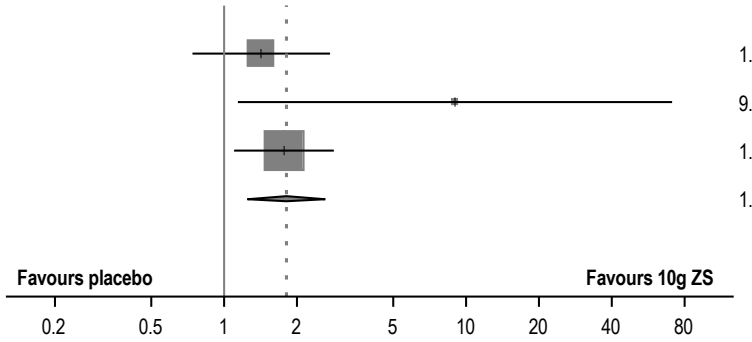
Study interaction p-value 0.4483

Relative risks for individual studies are estimated using a logistic regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: 30- <60 ml/min/1.73m2**



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	17	28	19	22	33.4	1.42	[0.74; 2.74]	0.2912
ZS-002 Japan	1	11	9	11	3.4	9.00	[1.14; 71.04]	0.0371
ZS-003	29	60	41	48	63.2	1.77	[1.10; 2.84]	0.0189
Pooled Estimate	**47**	**99**	**69**	**81**		1.81	[1.25; 2.62]	0.0017

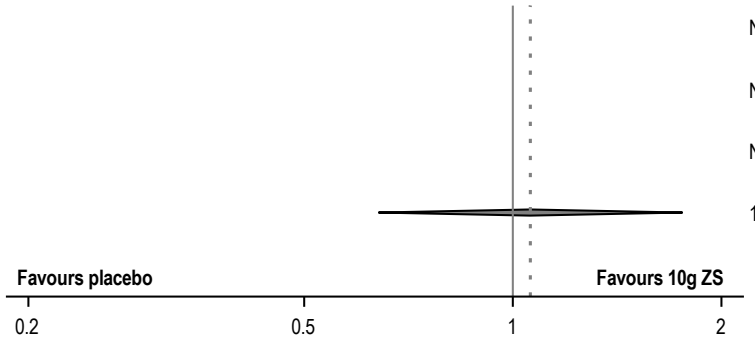
Study interaction p-value 0.2468

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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Baseline eGFR: >=60 ml/min/1.73m2**



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	1	1	1	1		NC	[NC; NC]	
ZS-002 Japan	0	0	3	3		NC	[NC; NC]	
ZS-003	27	38	31	41		NC	[NC; NC]	
Pooled Estimate	**28**	**39**	**35**	**45**		1.06	[0.64; 1.76]	0.8164

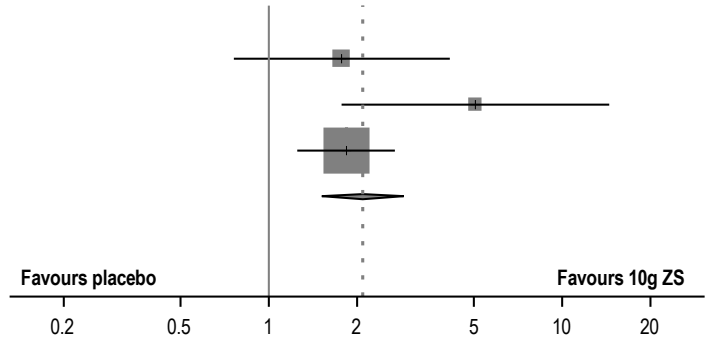
Study interaction p-value 0.9655

Relative risks for individual studies are estimated using a logistic regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Sex: Male



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	13	23	9	9	15.2	1.77	[0.76; 4.14]	0.1883
ZS-002 Japan	4	21	27	28	9.9	5.06	[1.77; 14.47]	0.0025
ZS-003	44	97	65	78	74.9	1.84	[1.25; 2.69]	0.0018
Pooled Estimate	**61**	**141**	**101**	**115**		2.09	[1.51; 2.88]	<0.0001

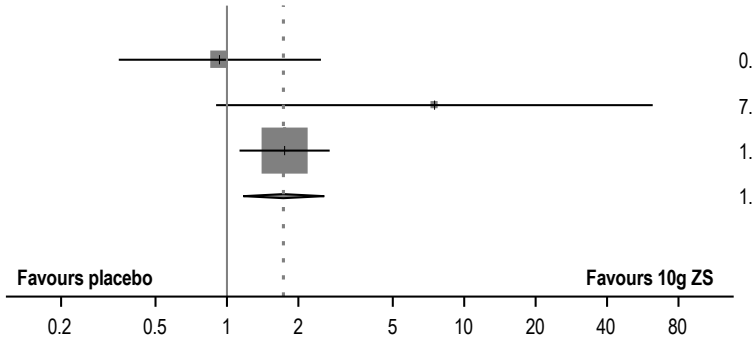
Study interaction p-value 0.1949

Relative risks for individual studies are estimated using a logistic regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Sex: Female



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	6	7	12	15	16.1	0.93	[0.35; 2.49]	0.8903
ZS-002 Japan	1	10	6	8	3.5	7.50	[0.90; 62.30]	0.0621
ZS-003	31	60	56	62	80.4	1.75	[1.13; 2.71]	0.0126
Pooled Estimate	**38**	**77**	**74**	**85**		1.73	[1.17; 2.56]	0.0065

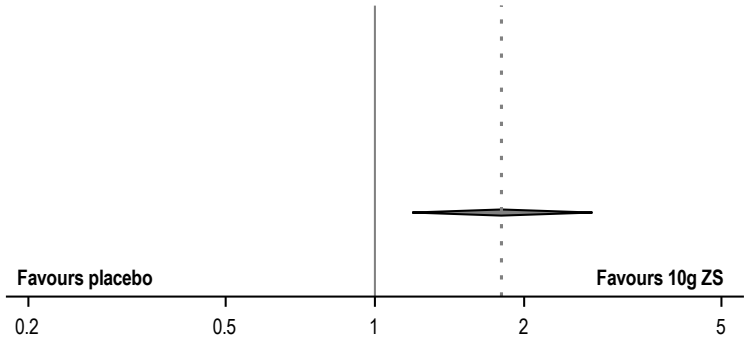
Study interaction p-value 0.1893

Relative risks for individual studies are estimated using a logistic regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Age (years): <65 years



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	5	9	7	7		NC	[NC; NC]	
ZS-002 Japan	1	1	4	5		NC	[NC; NC]	
ZS-003	31	65	46	52		NC	[NC; NC]	
Pooled Estimate	**37**	**75**	**57**	**64**		1.80	[1.19; 2.74]	0.0056

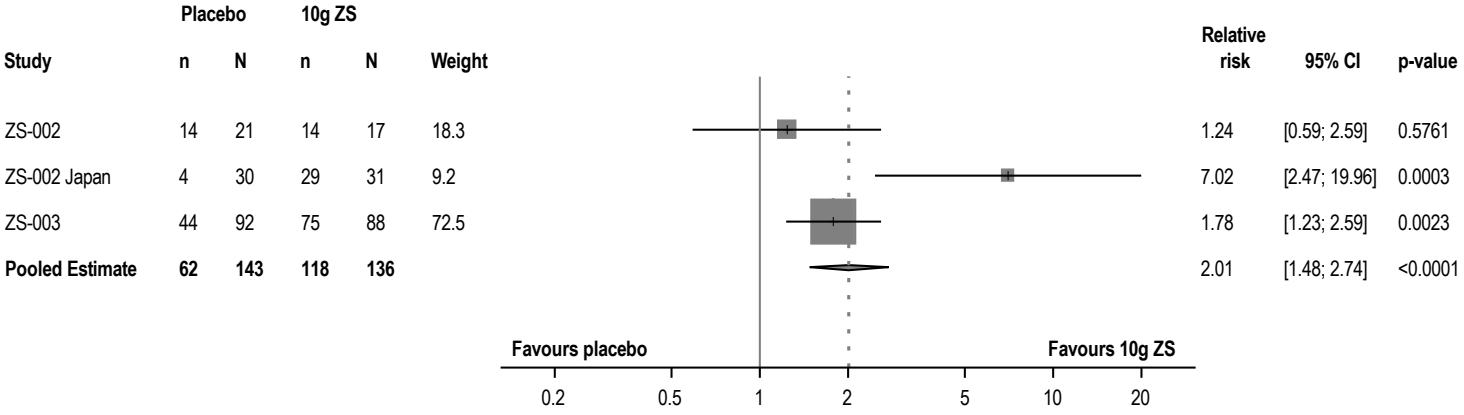
Study interaction p-value 0.7625

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Figure 3.1.5.2 - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Proportion of subjects with normalised serum potassium at timepoints up to 48 hours after first dose (Day 3 0hr pre-dose timepoint), ZS 10g TID vs. placebo, overall and by subgroups (intent-to-treat population)

Age (years): >=65 years



Study interaction p-value 0.0246

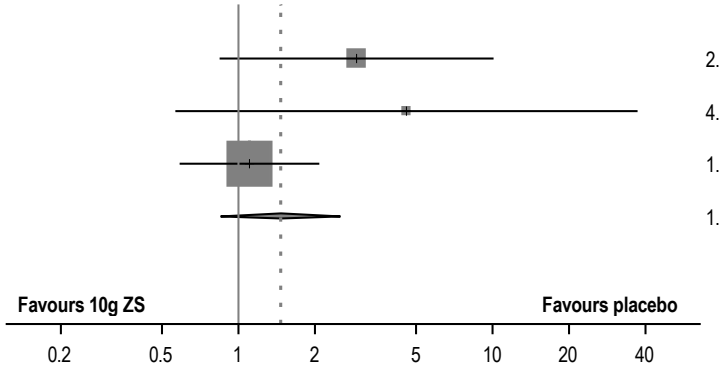
Significant heterogeneity between the studies; validity of pooled relative risk is questionable.

Relative risks for individual studies are estimated using a logistic regression model including treatment. Estimates presented may differ from those presented in Sections 1, 2 and 8 due to differences in the model specification.
The pooled estimate of relative risk is estimated using a logistic regression model including treatment and study.
The weights of the contribution of each individual study to the pooled estimate are approximate; these are calculated using the inverse variance of the individual study estimates of log(relative risk).
The study*treatment interaction p-value is presented as an indicator of inter-study heterogeneity and is estimated using a logistic regression model including treatment, study and study*treatment.
Normalization defined as S-K levels between 3.5-5.0 mmol
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Overall



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	3	30	7	24	19.2	2.92	[0.84; 10.09]	0.0910
ZS-002 Japan	1	33	5	36	6.8	4.58	[0.56; 37.22]	0.1542
ZS-003	17	158	17	143	74.0	1.10	[0.59; 2.08]	0.7575
Pooled Estimate	**21**	**221**	**29**	**203**	**100.0**	1.47	[0.85; 2.53]	0.1684

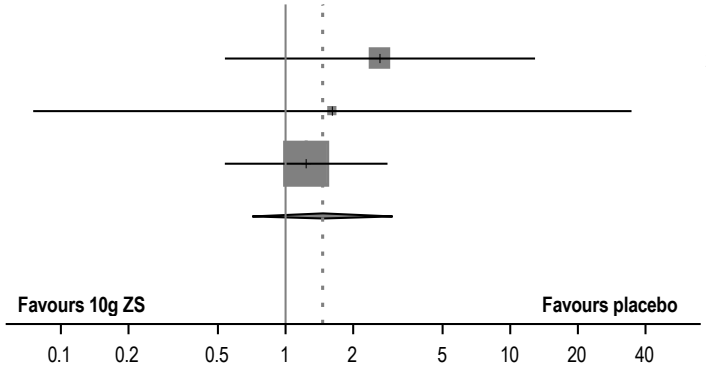
Study interaction p-value 0.2140

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline S-K: <=5.3 mmol/L



	Placebo		10g ZS			Relative		
Study	**n**	**N**	**n**	**N**	**Weight**	**risk**	**95% CI**	**p-value**
ZS-002	2	25	4	19	20.4	2.63	[0.54; 12.89]	0.2327
ZS-002 Japan	0	6	1	12	5.5	1.62	[0.08; 34.66]	0.7592
ZS-003	9	95	11	94	74.1	1.24	[0.54; 2.84]	0.6194
Pooled Estimate	**11**	**126**	**16**	**125**	**100.0**	1.46	[0.71; 3.00]	0.2991

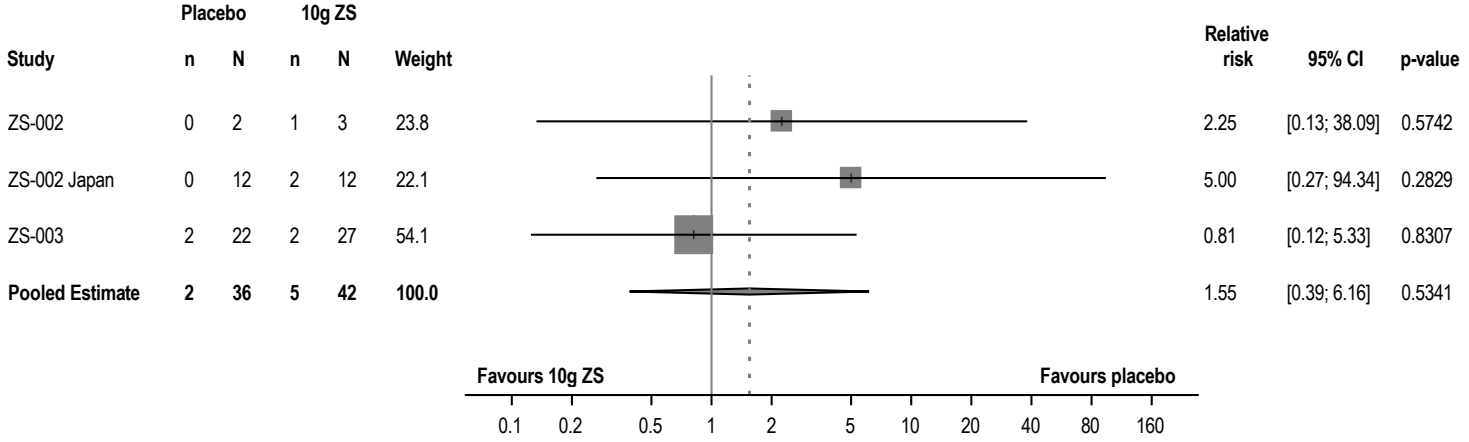
Study interaction p-value 0.7094

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline S-K: >5.3 - <=5.5 mmol/L



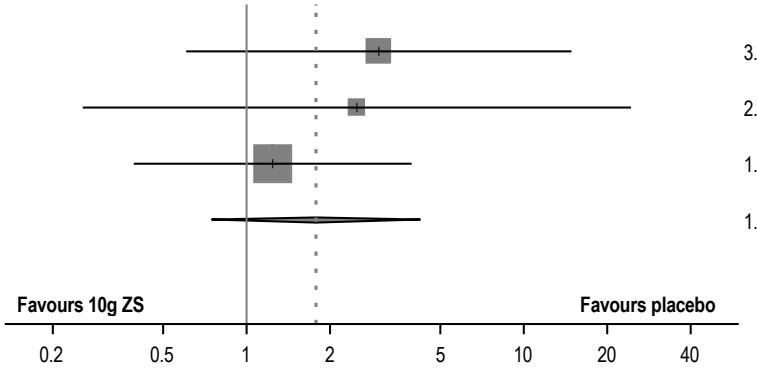
Study interaction p-value 0.5689

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline S-K: >5.5 mmol/L



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	1	3	2	2	29.3	3.00	[0.61; 14.86]	0.1785
ZS-002 Japan	1	15	2	12	14.5	2.50	[0.26; 24.38]	0.4303
ZS-003	6	41	4	22	56.3	1.24	[0.39; 3.94]	0.7124
Pooled Estimate	**8**	**59**	**8**	**36**	**100.0**	1.78	[0.75; 4.23]	0.1921

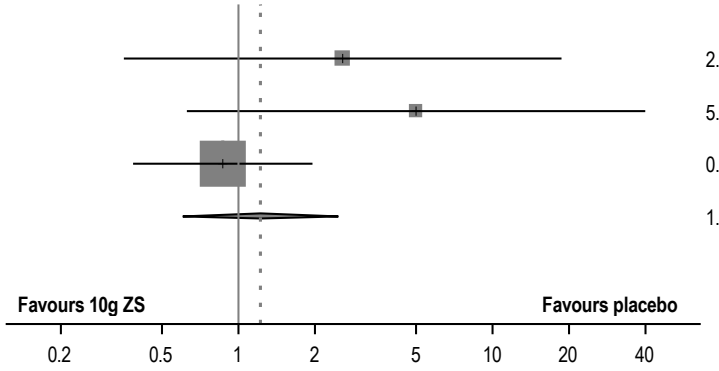
Study interaction p-value 0.6483

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Chronic kidney disease: Yes



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	1	6	3	7	12.7	2.57	[0.35; 18.68]	0.3506
ZS-002 Japan	1	26	5	26	11.6	5.00	[0.63; 39.91]	0.1288
ZS-003	12	96	9	83	75.7	0.87	[0.38; 1.96]	0.7317
Pooled Estimate	**14**	**128**	**17**	**116**	**100.0**	1.22	[0.60; 2.47]	0.5812

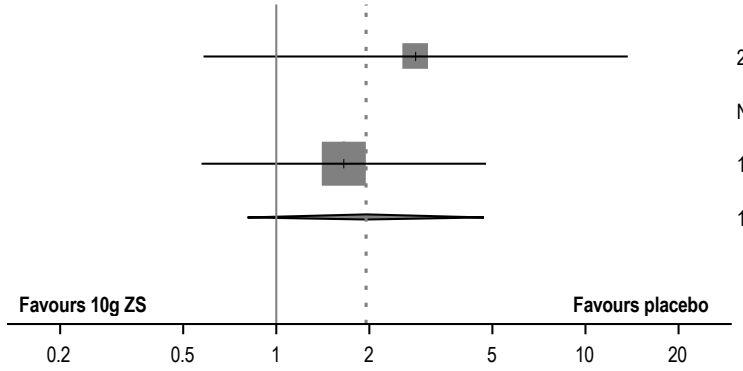
Study interaction p-value 0.2241

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Chronic kidney disease: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	2	24	4	17	31.0	2.82	[0.58; 13.70]	0.1978
ZS-002 Japan	0	7	0	10		NC	[NC; NC]	
ZS-003	5	62	8	60	69.0	1.65	[0.57; 4.77]	0.3523
Pooled Estimate	**7**	**93**	**12**	**87**	**100.0**	1.95	[0.81; 4.71]	0.1362

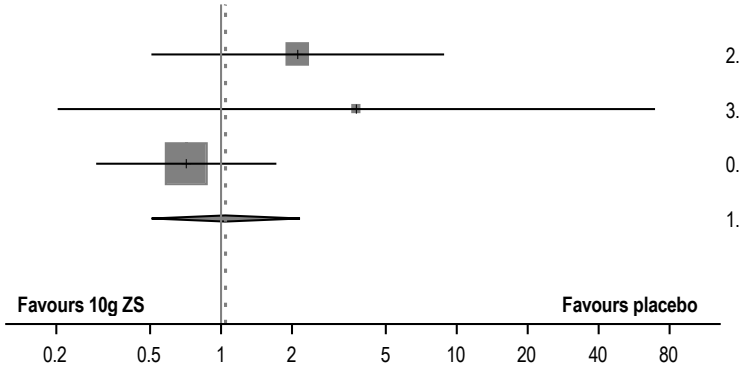
Study interaction p-value NC

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Congestive heart disease: Yes



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	2	11	5	13	25.8	2.12	[0.51; 8.84]	0.3044
ZS-002 Japan	0	4	1	3	6.2	3.75	[0.20; 69.40]	0.3747
ZS-003	11	66	7	59	68.0	0.71	[0.30; 1.72]	0.4492
Pooled Estimate	**13**	**81**	**13**	**75**	**100.0**	1.04	[0.51; 2.16]	0.9060

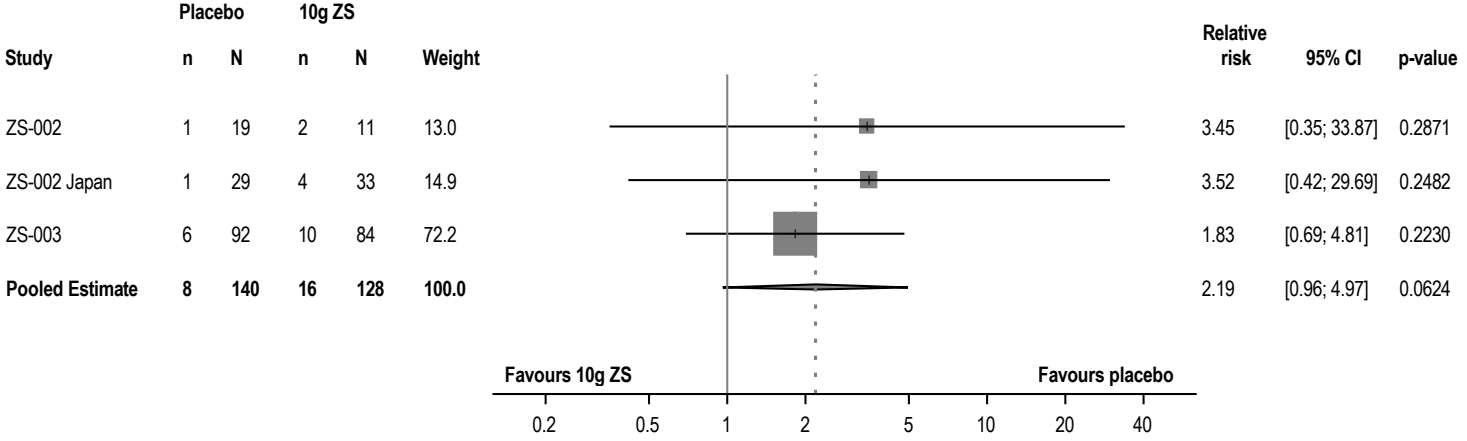
Study interaction p-value 0.3009

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Congestive heart disease: No



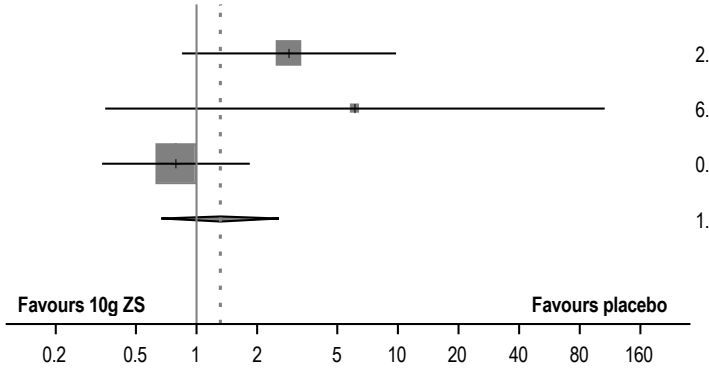
Study interaction p-value 0.7874

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Diabetes mellitus: Yes



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	3	19	5	11	30.4	2.88	[0.85; 9.79]	0.0903
ZS-002 Japan	0	16	4	24	5.6	6.12	[0.35; 106.44]	0.2138
ZS-003	12	96	8	81	64.0	0.79	[0.34; 1.84]	0.5845
Pooled Estimate	**15**	**131**	**17**	**116**	**100.0**	1.31	[0.67; 2.58]	0.4289

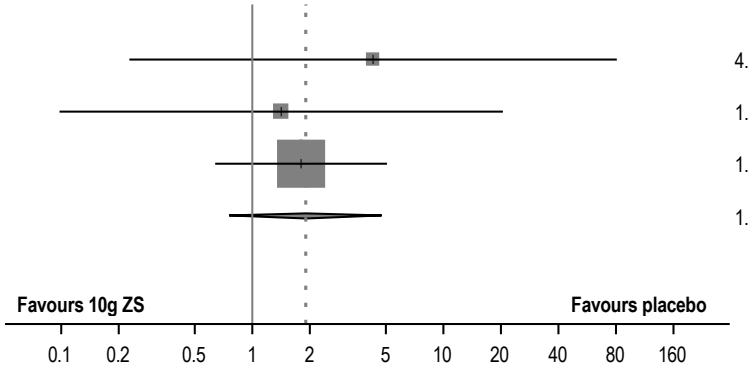
Study interaction p-value 0.1296

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Diabetes mellitus: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	0	11	2	13	9.7	4.29	[0.23; 80.81]	0.3314
ZS-002 Japan	1	17	1	12	11.8	1.42	[0.10; 20.49]	0.7983
ZS-003	5	62	9	62	78.5	1.80	[0.64; 5.07]	0.2657
Pooled Estimate	**6**	**90**	**12**	**87**	**100.0**	1.90	[0.76; 4.76]	0.1685

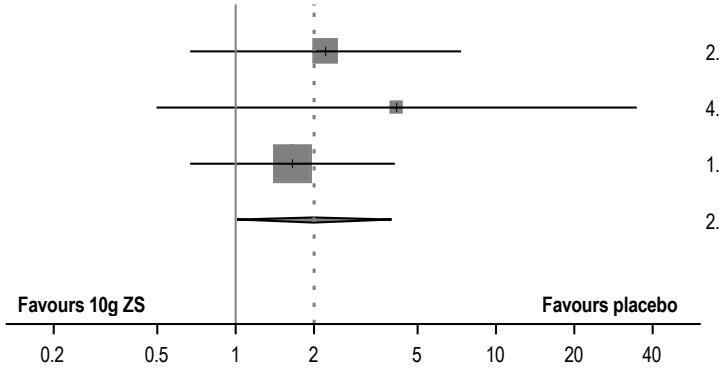
Study interaction p-value 0.8388

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

RAASi medications: Yes



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	3	19	7	20	32.6	2.22	[0.67; 7.34]	0.1928
ZS-002 Japan	1	27	4	26	10.4	4.15	[0.50; 34.75]	0.1888
ZS-003	7	101	11	96	57.0	1.65	[0.67; 4.09]	0.2765
Pooled Estimate	**11**	**147**	**22**	**142**	**100.0**	2.00	[1.01; 3.97]	0.0468

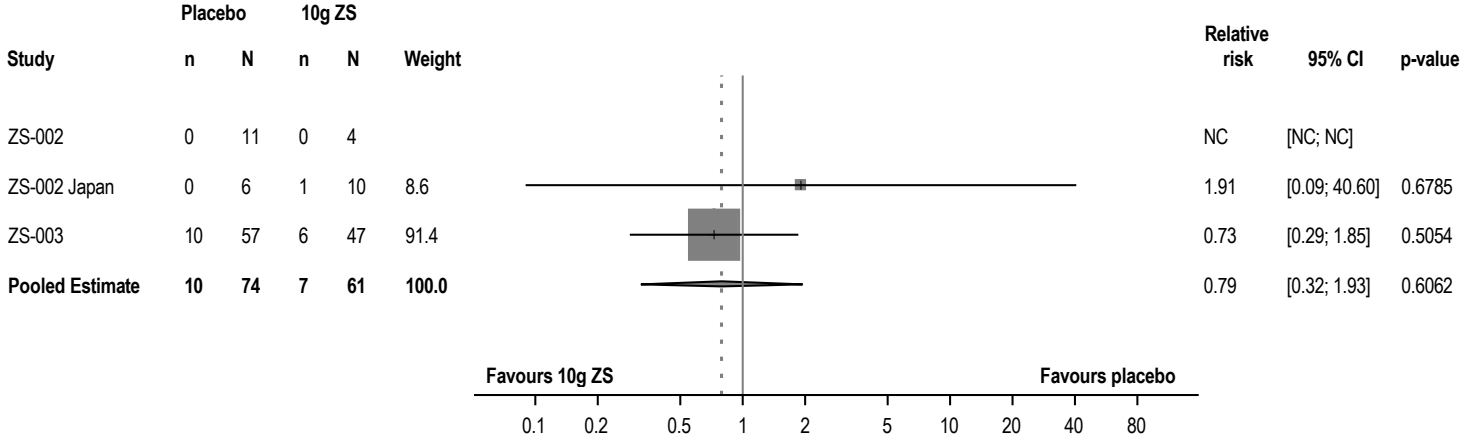
Study interaction p-value 0.7215

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

RAASi medications: No



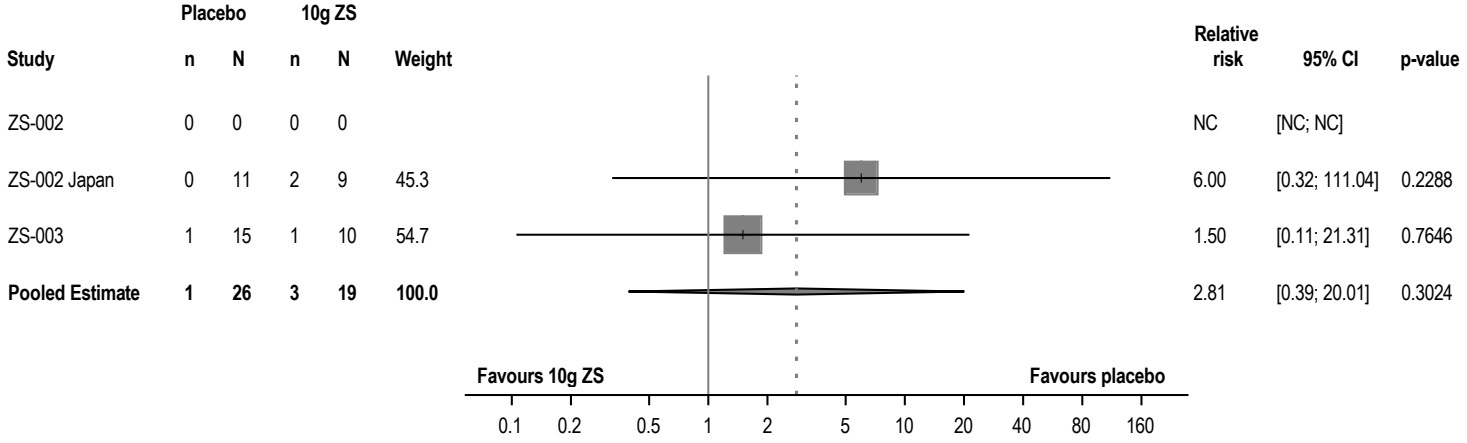
Study interaction p-value NC

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline eGFR: <15 ml/min/1.73m2**



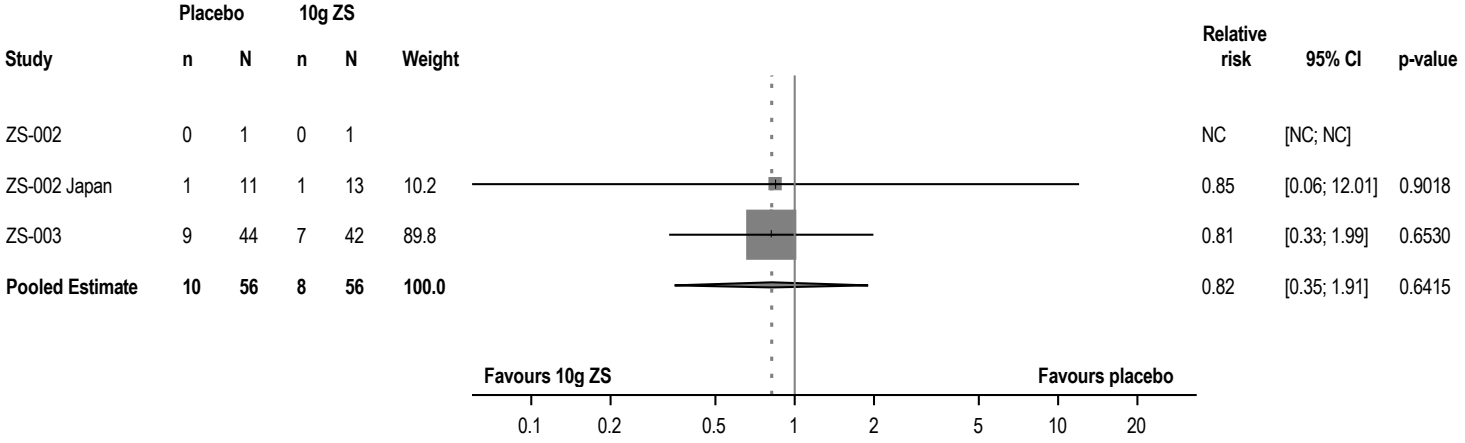
Study interaction p-value NC

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline eGFR: 15- <30 ml/min/1.73m2**



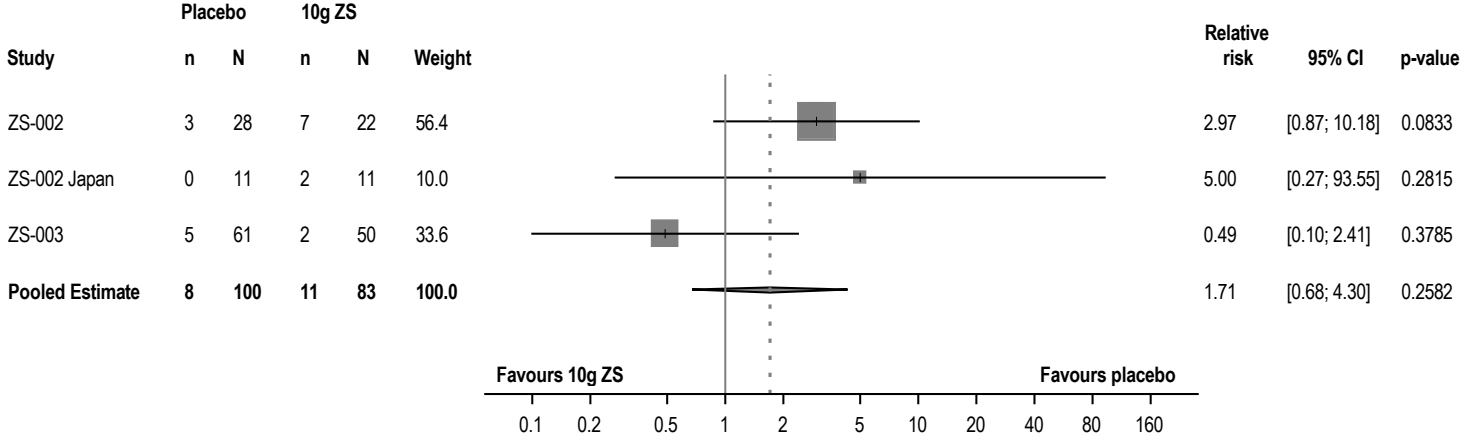
Study interaction p-value NC

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline eGFR: 30- <60 ml/min/1.73m2**



Study interaction p-value 0.1607

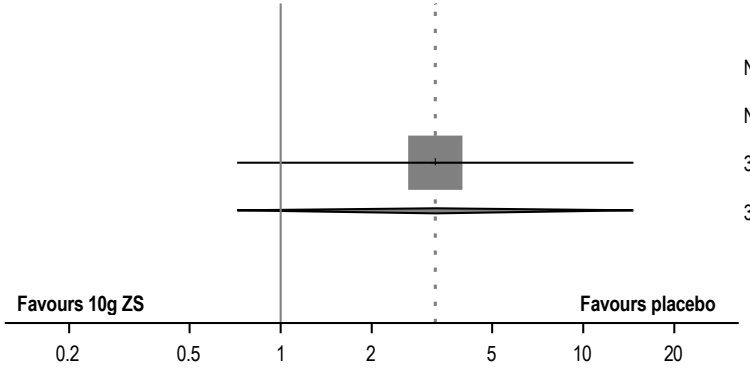
Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline eGFR: >=60 ml/min/1.73m2**

	Placebo		10g ZS			Relative		
Study	**n**	**N**	**n**	**N**	**Weight**	**risk**	**95% CI**	**p-value**
ZS-002	0	1	0	1		NC	[NC; NC]	
ZS-002 Japan	0	0	0	3		NC	[NC; NC]	
ZS-003	2	38	7	41	100.0	3.24	[0.72; 14.66]	0.1262
Pooled Estimate	**2**	**39**	**7**	**45**	**100.0**	3.24	[0.72; 14.66]	0.1262



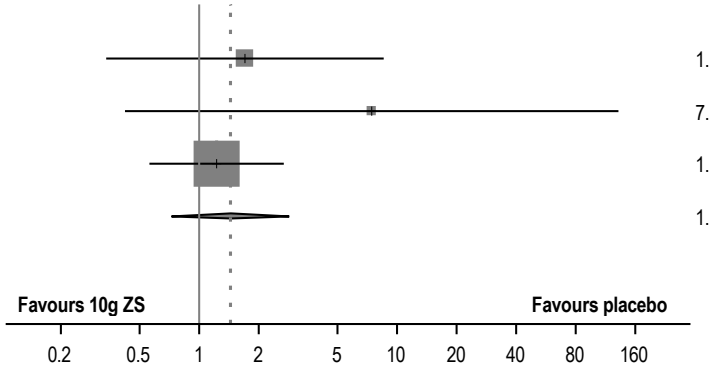
Study interaction p-value NC

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Sex: Male



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	3	23	2	9	17.9	1.70	[0.34; 8.56]	0.5178
ZS-002 Japan	0	23	4	28	5.7	7.45	[0.42; 131.53]	0.1705
ZS-003	11	98	11	80	76.4	1.23	[0.56; 2.68]	0.6109
Pooled Estimate	**14**	**144**	**17**	**117**	**100.0**	1.44	[0.73; 2.85]	0.2961

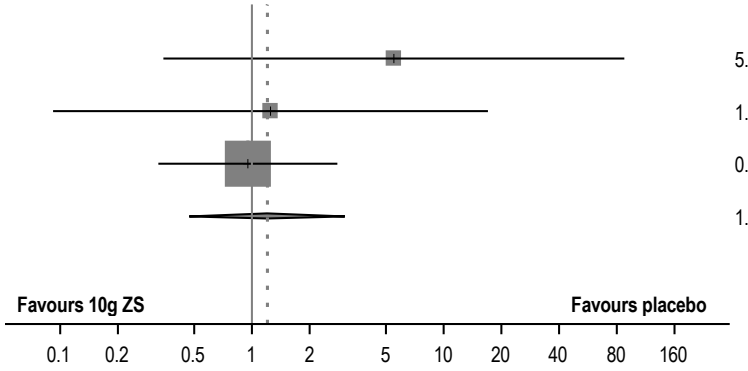
Study interaction p-value 0.4809

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Sex: Female



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	0	7	5	15	11.4	5.50	[0.35; 87.59]	0.2274
ZS-002 Japan	1	10	1	8	12.8	1.25	[0.09; 17.02]	0.8670
ZS-003	6	60	6	63	75.7	0.95	[0.33; 2.79]	0.9291
Pooled Estimate	**7**	**77**	**12**	**86**	**100.0**	1.20	[0.47; 3.07]	0.6961

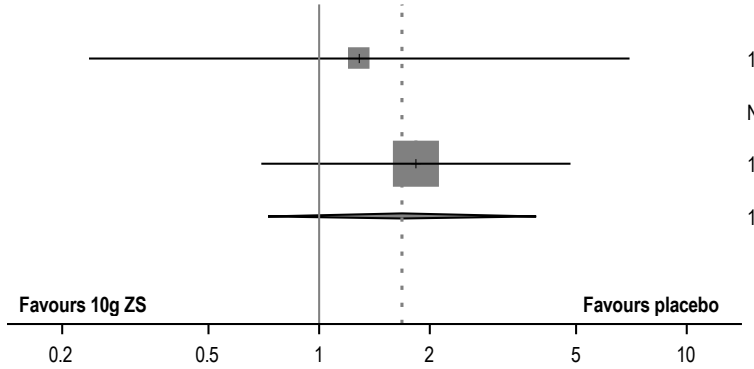
Study interaction p-value 0.5115

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Age (years): <65 years



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	2	9	2	7	24.7	1.29	[0.24; 6.99]	0.7711
ZS-002 Japan	0	1	0	5		NC	[NC; NC]	
ZS-003	6	66	9	54	75.3	1.83	[0.70; 4.83]	0.2199
Pooled Estimate	**8**	**76**	**11**	**66**	**100.0**	1.68	[0.72; 3.89]	0.2265

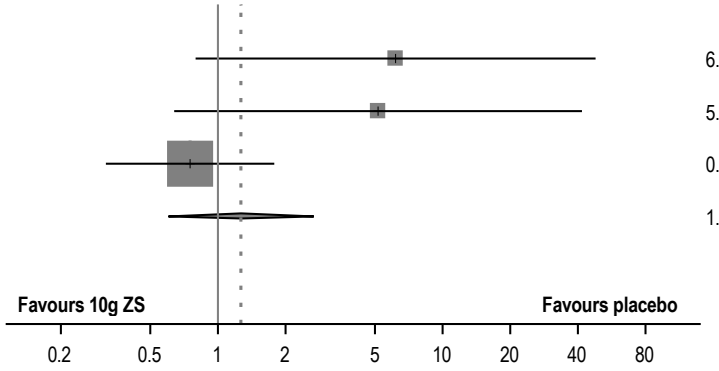
Study interaction p-value NC

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.1a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE), ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Age (years): >=65 years



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	1	21	5	17	13.1	6.18	[0.80; 47.96]	0.0817
ZS-002 Japan	1	32	5	31	12.7	5.16	[0.64; 41.71]	0.1237
ZS-003	11	92	8	89	74.2	0.75	[0.32; 1.78]	0.5169
Pooled Estimate	**13**	**145**	**18**	**137**	**100.0**	1.27	[0.60; 2.66]	0.5348

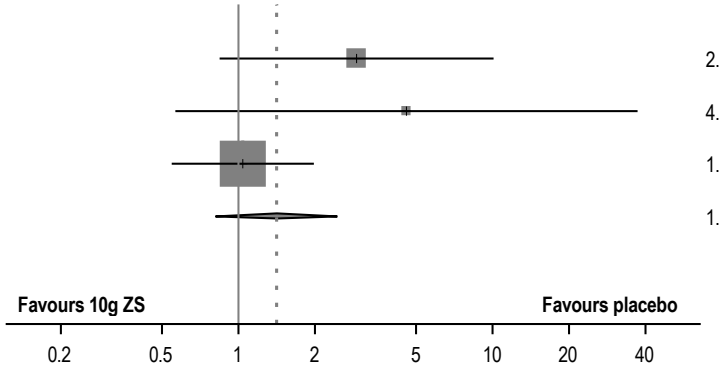
Study interaction p-value 0.0660

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Overall



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	3	30	7	24	19.7	2.92	[0.84; 10.09]	0.0910
ZS-002 Japan	1	33	5	36	6.9	4.58	[0.56; 37.22]	0.1542
ZS-003	17	158	16	143	73.3	1.04	[0.55; 1.98]	0.9052
Pooled Estimate	**21**	**221**	**28**	**203**	**100.0**	1.41	[0.81; 2.45]	0.2195

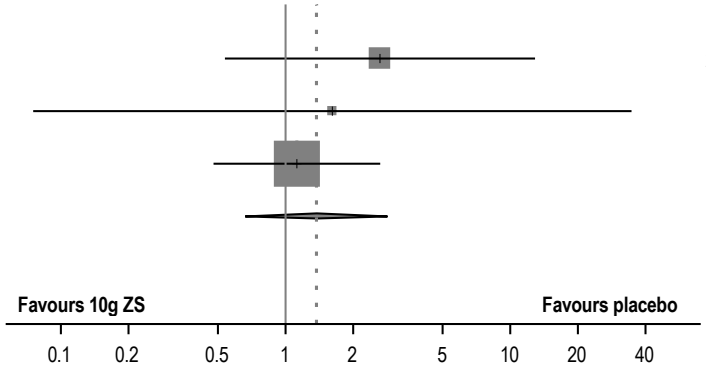
Study interaction p-value 0.1834

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline S-K: <=5.3 mmol/L



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	2	25	4	19	21.1	2.63	[0.54; 12.89]	0.2327
ZS-002 Japan	0	6	1	12	5.7	1.62	[0.08; 34.66]	0.7592
ZS-003	9	95	10	94	73.2	1.12	[0.48; 2.64]	0.7902
Pooled Estimate	**11**	**126**	**15**	**125**	**100.0**	1.37	[0.66; 2.85]	0.3957

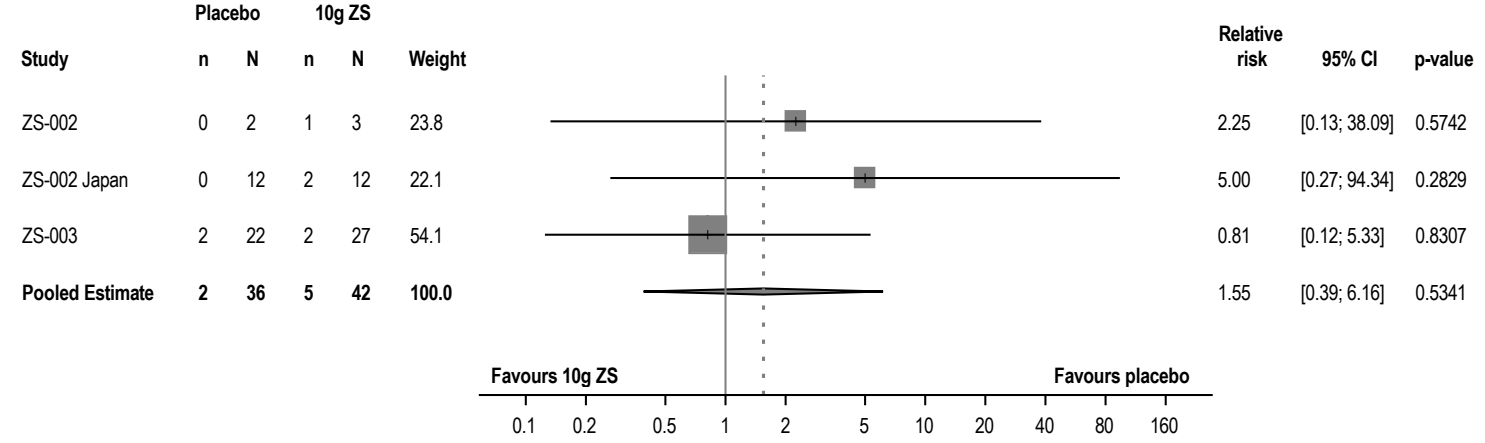
Study interaction p-value 0.6481

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline S-K: >5.3 - <=5.5 mmol/L



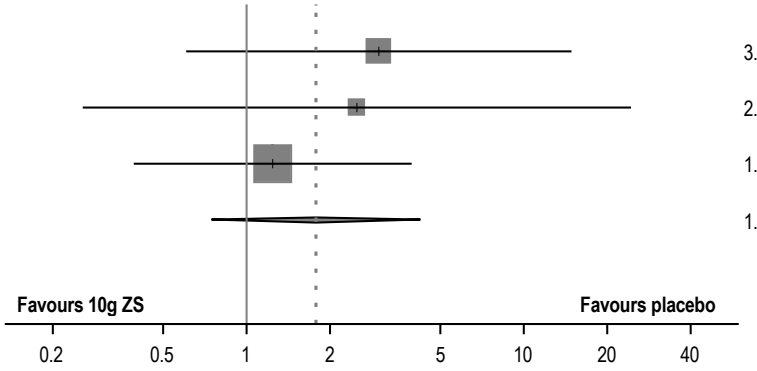
Study interaction p-value 0.5689

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline S-K: >5.5 mmol/L



	Placebo		10g ZS			Relative		
Study	**n**	**N**	**n**	**N**	**Weight**	**risk**	**95% CI**	**p-value**
ZS-002	1	3	2	2	29.3	3.00	[0.61; 14.86]	0.1785
ZS-002 Japan	1	15	2	12	14.5	2.50	[0.26; 24.38]	0.4303
ZS-003	6	41	4	22	56.3	1.24	[0.39; 3.94]	0.7124
Pooled Estimate	**8**	**59**	**8**	**36**	**100.0**	1.78	[0.75; 4.23]	0.1921

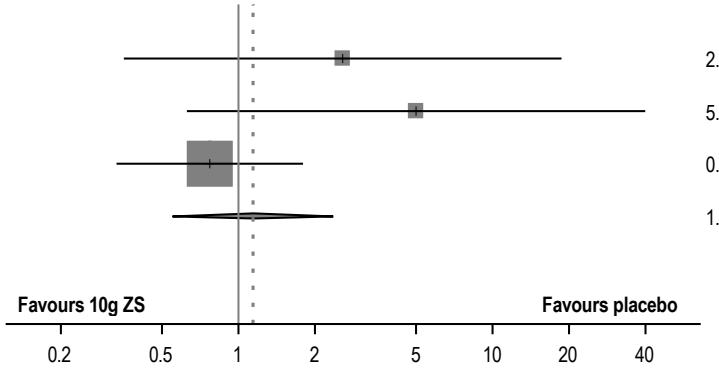
Study interaction p-value 0.6483

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Chronic kidney disease: Yes



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	1	6	3	7	13.5	2.57	[0.35; 18.68]	0.3506
ZS-002 Japan	1	26	5	26	12.3	5.00	[0.63; 39.91]	0.1288
ZS-003	12	96	8	83	74.2	0.77	[0.33; 1.80]	0.5465
Pooled Estimate	**14**	**128**	**16**	**116**	**100.0**	1.14	[0.55; 2.36]	0.7222

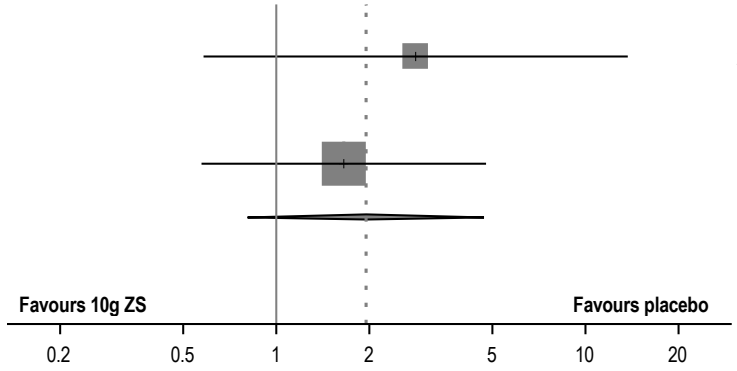
Study interaction p-value 0.1813

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Chronic kidney disease: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	2	24	4	17	31.0	2.82	[0.58; 13.70]	0.1978
ZS-002 Japan	0	7	0	10		NC	[NC; NC]	
ZS-003	5	62	8	60	69.0	1.65	[0.57; 4.77]	0.3523
Pooled Estimate	**7**	**93**	**12**	**87**	**100.0**	1.95	[0.81; 4.71]	0.1362

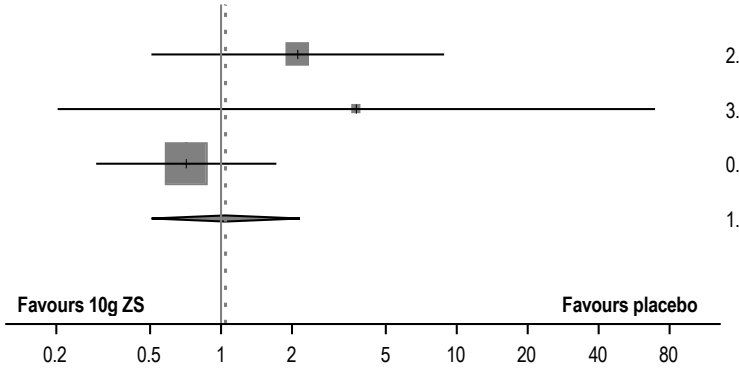
Study interaction p-value NC

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Congestive heart disease: Yes



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	2	11	5	13	25.8	2.12	[0.51; 8.84]	0.3044
ZS-002 Japan	0	4	1	3	6.2	3.75	[0.20; 69.40]	0.3747
ZS-003	11	66	7	59	68.0	0.71	[0.30; 1.72]	0.4492
Pooled Estimate	**13**	**81**	**13**	**75**	**100.0**	1.04	[0.51; 2.16]	0.9060

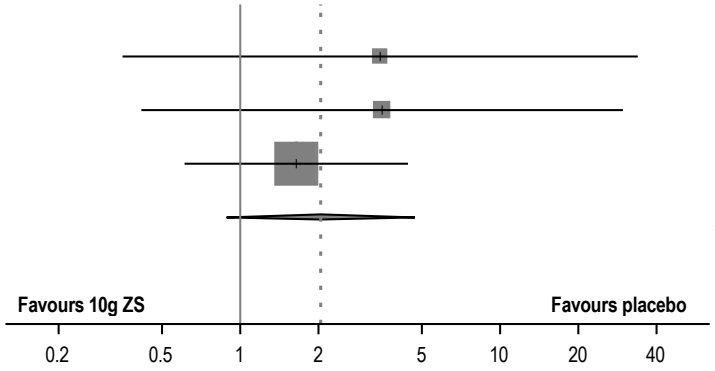
Study interaction p-value 0.3009

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Congestive heart disease: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	1	19	2	11	13.4	3.45	[0.35; 33.87]	0.2871
ZS-002 Japan	1	29	4	33	15.3	3.52	[0.42; 29.69]	0.2482
ZS-003	6	92	9	84	71.3	1.64	[0.61; 4.42]	0.3256
Pooled Estimate	**8**	**140**	**15**	**128**	**100.0**	2.04	[0.88; 4.70]	0.0946

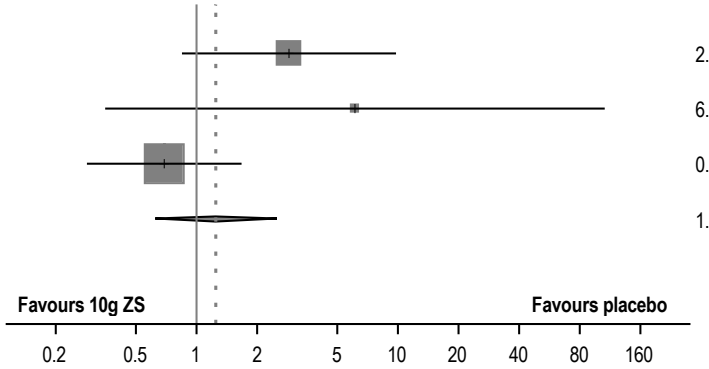
Study interaction p-value 0.7268

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Diabetes mellitus: Yes



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	3	19	5	11	32.3	2.88	[0.85; 9.79]	0.0903
ZS-002 Japan	0	16	4	24	5.9	6.12	[0.35; 106.44]	0.2138
ZS-003	12	96	7	81	61.8	0.69	[0.29; 1.67]	0.4132
Pooled Estimate	**15**	**131**	**16**	**116**	**100.0**	1.25	[0.62; 2.50]	0.5346

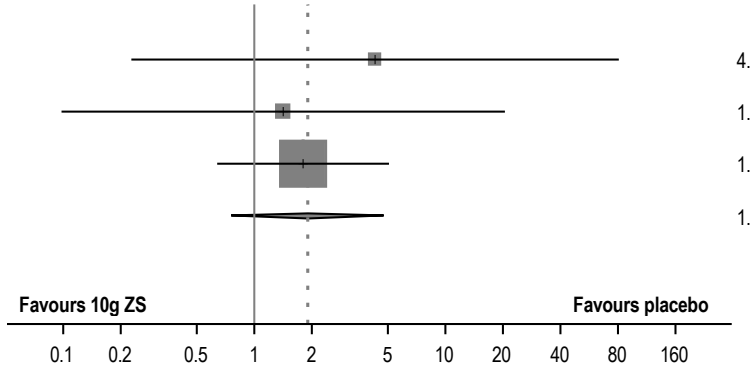
Study interaction p-value 0.0955

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The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Diabetes mellitus: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	0	11	2	13	9.7	4.29	[0.23; 80.81]	0.3314
ZS-002 Japan	1	17	1	12	11.8	1.42	[0.10; 20.49]	0.7983
ZS-003	5	62	9	62	78.5	1.80	[0.64; 5.07]	0.2657
Pooled Estimate	**6**	**90**	**12**	**87**	**100.0**	1.90	[0.76; 4.76]	0.1685

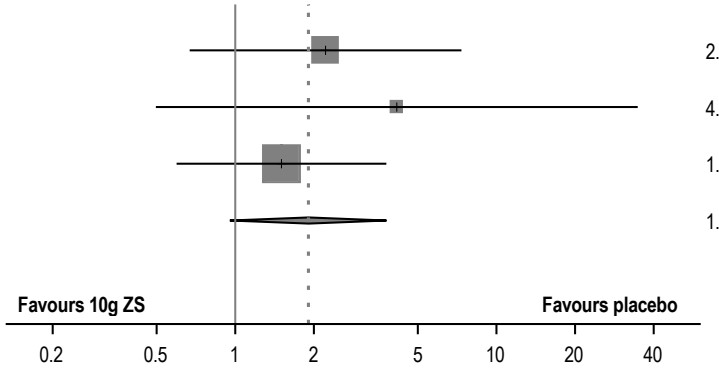
Study interaction p-value 0.8388

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The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

RAASi medications: Yes



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	3	19	7	20	33.4	2.22	[0.67; 7.34]	0.1928
ZS-002 Japan	1	27	4	26	10.6	4.15	[0.50; 34.75]	0.1888
ZS-003	7	101	10	96	56.0	1.50	[0.60; 3.79]	0.3877
Pooled Estimate	**11**	**147**	**21**	**142**	**100.0**	1.91	[0.95; 3.81]	0.0677

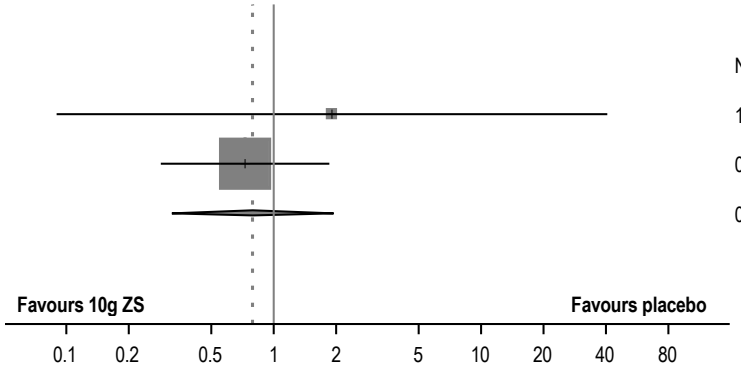
Study interaction p-value 0.6599

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The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

RAASi medications: No



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	0	11	0	4		NC	[NC; NC]	
ZS-002 Japan	0	6	1	10	8.6	1.91	[0.09; 40.60]	0.6785
ZS-003	10	57	6	47	91.4	0.73	[0.29; 1.85]	0.5054
Pooled Estimate	**10**	**74**	**7**	**61**	**100.0**	0.79	[0.32; 1.93]	0.6062

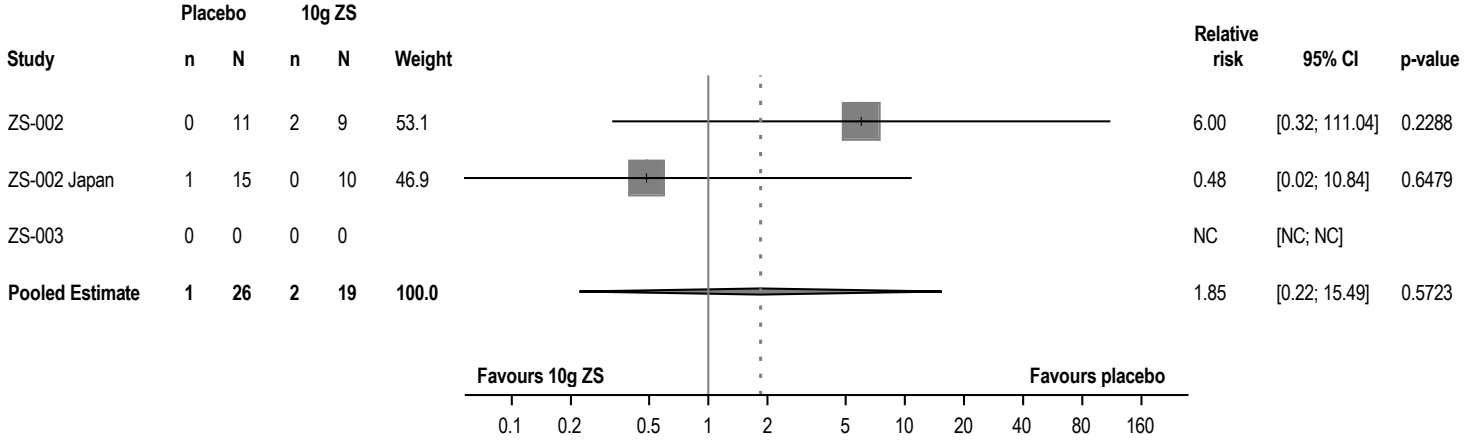
Study interaction p-value NC

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline eGFR: <15 ml/min/1.73m2**



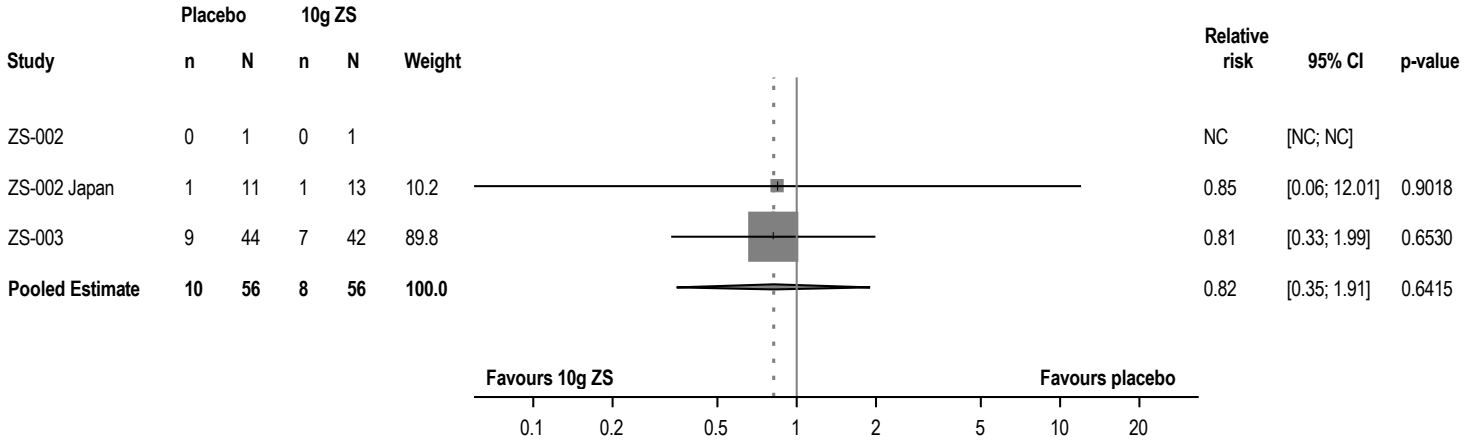
Study interaction p-value NC

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline eGFR: 15- <30 ml/min/1.73m2**



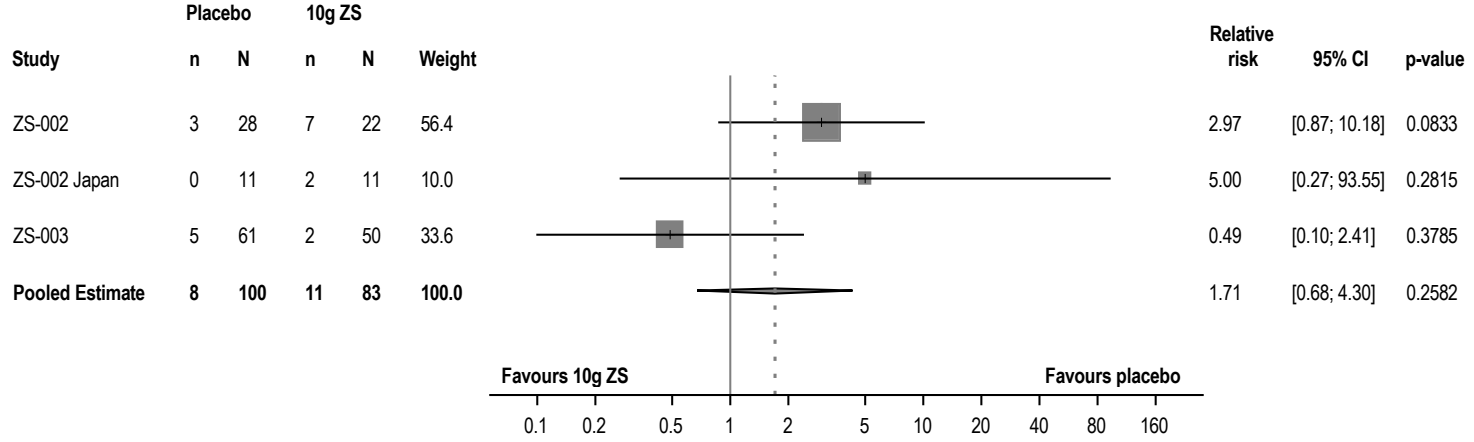
Study interaction p-value NC

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline eGFR: 30- <60 ml/min/1.73m2**



Study interaction p-value 0.1607

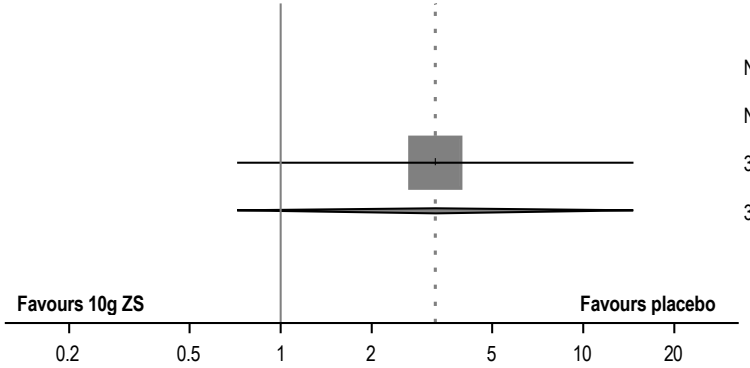
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The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Baseline eGFR: >=60 ml/min/1.73m2**

	Placebo		10g ZS			Relative		
Study	**n**	**N**	**n**	**N**	**Weight**	**risk**	**95% CI**	**p-value**
ZS-002	0	1	0	1		NC	[NC; NC]	
ZS-002 Japan	0	0	0	3		NC	[NC; NC]	
ZS-003	2	38	7	41	100.0	3.24	[0.72; 14.66]	0.1262
Pooled Estimate	**2**	**39**	**7**	**45**	**100.0**	3.24	[0.72; 14.66]	0.1262



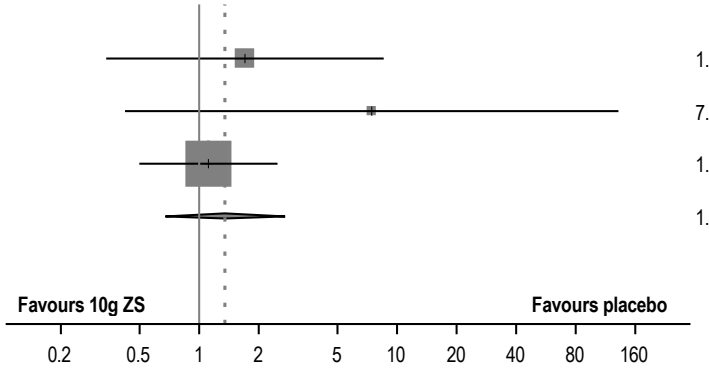
Study interaction p-value NC

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Sex: Male



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	3	23	2	9	18.7	1.70	[0.34; 8.56]	0.5178
ZS-002 Japan	0	23	4	28	5.9	7.45	[0.42; 131.53]	0.1705
ZS-003	11	98	10	80	75.4	1.11	[0.50; 2.49]	0.7930
Pooled Estimate	**14**	**144**	**16**	**117**	**100.0**	1.35	[0.67; 2.71]	0.4005

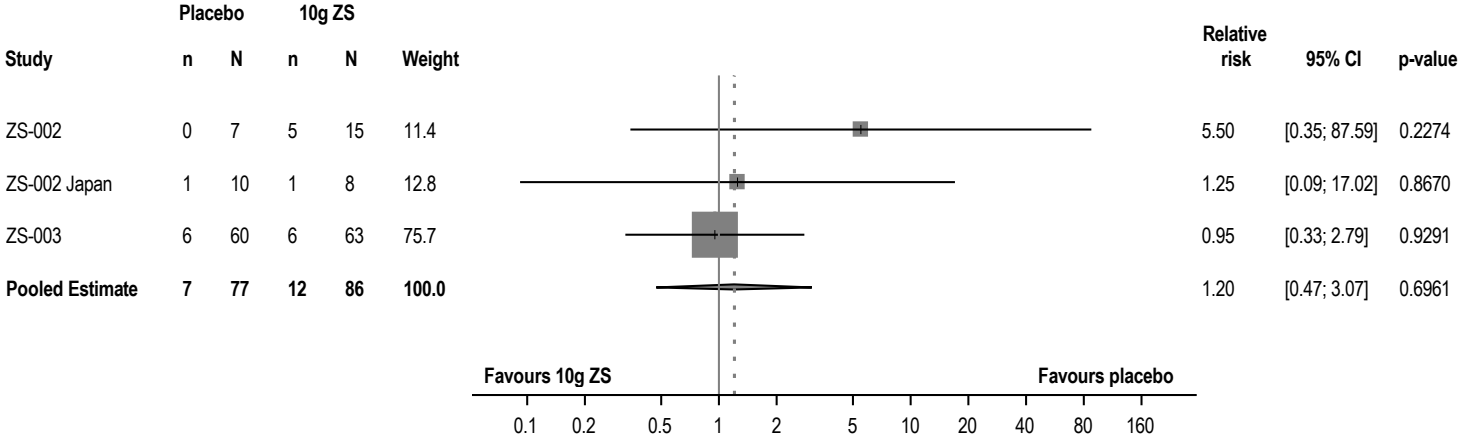
Study interaction p-value 0.4362

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Sex: Female



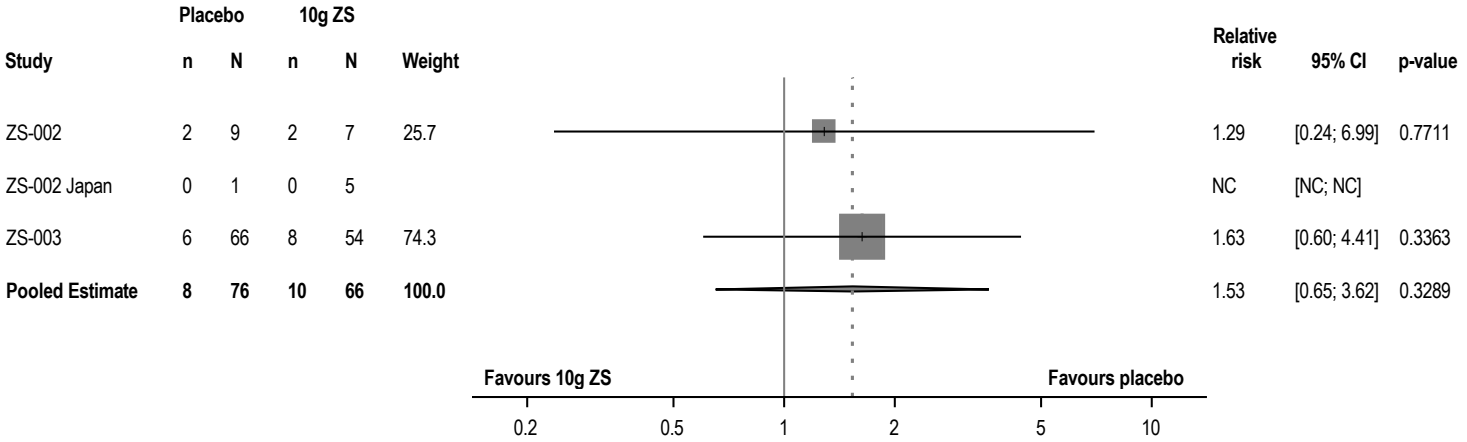
Study interaction p-value 0.5115

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Age (years): <65 years



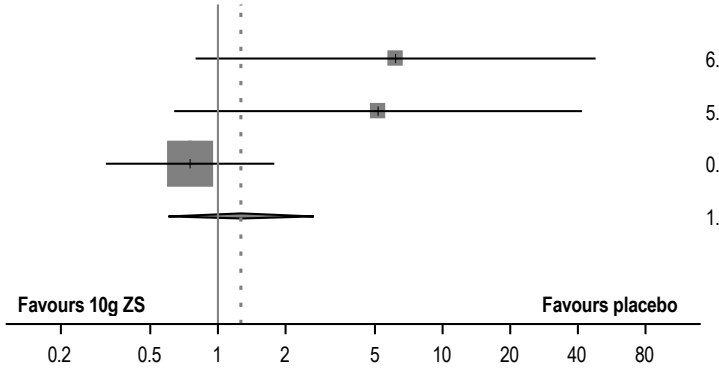
Study interaction p-value NC

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Figure 3.2.1.5a - Study ZS-002, ZS-002 Japan and ZS-003 acute pooled: Subjects experiencing any adverse event (AE) graded as non-severe, ZS 10g TID vs. placebo, overall and by subgroups (safety population)

Age (years): >=65 years



Study	Placebo n	Placebo N	10g ZS n	10g ZS N	Weight	Relative risk	95% CI	p-value
ZS-002	1	21	5	17	13.1	6.18	[0.80; 47.96]	0.0817
ZS-002 Japan	1	32	5	31	12.7	5.16	[0.64; 41.71]	0.1237
ZS-003	11	92	8	89	74.2	0.75	[0.32; 1.78]	0.5169
Pooled Estimate	**13**	**145**	**18**	**137**	**100.0**	1.27	[0.60; 2.66]	0.5348

Study interaction p-value 0.0660

Relative risks for individual studies are estimated using naive calculations from the frequency table. Confidence intervals are estimated using the Wald method.
The pooled estimate of relative risk is estimated using the inverse-variance method.
CI = Confidence Intervals, NC = Not calculated
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Anhang 4-G6: Studie Energize

Lokelma

Table 7.1.1.1 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)

	Placebo (N=37)						Lokelma 10g QD (N=33)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Overall																
Baseline																
Absolute value	36	6.48 (0.757)	6.5 (6.1, 7.0)	4.6, 8.9			32	6.38 (0.627)	6.5 (6.1, 6.8)	4.9, 7.3						
1h																
Absolute value	36	5.87 (0.770)	5.7 (5.3, 6.6)	4.6, 7.5			32	5.79 (0.669)	5.8 (5.4, 6.1)	4.6, 7.3						
Change from baseline	36	-0.61 (0.851)	-0.5 (-1.0, 0.0)	-4.0, 0.6	-0.62 (0.107)	(-0.83, -0.40)	32	-0.59 (0.566)	-0.5 (-1.2, -0.1)	-1.6, 0.5	-0.64 (0.114)	(-0.86, -0.41)	-0.02 (-0.33, 0.29)	0.8994	0.04 (-0.44, 0.51)	
Percent change from baseline	36	-8.88 (10.972)	-7.6 (-14.5, 0.0)	-44.9, 8.7			32	-8.94 (8.522)	-7.8 (-17.4, -1.7)	-24.2, 7.4						
2h																
Absolute value	36	6.13 (0.845)	6.0 (5.7, 6.6)	4.2, 8.8			32	5.78 (0.690)	5.7 (5.2, 6.3)	4.9, 7.3						
Change from baseline	36	-0.35 (0.639)	-0.3 (-0.7, -0.0)	-3.1, 0.7	-0.35 (0.103)	(-0.56, -0.15)	32	-0.61 (0.646)	-0.5 (-1.1, -0.0)	-2.3, 0.6	-0.66 (0.110)	(-0.88, -0.44)	-0.31 (-0.61, -0.00)	0.0466	-0.40 (-0.88, 0.08)	
Percent change from baseline	36	-5.10 (9.136)	-4.3 (-10.6, -0.6)	-42.5, 10.6			32	-9.16 (9.552)	-7.0 (-17.3, -0.9)	-31.9, 10.0						
4h																
Absolute value	36	6.23 (0.809)	6.3 (5.7, 6.7)	4.6, 8.9			32	6.03 (0.604)	6.1 (5.7, 6.5)	4.9, 7.4						
Change from baseline	36	-0.25 (0.626)	-0.0 (-0.5, 0.1)	-2.4, 1.1	-0.26 (0.094)	(-0.44, -0.07)	32	-0.36 (0.573)	-0.3 (-0.6, 0.0)	-1.6, 1.1	-0.41 (0.100)	(-0.61, -0.21)	-0.15 (-0.42, 0.12)	0.2782	-0.17 (-0.65, 0.31)	
Percent change from baseline	36	-3.56 (9.311)	-0.7 (-8.3, 2.4)	-32.9, 20.4			32	-5.19 (8.702)	-5.5 (-9.1, 0.0)	-24.6, 17.5						
6h																
Absolute value	21	6.38 (0.687)	6.6 (5.8, 6.8)	4.8, 7.3			23	5.90 (0.658)	5.8 (5.6, 6.3)	4.9, 7.3						
Change from baseline	21	-0.31 (1.013)	0.0 (-0.6, 0.2)	-4.1, 1.1	-0.26 (0.151)	(-0.57, 0.04)	23	-0.49 (0.703)	-0.5 (-1.1, -0.1)	-1.6, 1.0	-0.52 (0.144)	(-0.81, -0.23)	-0.26 (-0.68, 0.16)	0.2252	-0.20 (-0.80, 0.39)	
Percent change from baseline	21	-3.74 (12.780)	0.0 (-9.6, 2.8)	-46.1, 20.4			23	-7.27 (10.893)	-7.4 (-18.3, -2.0)	-24.6, 16.7						
8h																
Absolute value	17	6.52 (0.671)	6.4 (5.9, 7.2)	5.6, 7.6			22	5.90 (0.545)	5.8 (5.5, 6.1)	5.1, 7.3						
Change from baseline	17	-0.30 (0.597)	-0.2 (-0.9, 0.2)	-1.3, 0.6	-0.14 (0.143)	(-0.43, 0.15)	22	-0.48 (0.788)	-0.3 (-1.1, 0.0)	-1.7, 1.1	-0.51 (0.128)	(-0.77, -0.25)	-0.38 (-0.77, 0.01)	0.0573	-0.25 (-0.88, 0.39)	
Percent change from baseline	17	-4.06 (8.288)	-3.3 (-12.3, 2.8)	-14.9, 9.1			22	-6.69 (12.363)	-5.7 (-16.7, 0.0)	-25.0, 22.0						
10h																
Absolute value	18	6.56 (0.686)	6.5 (6.2, 7.3)	5.4, 7.6			21	5.88 (0.660)	5.9 (5.5, 6.3)	4.1, 7.3						
Change from baseline	18	-0.21 (0.644)	-0.3 (-0.6, 0.3)	-1.3, 0.8	-0.11 (0.130)	(-0.37, 0.15)	21	-0.43 (0.680)	-0.4 (-0.8, 0.1)	-1.9, 1.0	-0.56 (0.124)	(-0.81, -0.31)	-0.45 (-0.81, -0.08)	0.0167	-0.33 (-0.96, 0.31)	
Percent change from baseline	18	-2.69 (9.305)	-5.2 (-9.8, 4.5)	-16.4, 13.1			21	-6.26 (11.142)	-6.6 (-13.3, 1.6)	-31.7, 20.0						
12h																
Absolute value	18	6.54 (0.688)	6.8 (6.0, 7.1)	5.5, 7.3			20	5.81 (0.720)	5.9 (5.4, 6.2)	4.3, 7.3						
Change from baseline	18	-0.20 (1.091)	0.1 (-0.6, 0.3)	-3.4, 1.9	-0.17 (0.177)	(-0.52, 0.19)	20	-0.47 (0.873)	-0.5 (-0.8, 0.0)	-2.1, 1.6	-0.71 (0.168)	(-1.05, -0.37)	-0.54 (-1.04, -0.05)	0.0316	-0.27 (-0.91, 0.37)	
Percent change from baseline	18	-1.73 (15.223)	1.4 (-9.8, 4.5)	-38.2, 35.2			20	-6.62 (14.459)	-8.5 (-13.6, 0.0)	-32.8, 32.0						
24h																
Absolute value	12	5.94 (0.884)	6.1 (5.7, 6.4)	3.6, 7.3			16	5.43 (0.709)	5.3 (5.2, 5.9)	4.0, 6.7						
Change from baseline	12	-1.06 (1.436)	-0.8 (-1.0, -0.6)	-5.3, 0.7	-0.88 (0.205)	(-1.29, -0.46)	16	-0.97 (0.717)	-0.8 (-1.6, -0.5)	-2.2, 0.1	-1.10 (0.184)	(-1.48, -0.73)	-0.23 (-0.79, 0.33)	0.4156	0.08 (-0.67, 0.83)	
Percent change from baseline	12	-13.83 (16.263)	-11.1 (-15.0, -8.6)	-59.6, 10.6			16	-14.91 (10.783)	-12.4 (-23.5, -7.0)	-35.5, 1.6						
EOT																
Absolute value	30	5.95 (0.676)	6.0 (5.6, 6.4)	3.6, 7.3			24	5.49 (0.642)	5.4 (5.2, 5.7)	4.0, 6.7						
Change from baseline	30	-0.58 (1.134)	-0.6 (-0.9, 0.0)	-5.3, 1.3			24	-0.88 (0.669)	-0.7 (-1.3, -0.5)	-2.2, 0.1						
Percent change from baseline	30	-7.55 (14.452)	-8.6 (-13.0, 0.0)	-59.6, 24.1			24	-13.47 (10.018)	-11.4 (-21.3, -7.0)	-35.5, 1.6						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

Lokelma

Table 7.1.1.1 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)

	Placebo (N=37)						Lokelma 10g QD (N=33)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value																
<=5.3 mmol/L																
Baseline																
Absolute value	2	4.80 (0.283)	4.8 (4.6, 5.0)	4.6, 5.0			4	5.10 (0.183)	5.1 (5.0, 5.3)	4.9, 5.3						
1h																
Absolute value	2	4.85 (0.354)	4.9 (4.6, 5.1)	4.6, 5.1			4	4.98 (0.330)	5.0 (4.8, 5.2)	4.6, 5.4						
Change from baseline	2	0.05 (0.071)	0.0 (0.0, 0.1)	0.0, 0.1			4	-0.13 (0.395)	0.0 (-0.4, 0.1)	-0.7, 0.2						
Percent change from baseline	2	1.00 (1.414)	1.0 (0.0, 2.0)	0.0, 2.0			4	-2.34 (7.470)	0.0 (-6.6, 1.9)	-13.2, 3.9						
2h																
Absolute value	2	4.85 (0.354)	4.9 (4.6, 5.1)	4.6, 5.1			4	5.03 (0.150)	5.0 (4.9, 5.2)	4.9, 5.2						
Change from baseline	2	0.05 (0.071)	0.0 (0.0, 0.1)	0.0, 0.1			4	-0.07 (0.171)	-0.0 (-0.2, 0.0)	-0.3, 0.1						
Percent change from baseline	2	1.00 (1.414)	1.0 (0.0, 2.0)	0.0, 2.0			4	-1.41 (3.309)	-0.9 (-3.8, 1.0)	-5.8, 2.0						
4h																
Absolute value	2	4.85 (0.354)	4.9 (4.6, 5.1)	4.6, 5.1			4	5.20 (0.245)	5.3 (5.0, 5.4)	4.9, 5.4						
Change from baseline	2	0.05 (0.071)	0.0 (0.0, 0.1)	0.0, 0.1			4	0.10 (0.216)	0.1 (-0.1, 0.3)	-0.1, 0.4						
Percent change from baseline	2	1.00 (1.414)	1.0 (0.0, 2.0)	0.0, 2.0			4	1.99 (4.296)	0.9 (-1.0, 4.9)	-1.9, 8.0						
6h																
Absolute value	0						2	5.40 (0.707)	5.4 (4.9, 5.9)	4.9, 5.9						
Change from baseline	0						2	0.25 (0.495)	0.3 (-0.1, 0.6)	-0.1, 0.6						
Percent change from baseline	0						2	4.66 (9.419)	4.7 (-2.0, 11.3)	-2.0, 11.3						
8h																
Absolute value	0						2	5.90 (0.283)	5.9 (5.7, 6.1)	5.7, 6.1						
Change from baseline	0						2	0.75 (0.495)	0.8 (0.4, 1.1)	0.4, 1.1						
Percent change from baseline	0						2	14.78 (10.218)	14.8 (7.6, 22.0)	7.6, 22.0						
10h																
Absolute value	0						3	5.63 (0.321)	5.5 (5.4, 6.0)	5.4, 6.0						
Change from baseline	0						3	0.47 (0.462)	0.2 (0.2, 1.0)	0.2, 1.0						
Percent change from baseline	0						3	9.21 (9.347)	3.9 (3.8, 20.0)	3.8, 20.0						
12h																
Absolute value	0						3	5.73 (1.026)	6.0 (4.6, 6.6)	4.6, 6.6						
Change from baseline	0						3	0.57 (1.168)	0.8 (-0.7, 1.6)	-0.7, 1.6						
Percent change from baseline	0						3	11.39 (22.868)	15.4 (-13.2, 32.0)	-13.2, 32.0						
24h																
Absolute value							1	5.10 (NC)	5.1 (5.1, 5.1)	5.1, 5.1						
Change from baseline							1	-0.20 (NC)	-0.2 (-0.2, -0.2)	-0.2, -0.2						
Percent change from baseline							1	-3.77 (NC)	-3.8 (-3.8, -3.8)	-3.8, -3.8						
EOT																
Absolute value	1	5.10 (NC)	5.1 (5.1, 5.1)	5.1, 5.1			2	5.10 (0.000)	5.1 (5.1, 5.1)	5.1, 5.1						
Change from baseline	1	0.10 (NC)	0.1 (0.1, 0.1)	0.1, 0.1			2	-0.15 (0.071)	-0.2 (-0.2, -0.1)	-0.2, -0.1						
Percent change from baseline	1	2.00 (NC)	2.0 (2.0, 2.0)	2.0, 2.0			2	-2.85 (1.308)	-2.8 (-3.8, -1.9)	-3.8, -1.9						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

Lokelma

Table 7.1.1.1 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)

	Placebo (N=37)						Lokelma 10g QD (N=33)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value *(contd.)*																
5.4-5.5 mmol/L																
Baseline																
Absolute value	1	5.40 (NC)	5.4 (5.4, 5.4)	5.4, 5.4												
1h																
Absolute value	1	4.80 (NC)	4.8 (4.8, 4.8)	4.8, 4.8												
Change from baseline	1	-0.60 (NC)	-0.6 (-0.6, -0.6)	-0.6, -0.6												
Percent change from baseline	1	-11.11 (NC)	-11.1 (-11.1, -11.1)	-11.1, -11.1												
2h																
Absolute value	1	5.30 (NC)	5.3 (5.3, 5.3)	5.3, 5.3												
Change from baseline	1	-0.10 (NC)	-0.1 (-0.1, -0.1)	-0.1, -0.1												
Percent change from baseline	1	-1.85 (NC)	-1.9 (-1.9, -1.9)	-1.9, -1.9												
4h																
Absolute value	1	6.50 (NC)	6.5 (6.5, 6.5)	6.5, 6.5												
Change from baseline	1	1.10 (NC)	1.1 (1.1, 1.1)	1.1, 1.1												
Percent change from baseline	1	20.37 (NC)	20.4 (20.4, 20.4)	20.4, 20.4												
6h																
Absolute value	1	6.50 (NC)	6.5 (6.5, 6.5)	6.5, 6.5												
Change from baseline	1	1.10 (NC)	1.1 (1.1, 1.1)	1.1, 1.1												
Percent change from baseline	1	20.37 (NC)	20.4 (20.4, 20.4)	20.4, 20.4												
8h																
Absolute value	0															
Change from baseline	0															
Percent change from baseline	0															
10h																
Absolute value	0															
Change from baseline	0															
Percent change from baseline	0															
12h																
Absolute value	1	7.30 (NC)	7.3 (7.3, 7.3)	7.3, 7.3												
Change from baseline	1	1.90 (NC)	1.9 (1.9, 1.9)	1.9, 1.9												
Percent change from baseline	1	35.19 (NC)	35.2 (35.2, 35.2)	35.2, 35.2												
EOT																
Absolute value	1	6.70 (NC)	6.7 (6.7, 6.7)	6.7, 6.7												
Change from baseline	1	1.30 (NC)	1.3 (1.3, 1.3)	1.3, 1.3												
Percent change from baseline	1	24.07 (NC)	24.1 (24.1, 24.1)	24.1, 24.1												
>5.5 mmol/L																
Baseline																
Absolute value	33	6.62 (0.626)	6.6 (6.1, 7.0)	5.8, 8.9			28	6.56 (0.411)	6.6 (6.3, 6.9)	6.0, 7.3						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

Lokelma

Table 7.1.1.1 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)

	Placebo (N=37)						Lokelma 10g QD (N=33)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Acute Baseline S-K value *(contd.)*																
>5.5 mmol/L *(contd.)*																
1h																
Absolute value	33	5.96 (0.731)	5.8 (5.5, 6.6)	4.8, 7.5			28	5.91 (0.623)	5.9 (5.5, 6.2)	5.0, 7.3						
Change from baseline	33	-0.65 (0.873)	-0.5 (-1.0, 0.0)	-4.0, 0.6	-0.66 (0.116)	(-0.89, -0.42)	28	-0.65 (0.561)	-0.6 (-1.2, -0.1)	-1.6, 0.5	-0.68 (0.126)	(-0.93, -0.43)	-0.02 (-0.37, 0.32)	0.8864	0.00 (-0.50, 0.50)	
Percent change from baseline	33	-9.41 (11.182)	-8.2 (-15.3, 0.0)	-44.9, 8.7			28	-9.88 (8.356)	-8.8 (-18.4, -2.4)	-24.2, 7.4						
2h																
Absolute value	33	6.24 (0.801)	6.2 (5.8, 6.6)	4.2, 8.8			28	5.88 (0.669)	5.9 (5.3, 6.4)	4.9, 7.3						
Change from baseline	33	-0.38 (0.659)	-0.3 (-0.7, -0.1)	-3.1, 0.7	-0.38 (0.113)	(-0.61, -0.15)	28	-0.68 (0.654)	-0.7 (-1.1, -0.2)	-2.3, 0.6	-0.71 (0.123)	(-0.96, -0.46)	-0.33 (-0.66, 0.01)	0.0541	-0.46 (-0.97, 0.05)	
Percent change from baseline	33	-5.56 (9.399)	-4.4 (-10.8, -1.6)	-42.5, 10.6			28	-10.27 (9.663)	-10.2 (-17.9, -3.1)	-31.9, 10.0						
4h																
Absolute value	33	6.30 (0.765)	6.3 (5.8, 6.7)	4.9, 8.9			28	6.14 (0.545)	6.1 (5.7, 6.5)	4.9, 7.4						
Change from baseline	33	-0.31 (0.601)	-0.1 (-0.6, 0.1)	-2.4, 0.5	-0.31 (0.100)	(-0.52, -0.11)	28	-0.42 (0.580)	-0.4 (-0.6, -0.1)	-1.6, 1.1	-0.45 (0.109)	(-0.67, -0.23)	-0.13 (-0.43, 0.16)	0.3670	-0.18 (-0.69, 0.32)	
Percent change from baseline	33	-4.56 (8.634)	-1.6 (-8.5, 1.7)	-32.9, 8.1			28	-6.21 (8.727)	-6.6 (-9.5, -1.5)	-24.6, 17.5						
6h																
Absolute value	20	6.37 (0.704)	6.7 (5.8, 6.8)	4.8, 7.3			21	5.94 (0.652)	5.8 (5.7, 6.3)	4.9, 7.3						
Change from baseline	20	-0.39 (0.984)	-0.1 (-0.7, 0.1)	-4.1, 0.7	-0.36 (0.153)	(-0.67, -0.05)	21	-0.56 (0.687)	-0.5 (-1.1, -0.3)	-1.6, 1.0	-0.63 (0.151)	(-0.93, -0.32)	-0.27 (-0.71, 0.16)	0.2169	-0.21 (-0.82, 0.40)	
Percent change from baseline	20	-4.94 (11.824)	-0.8 (-9.6, 1.4)	-46.1, 11.5			21	-8.40 (10.512)	-8.1 (-18.3, -4.3)	-24.6, 16.7						
8h																
Absolute value	17	6.52 (0.671)	6.4 (5.9, 7.2)	5.6, 7.6			20	5.91 (0.569)	5.8 (5.5, 6.3)	5.1, 7.3						
Change from baseline	17	-0.30 (0.597)	-0.2 (-0.9, 0.2)	-1.3, 0.6	-0.23 (0.140)	(-0.51, 0.06)	20	-0.60 (0.706)	-0.5 (-1.2, -0.1)	-1.7, 1.0	-0.65 (0.131)	(-0.91, -0.38)	-0.42 (-0.81, -0.03)	0.0368	-0.46 (-1.11, 0.20)	
Percent change from baseline	17	-4.06 (8.288)	-3.3 (-12.3, 2.8)	-14.9, 9.1			20	-8.84 (10.493)	-8.8 (-17.0, -1.7)	-25.0, 16.7						
10h																
Absolute value	18	6.56 (0.686)	6.5 (6.2, 7.3)	5.4, 7.6			18	5.92 (0.698)	6.0 (5.5, 6.4)	4.1, 7.3						
Change from baseline	18	-0.21 (0.644)	-0.3 (-0.6, 0.3)	-1.3, 0.8	-0.20 (0.130)	(-0.46, 0.06)	18	-0.58 (0.595)	-0.5 (-0.9, -0.3)	-1.9, 0.4	-0.67 (0.132)	(-0.94, -0.41)	-0.47 (-0.84, -0.10)	0.0148	-0.59 (-1.26, 0.08)	
Percent change from baseline	18	-2.69 (9.305)	-5.2 (-9.8, 4.5)	-16.4, 13.1			18	-8.84 (9.302)	-7.5 (-14.1, -4.3)	-31.7, 6.7						
12h																
Absolute value	17	6.50 (0.682)	6.7 (6.0, 7.1)	5.5, 7.3			17	5.82 (0.695)	5.9 (5.4, 6.2)	4.3, 7.3						
Change from baseline	17	-0.32 (0.986)	0.0 (-0.6, 0.3)	-3.4, 0.6	-0.31 (0.160)	(-0.63, 0.01)	17	-0.65 (0.706)	-0.6 (-0.9, -0.1)	-2.1, 0.2	-0.86 (0.161)	(-1.18, -0.53)	-0.55 (-1.01, -0.09)	0.0207	-0.38 (-1.06, 0.30)	
Percent change from baseline	17	-3.90 (12.492)	0.0 (-9.8, 4.3)	-38.2, 10.2			17	-9.79 (10.553)	-8.8 (-14.1, -1.7)	-32.8, 3.3						
24h																
Absolute value	12	5.94 (0.884)	6.1 (5.7, 6.4)	3.6, 7.3			15	5.45 (0.729)	5.3 (5.2, 6.2)	4.0, 6.7						
Change from baseline	12	-1.06 (1.436)	-0.8 (-1.0, -0.6)	-5.3, 0.7	-0.98 (0.207)	(-1.40, -0.56)	15	-1.02 (0.711)	-0.8 (-1.8, -0.5)	-2.2, 0.1	-1.26 (0.193)	(-1.65, -0.87)	-0.28 (-0.85, 0.30)	0.3362	0.04 (-0.72, 0.79)	
Percent change from baseline	12	-13.83 (16.263)	-11.1 (-15.0, -8.6)	-59.6, 10.6			15	-15.65 (10.730)	-13.1 (-25.7, -7.4)	-35.5, 1.6						
EOT																
Absolute value	28	5.95 (0.665)	6.0 (5.7, 6.4)	3.6, 7.3			22	5.52 (0.660)	5.5 (5.2, 5.7)	4.0, 6.7						
Change from baseline	28	-0.67 (1.107)	-0.6 (-0.9, -0.1)	-5.3, 0.7			22	-0.94 (0.660)	-0.8 (-1.4, -0.5)	-2.2, 0.1						
Percent change from baseline	28	-9.02 (13.478)	-8.8 (-13.4, -1.6)	-59.6, 10.6			22	-14.43 (9.905)	-12.4 (-21.3, -8.2)	-35.5, 1.6						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

Lokelma

Table 7.1.1.1 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)

	Placebo (N=37)						Lokelma 10g QD (N=33)								
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Sex																0.4524
Male																
Baseline																
Absolute value	18	6.53 (0.885)	6.6 (6.0, 6.9)	4.6, 8.9			16	6.22 (0.749)	6.5 (5.7, 6.8)	4.9, 7.2						
1h																
Absolute value	18	5.95 (0.877)	5.9 (5.3, 6.7)	4.6, 7.5			16	5.80 (0.740)	5.8 (5.3, 6.3)	4.6, 7.3						
Change from baseline	18	-0.58 (1.114)	-0.2 (-0.9, 0.0)	-4.0, 0.6			16	-0.42 (0.569)	-0.4 (-0.9, 0.0)	-1.5, 0.5						
Percent change from baseline	18	-7.92 (13.806)	-4.1 (-13.7, 0.0)	-44.9, 8.7			16	-6.39 (8.555)	-5.4 (-14.3, 0.0)	-21.4, 7.4						
2h																
Absolute value	18	6.12 (1.052)	5.9 (5.6, 6.6)	4.2, 8.8			16	5.63 (0.747)	5.4 (5.0, 6.3)	4.9, 6.9						
Change from baseline	18	-0.42 (0.844)	-0.3 (-0.7, 0.0)	-3.1, 0.7			16	-0.59 (0.707)	-0.3 (-1.1, 0.0)	-2.3, 0.1						
Percent change from baseline	18	-6.02 (11.932)	-4.7 (-10.8, 0.0)	-42.5, 10.6			16	-8.93 (10.279)	-5.4 (-17.8, 0.0)	-31.9, 2.0						
4h																
Absolute value	18	6.14 (1.002)	6.1 (5.5, 6.7)	4.6, 8.9			16	5.81 (0.601)	5.8 (5.4, 6.4)	4.9, 6.8						
Change from baseline	18	-0.39 (0.651)	-0.2 (-0.6, 0.0)	-2.4, 0.2			16	-0.41 (0.590)	-0.3 (-0.6, 0.0)	-1.6, 0.4						
Percent change from baseline	18	-5.77 (9.250)	-3.1 (-8.5, 0.0)	-32.9, 3.3			16	-5.92 (8.868)	-4.1 (-9.1, 0.0)	-24.6, 8.0						
6h																
Absolute value	10	6.11 (0.717)	5.9 (5.7, 6.8)	4.8, 7.1			11	5.66 (0.721)	5.7 (4.9, 6.3)	4.9, 6.8						
Change from baseline	10	-0.71 (1.304)	-0.4 (-0.9, -0.1)	-4.1, 0.7			11	-0.61 (0.729)	-0.7 (-1.1, -0.1)	-1.6, 0.6						
Percent change from baseline	10	-8.95 (15.360)	-6.6 (-13.0, -1.7)	-46.1, 11.5			11	-9.22 (11.596)	-10.9 (-18.3, -2.0)	-24.6, 11.3						
8h																
Absolute value	9	6.32 (0.698)	6.1 (5.8, 6.6)	5.6, 7.6			10	5.95 (0.395)	5.8 (5.7, 6.4)	5.5, 6.5						
Change from baseline	9	-0.58 (0.591)	-0.7 (-1.0, -0.3)	-1.3, 0.6			10	-0.30 (0.834)	-0.2 (-1.0, 0.2)	-1.7, 1.1						
Percent change from baseline	9	-7.92 (8.074)	-9.6 (-14.5, -5.1)	-14.9, 9.1			10	-3.59 (13.344)	-3.3 (-15.4, 3.2)	-23.6, 22.0						
10h																
Absolute value	10	6.44 (0.728)	6.3 (6.1, 6.9)	5.4, 7.6			11	5.72 (0.708)	5.8 (5.4, 6.3)	4.1, 6.7						
Change from baseline	10	-0.35 (0.755)	-0.5 (-1.0, 0.4)	-1.3, 0.8			11	-0.44 (0.813)	-0.5 (-0.9, 0.2)	-1.9, 1.0						
Percent change from baseline	10	-4.46 (10.880)	-6.9 (-14.6, 6.8)	-16.4, 13.1			11	-6.24 (13.753)	-7.4 (-14.1, 3.8)	-31.7, 20.0						
12h																
Absolute value	9	6.24 (0.658)	6.3 (5.5, 6.7)	5.5, 7.1			10	5.72 (0.842)	6.0 (5.1, 6.3)	4.3, 6.8						
Change from baseline	9	-0.66 (1.243)	-0.2 (-1.2, 0.2)	-3.4, 0.6			10	-0.33 (1.040)	-0.4 (-0.7, 0.0)	-2.1, 1.6						
Percent change from baseline	9	-8.07 (15.399)	-2.9 (-17.8, 3.3)	-38.2, 10.2			10	-4.35 (18.181)	-5.8 (-13.2, 0.0)	-32.8, 32.0						
24h																
Absolute value	7	5.69 (1.105)	5.8 (5.4, 6.1)	3.6, 7.3			7	5.34 (0.519)	5.3 (5.1, 5.6)	4.6, 6.3						
Change from baseline	7	-1.27 (1.905)	-0.9 (-1.5, -0.3)	-5.3, 0.7			7	-0.94 (0.663)	-0.7 (-1.8, -0.4)	-1.8, -0.2						
Percent change from baseline	7	-16.03 (21.614)	-13.0 (-20.6, -5.1)	-59.6, 10.6			7	-14.54 (9.684)	-11.7 (-25.7, -6.7)	-28.1, -3.8						
EOT																
Absolute value	16	5.84 (0.837)	5.8 (5.5, 6.5)	3.6, 7.3			10	5.37 (0.447)	5.3 (5.1, 5.6)	4.6, 6.3						
Change from baseline	16	-0.80 (1.432)	-0.6 (-1.1, 0.0)	-5.3, 0.7			10	-0.83 (0.604)	-0.7 (-1.2, -0.4)	-1.8, -0.1						
Percent change from baseline	16	-10.42 (17.277)	-9.3 (-16.2, 0.0)	-59.6, 10.6			10	-12.86 (8.858)	-11.4 (-18.5, -6.7)	-28.1, -1.9						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

Lokelma

Table 7.1.1.1 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)

	Placebo (N=37)						Lokelma 10g QD (N=33)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Sex *(contd.)*																
Female																
Baseline																
Absolute value	18	6.43 (0.624)	6.5 (6.1, 7.0)	5.0, 7.3			16	6.54 (0.441)	6.5 (6.2, 6.9)	6.0, 7.3						
1h																
Absolute value	18	5.78 (0.660)	5.7 (5.2, 6.5)	4.8, 7.0			16	5.79 (0.614)	5.8 (5.4, 6.1)	5.0, 7.3						
Change from baseline	18	-0.64 (0.497)	-0.5 (-1.0, -0.4)	-1.7, 0.1	-0.68 (0.118)	(-0.92, -0.44)	16	-0.76 (0.527)	-0.8 (-1.3, -0.2)	-1.6, 0.0	-0.75 (0.124)	(-1.01, -0.50)	-0.07 (-0.42, 0.28)	0.6707	-0.22 (-0.89, 0.46)	
Percent change from baseline	18	-9.85 (7.434)	-8.3 (-15.4, -6.9)	-25.0, 2.0			16	-11.48 (7.943)	-11.3 (-19.0, -3.2)	-24.2, 0.0						
2h																
Absolute value	18	6.15 (0.603)	6.1 (5.7, 6.5)	5.1, 7.2			16	5.92 (0.617)	6.0 (5.4, 6.3)	5.1, 7.3						
Change from baseline	18	-0.28 (0.346)	-0.3 (-0.4, -0.1)	-0.9, 0.4	-0.31 (0.111)	(-0.54, -0.09)	16	-0.63 (0.602)	-0.6 (-1.1, -0.2)	-1.5, 0.6	-0.62 (0.116)	(-0.86, -0.38)	-0.31 (-0.64, 0.02)	0.0635	-0.72 (-1.41, -0.02)	
Percent change from baseline	18	-4.17 (5.259)	-3.8 (-6.3, -1.7)	-12.9, 6.6			16	-9.39 (9.098)	-9.3 (-16.9, -4.0)	-22.7, 10.0						
4h																
Absolute value	18	6.31 (0.574)	6.3 (5.9, 6.7)	5.1, 7.3			16	6.24 (0.545)	6.2 (5.8, 6.5)	5.6, 7.4						
Change from baseline	18	-0.12 (0.586)	0.0 (-0.4, 0.2)	-1.5, 1.1	-0.15 (0.122)	(-0.40, 0.10)	16	-0.31 (0.570)	-0.4 (-0.6, -0.1)	-1.1, 1.1	-0.30 (0.129)	(-0.56, -0.04)	-0.15 (-0.51, 0.21)	0.4013	-0.33 (-1.01, 0.35)	
Percent change from baseline	18	-1.35 (9.087)	0.0 (-6.3, 3.3)	-20.6, 20.4			16	-4.46 (8.758)	-6.6 (-9.2, -1.5)	-16.4, 17.5						
6h																
Absolute value	11	6.62 (0.588)	6.7 (6.1, 7.3)	5.6, 7.3			12	6.11 (0.538)	5.9 (5.8, 6.3)	5.6, 7.3						
Change from baseline	11	0.05 (0.470)	0.0 (0.0, 0.2)	-0.7, 1.1	0.06 (0.155)	(-0.26, 0.38)	12	-0.38 (0.693)	-0.3 (-0.7, -0.1)	-1.6, 1.0	-0.54 (0.148)	(-0.85, -0.24)	-0.61 (-1.05, -0.16)	0.0094	-0.72 (-1.56, 0.13)	
Percent change from baseline	11	1.00 (7.898)	0.0 (0.0, 2.8)	-9.7, 20.4			12	-5.48 (10.381)	-5.6 (-10.5, -1.6)	-21.9, 16.7						
8h																
Absolute value	8	6.75 (0.602)	6.9 (6.2, 7.3)	5.9, 7.3			12	5.87 (0.660)	5.7 (5.5, 6.0)	5.1, 7.3						
Change from baseline	8	0.01 (0.452)	0.2 (-0.2, 0.3)	-0.9, 0.6	0.12 (0.212)	(-0.32, 0.56)	12	-0.63 (0.751)	-0.8 (-1.2, -0.1)	-1.7, 1.0	-0.80 (0.186)	(-1.19, -0.41)	-0.92 (-1.51, -0.34)	0.0036	-0.98 (-1.92, -0.03)	
Percent change from baseline	8	0.30 (6.450)	2.1 (-3.1, 3.9)	-12.3, 9.0			12	-9.27 (11.407)	-12.0 (-17.0, -2.5)	-25.0, 16.7						
10h																
Absolute value	8	6.70 (0.648)	6.8 (6.4, 7.3)	5.5, 7.3			10	6.06 (0.585)	6.0 (5.6, 6.4)	5.4, 7.3						
Change from baseline	8	-0.04 (0.463)	0.2 (-0.4, 0.3)	-0.8, 0.4	0.10 (0.174)	(-0.27, 0.46)	10	-0.42 (0.541)	-0.4 (-0.8, 0.0)	-1.3, 0.4	-0.62 (0.154)	(-0.94, -0.29)	-0.71 (-1.20, -0.22)	0.0070	-0.75 (-1.71, 0.21)	
Percent change from baseline	8	-0.49 (6.933)	2.8 (-7.1, 4.4)	-11.0, 6.9			10	-6.28 (8.108)	-6.5 (-12.9, 0.0)	-17.8, 6.7						
12h																
Absolute value	9	6.84 (0.609)	7.0 (6.8, 7.3)	5.5, 7.3			10	5.90 (0.607)	5.8 (5.5, 6.2)	5.2, 7.3						
Change from baseline	9	0.26 (0.720)	0.2 (0.0, 0.3)	-0.6, 1.9	0.21 (0.206)	(-0.22, 0.64)	10	-0.60 (0.696)	-0.5 (-0.9, 0.0)	-2.0, 0.2	-0.87 (0.188)	(-1.26, -0.47)	-1.08 (-1.66, -0.49)	0.0011	-1.21 (-2.19, -0.23)	
Percent change from baseline	9	4.61 (12.841)	2.8 (0.0, 4.5)	-9.8, 35.2			10	-8.88 (9.972)	-8.9 (-14.1, 0.0)	-27.4, 3.3						
24h																
Absolute value	5	6.30 (0.200)	6.4 (6.2, 6.4)	6.0, 6.5			9	5.49 (0.855)	5.3 (5.2, 6.2)	4.0, 6.7						
Change from baseline	5	-0.76 (0.182)	-0.7 (-0.9, -0.6)	-1.0, -0.6	-0.68 (0.286)	(-1.31, -0.04)	9	-0.99 (0.796)	-0.8 (-1.4, -0.6)	-2.2, 0.1	-1.12 (0.240)	(-1.65, -0.59)	-0.44 (-1.27, 0.38)	0.2612	-0.35 (-1.45, 0.75)	
Percent change from baseline	5	-10.75 (2.492)	-9.9 (-12.3, -8.8)	-14.3, -8.5			9	-15.20 (12.144)	-13.1 (-21.3, -8.2)	-35.5, 1.6						
EOT																
Absolute value	14	6.07 (0.423)	6.1 (5.8, 6.4)	5.1, 6.7			14	5.57 (0.756)	5.5 (5.2, 6.2)	4.0, 6.7						
Change from baseline	14	-0.32 (0.609)	-0.5 (-0.7, 0.0)	-1.0, 1.3			14	-0.91 (0.733)	-0.8 (-1.4, -0.5)	-2.2, 0.1						
Percent change from baseline	14	-4.28 (9.992)	-7.4 (-9.9, 0.0)	-14.3, 24.1			14	-13.90 (11.079)	-12.1 (-21.3, -8.2)	-35.5, 1.6						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Lokelma

Table 7.1.1.1 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)

	Placebo (N=37)						Lokelma 10g QD (N=33)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Age																0.6598
<65 years																
Baseline																
Absolute value	28	6.50 (0.731)	6.5 (6.1, 6.8)	5.0, 8.9			16	6.42 (0.613)	6.6 (6.2, 6.8)	5.0, 7.3						
1h																
Absolute value	28	5.80 (0.690)	5.7 (5.3, 6.2)	4.8, 7.3			16	5.79 (0.752)	5.7 (5.2, 6.4)	4.6, 7.3						
Change from baseline	28	-0.70 (0.918)	-0.5 (-1.0, 0.0)	-4.0, 0.5			16	-0.63 (0.609)	-0.7 (-1.2, -0.0)	-1.6, 0.5						
Percent change from baseline	28	-9.96 (11.626)	-8.3 (-15.3, 0.0)	-44.9, 7.5			16	-9.69 (9.150)	-11.4 (-17.4, -0.8)	-24.2, 7.4						
2h																
Absolute value	28	6.18 (0.849)	6.0 (5.7, 6.5)	4.2, 8.8			16	5.61 (0.687)	5.2 (5.1, 6.1)	4.9, 6.9						
Change from baseline	28	-0.33 (0.704)	-0.3 (-0.6, -0.0)	-3.1, 0.7			16	-0.81 (0.722)	-0.9 (-1.4, -0.0)	-2.3, 0.1						
Percent change from baseline	28	-4.69 (10.000)	-3.8 (-9.5, -0.6)	-42.5, 10.6			16	-12.24 (10.559)	-14.0 (-20.4, -0.9)	-31.9, 2.0						
4h																
Absolute value	28	6.25 (0.803)	6.3 (5.7, 6.6)	4.9, 8.9			16	6.04 (0.609)	6.1 (5.7, 6.4)	4.9, 7.4						
Change from baseline	28	-0.25 (0.641)	-0.0 (-0.5, 0.2)	-2.4, 1.1			16	-0.38 (0.663)	-0.3 (-0.8, 0.0)	-1.6, 1.1						
Percent change from baseline	28	-3.45 (9.611)	-0.7 (-8.3, 2.4)	-32.9, 20.4			16	-5.45 (10.141)	-5.5 (-10.6, 0.0)	-24.6, 17.5						
6h																
Absolute value	16	6.42 (0.698)	6.7 (5.8, 6.8)	4.8, 7.3			12	5.72 (0.581)	5.9 (5.3, 6.0)	4.9, 6.8						
Change from baseline	16	-0.24 (1.138)	0.0 (-0.3, 0.2)	-4.1, 1.1			12	-0.62 (0.773)	-0.4 (-1.4, -0.1)	-1.6, 0.6						
Percent change from baseline	16	-2.38 (14.109)	0.0 (-3.8, 2.9)	-46.1, 20.4			12	-8.97 (11.728)	-6.9 (-19.1, -2.6)	-24.6, 11.3						
8h																
Absolute value	13	6.58 (0.686)	6.6 (6.0, 7.2)	5.6, 7.6			11	5.85 (0.380)	5.8 (5.6, 6.1)	5.3, 6.5						
Change from baseline	13	-0.22 (0.607)	-0.2 (-0.7, 0.2)	-1.3, 0.6			11	-0.46 (0.839)	-0.3 (-1.2, 0.2)	-1.7, 1.1						
Percent change from baseline	13	-2.74 (8.284)	-2.9 (-9.6, 3.5)	-14.9, 9.1			11	-6.10 (13.415)	-4.9 (-17.4, 3.2)	-23.6, 22.0						
10h																
Absolute value	13	6.70 (0.608)	6.8 (6.3, 7.3)	5.5, 7.6			10	5.82 (0.696)	6.0 (5.6, 6.3)	4.1, 6.6						
Change from baseline	13	-0.09 (0.680)	0.2 (-0.5, 0.4)	-1.3, 0.8			10	-0.50 (0.854)	-0.4 (-1.3, 0.1)	-1.9, 1.0						
Percent change from baseline	13	-0.70 (9.577)	2.8 (-6.9, 6.8)	-16.4, 13.1			10	-6.98 (14.174)	-6.9 (-17.8, 1.6)	-31.7, 20.0						
12h																
Absolute value	14	6.54 (0.696)	6.7 (6.0, 7.1)	5.5, 7.3			9	5.80 (0.620)	5.9 (5.4, 6.2)	4.6, 6.6						
Change from baseline	14	-0.16 (1.224)	0.2 (-0.6, 0.5)	-3.4, 1.9			9	-0.42 (0.939)	-0.6 (-0.7, -0.2)	-2.0, 1.6						
Percent change from baseline	14	-0.72 (16.927)	3.1 (-9.8, 7.6)	-38.2, 35.2			9	-5.60 (16.005)	-9.5 (-10.1, -3.3)	-27.4, 32.0						
24h																
Absolute value	8	5.87 (1.051)	6.1 (5.7, 6.3)	3.6, 7.3			6	5.55 (0.602)	5.5 (5.1, 6.2)	4.8, 6.3						
Change from baseline	8	-1.16 (1.786)	-0.7 (-1.3, -0.5)	-5.3, 0.7			6	-0.75 (0.745)	-0.5 (-1.3, -0.2)	-2.0, -0.1						
Percent change from baseline	8	-14.56 (20.248)	-9.4 (-17.4, -7.0)	-59.6, 10.6			6	-11.35 (10.463)	-7.0 (-21.3, -3.8)	-27.4, -1.6						
EOT																
Absolute value	24	5.93 (0.734)	6.0 (5.6, 6.4)	3.6, 7.3			11	5.68 (0.546)	5.6 (5.3, 6.2)	4.8, 6.7						
Change from baseline	24	-0.57 (1.259)	-0.5 (-0.8, 0.0)	-5.3, 1.3			11	-0.70 (0.597)	-0.7 (-1.0, -0.2)	-2.0, 0.1						
Percent change from baseline	24	-7.25 (15.961)	-7.5 (-11.9, 1.0)	-59.6, 24.1			11	-10.69 (8.529)	-11.1 (-14.9, -3.8)	-27.4, 1.5						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Lokelma

Table 7.1.1.1 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)

	Placebo (N=37)						Lokelma 10g QD (N=33)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Age *(contd.)*																
>= 65 years																
Baseline																
Absolute value	8	6.41 (0.890)	6.7 (6.0, 7.1)	4.6, 7.3			16	6.34 (0.657)	6.4 (6.0, 6.9)	4.9, 7.3						
1h																
Absolute value	8	6.09 (1.026)	6.2 (5.3, 6.9)	4.6, 7.5			16	5.80 (0.600)	5.8 (5.5, 6.1)	4.9, 7.3						
Change from baseline	8	-0.33 (0.501)	-0.5 (-0.6, 0.0)	-1.0, 0.6			16	-0.54 (0.537)	-0.5 (-1.0, -0.1)	-1.5, 0.2						
Percent change from baseline	8	-5.11 (7.722)	-6.9 (-9.8, 0.0)	-16.1, 8.7			16	-8.18 (8.072)	-6.6 (-15.0, -1.7)	-21.4, 3.9						
2h																
Absolute value	8	5.99 (0.872)	6.1 (5.3, 6.8)	4.6, 7.0			16	5.94 (0.670)	5.9 (5.5, 6.4)	4.9, 7.3						
Change from baseline	8	-0.43 (0.349)	-0.5 (-0.7, -0.1)	-0.9, 0.0			16	-0.40 (0.501)	-0.3 (-0.7, -0.1)	-1.5, 0.6						
Percent change from baseline	8	-6.52 (5.354)	-6.9 (-11.3, -1.4)	-12.9, 0.0			16	-6.08 (7.536)	-5.9 (-10.3, -1.4)	-21.4, 10.0						
4h																
Absolute value	8	6.14 (0.881)	6.3 (5.6, 6.9)	4.6, 7.1			16	6.01 (0.620)	6.0 (5.7, 6.5)	4.9, 7.3						
Change from baseline	8	-0.28 (0.611)	-0.2 (-0.5, 0.1)	-1.5, 0.5			16	-0.33 (0.488)	-0.3 (-0.6, 0.0)	-1.5, 0.7						
Percent change from baseline	8	-3.94 (8.774)	-2.8 (-8.1, 1.5)	-20.6, 8.1			16	-4.92 (7.315)	-5.8 (-8.6, 0.0)	-21.4, 11.7						
6h																
Absolute value	5	6.24 (0.709)	6.0 (5.7, 6.6)	5.6, 7.3			11	6.09 (0.708)	5.8 (5.7, 6.7)	4.9, 7.3						
Change from baseline	5	-0.54 (0.428)	-0.7 (-0.7, -0.6)	-0.9, 0.2			11	-0.35 (0.625)	-0.5 (-0.8, 0.0)	-1.1, 1.0						
Percent change from baseline	5	-8.09 (6.254)	-9.7 (-10.9, -9.6)	-13.0, 2.8			11	-5.41 (10.123)	-8.1 (-12.1, 0.0)	-18.3, 16.7						
8h																
Absolute value	4	6.35 (0.686)	6.2 (5.9, 6.9)	5.8, 7.3			11	5.95 (0.688)	5.7 (5.5, 6.4)	5.1, 7.3						
Change from baseline	4	-0.58 (0.544)	-0.8 (-1.0, -0.2)	-1.0, 0.2			11	-0.49 (0.774)	-0.4 (-1.1, 0.0)	-1.7, 1.0						
Percent change from baseline	4	-8.35 (7.732)	-10.9 (-13.4, -3.3)	-14.5, 2.8			11	-7.28 (11.843)	-6.6 (-16.7, 0.0)	-25.0, 16.7						
10h																
Absolute value	5	6.18 (0.804)	6.3 (5.4, 6.5)	5.4, 7.3			11	5.94 (0.655)	5.7 (5.4, 6.4)	5.2, 7.3						
Change from baseline	5	-0.52 (0.460)	-0.6 (-0.8, -0.4)	-1.0, 0.2			11	-0.36 (0.508)	-0.4 (-0.8, 0.2)	-1.1, 0.4						
Percent change from baseline	5	-7.87 (6.813)	-8.7 (-11.0, -6.9)	-15.6, 2.8			11	-5.60 (8.156)	-6.6 (-13.3, 3.3)	-16.7, 6.7						
12h																
Absolute value	4	6.58 (0.763)	6.8 (6.1, 7.1)	5.5, 7.3			11	5.82 (0.823)	5.9 (5.2, 6.2)	4.3, 7.3						
Change from baseline	4	-0.35 (0.465)	-0.4 (-0.7, 0.0)	-0.9, 0.2			11	-0.50 (0.859)	-0.2 (-1.4, 0.1)	-2.1, 0.8						
Percent change from baseline	4	-5.25 (7.090)	-4.9 (-10.5, -0.0)	-14.1, 2.8			11	-7.45 (13.805)	-2.9 (-21.2, 1.7)	-32.8, 15.4						
24h																
Absolute value	4	6.08 (0.499)	6.2 (5.7, 6.5)	5.4, 6.5			10	5.35 (0.788)	5.3 (5.2, 5.4)	4.0, 6.7						
Change from baseline	4	-0.85 (0.173)	-0.9 (-1.0, -0.7)	-1.0, -0.6			10	-1.10 (0.706)	-1.0 (-1.8, -0.6)	-2.2, 0.1						
Percent change from baseline	4	-12.36 (2.969)	-12.7 (-14.3, -10.4)	-15.6, -8.5			10	-17.04 (10.930)	-15.8 (-25.7, -10.0)	-35.5, 1.6						
EOT																
Absolute value	6	6.02 (0.402)	6.0 (5.8, 6.4)	5.4, 6.5			13	5.32 (0.691)	5.3 (5.1, 5.4)	4.0, 6.7						
Change from baseline	6	-0.60 (0.415)	-0.7 (-0.9, -0.2)	-1.0, 0.0			13	-1.02 (0.714)	-0.8 (-1.7, -0.6)	-2.2, 0.1						
Percent change from baseline	6	-8.78 (6.094)	-10.4 (-13.0, -3.2)	-15.6, 0.0			13	-15.82 (10.892)	-13.1 (-25.0, -8.3)	-35.5, 1.6						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

Lokelma

Table 7.1.1.1 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)

	Placebo (N=37)						Lokelma 10g QD (N=33)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Region																0.5806
USA																
Baseline																
Absolute value	19	6.17 (0.650)	6.1 (5.9, 6.5)	4.6, 7.3			18	6.38 (0.684)	6.6 (6.3, 6.8)	4.9, 7.2						
1h																
Absolute value	19	5.56 (0.514)	5.5 (5.2, 5.8)	4.6, 6.7			18	5.58 (0.537)	5.5 (5.2, 5.8)	4.9, 6.8						
Change from baseline	19	-0.62 (0.600)	-0.5 (-1.0, 0.0)	-2.5, 0.1			18	-0.80 (0.602)	-1.0 (-1.3, 0.0)	-1.6, 0.2						
Percent change from baseline	19	-9.42 (8.538)	-8.6 (-15.3, 0.0)	-34.3, 2.0			18	-11.95 (9.038)	-14.8 (-19.1, 0.0)	-24.2, 3.9						
2h																
Absolute value	19	5.72 (0.632)	5.8 (5.4, 6.2)	4.2, 6.7			18	5.60 (0.642)	5.4 (5.1, 6.2)	4.9, 6.8						
Change from baseline	19	-0.45 (0.773)	-0.3 (-0.7, 0.0)	-3.1, 0.5			18	-0.78 (0.693)	-0.8 (-1.4, 0.0)	-2.3, 0.1						
Percent change from baseline	19	-6.67 (10.942)	-4.6 (-10.9, 0.0)	-42.5, 8.3			18	-11.72 (10.088)	-11.4 (-21.4, 0.0)	-31.9, 2.0						
4h																
Absolute value	19	5.92 (0.632)	6.0 (5.5, 6.5)	4.6, 6.7			18	5.93 (0.670)	5.9 (5.5, 6.3)	4.9, 7.4						
Change from baseline	19	-0.25 (0.650)	0.0 (-0.4, 0.2)	-2.4, 0.5			18	-0.45 (0.678)	-0.4 (-0.9, 0.0)	-1.6, 1.1						
Percent change from baseline	19	-3.62 (9.342)	0.0 (-6.9, 3.3)	-32.9, 8.1			18	-6.52 (10.297)	-6.9 (-12.7, 0.0)	-24.6, 17.5						
6h																
Absolute value	5	6.08 (0.597)	5.8 (5.8, 6.1)	5.6, 7.1			9	5.72 (0.591)	5.7 (5.6, 5.9)	4.9, 6.8						
Change from baseline	5	-0.22 (0.249)	-0.2 (-0.3, 0.0)	-0.6, 0.0			9	-0.68 (0.670)	-0.6 (-1.3, -0.4)	-1.6, 0.5						
Percent change from baseline	5	-3.47 (4.040)	-2.7 (-4.9, 0.0)	-9.7, 0.0			9	-10.13 (9.913)	-8.8 (-18.8, -6.4)	-24.6, 7.9						
8h																
Absolute value	3	6.10 (0.265)	6.0 (5.9, 6.4)	5.9, 6.4			8	5.79 (0.497)	5.7 (5.5, 6.3)	5.1, 6.5						
Change from baseline	3	-0.30 (0.557)	-0.2 (-0.9, 0.2)	-0.9, 0.2			8	-0.60 (0.980)	-0.8 (-1.5, 0.1)	-1.7, 1.1						
Percent change from baseline	3	-4.05 (7.918)	-3.3 (-12.3, 3.5)	-12.3, 3.5			8	-8.11 (15.781)	-12.0 (-20.5, 1.6)	-25.0, 22.0						
10h																
Absolute value	4	5.80 (0.408)	5.8 (5.5, 6.2)	5.4, 6.2			7	5.87 (0.486)	5.8 (5.4, 6.4)	5.4, 6.6						
Change from baseline	4	-0.45 (0.661)	-0.5 (-0.9, 0.0)	-1.2, 0.4			7	-0.30 (0.808)	-0.3 (-0.9, 0.2)	-1.4, 1.0						
Percent change from baseline	4	-6.57 (9.826)	-8.4 (-13.1, 0.0)	-16.4, 6.9			7	-3.62 (13.458)	-4.4 (-14.1, 3.9)	-19.4, 20.0						
12h																
Absolute value	3	5.93 (0.404)	6.0 (5.5, 6.3)	5.5, 6.3			6	5.82 (0.828)	6.1 (5.5, 6.3)	4.3, 6.6						
Change from baseline	3	-0.47 (0.907)	-0.6 (-1.3, 0.5)	-1.3, 0.5			6	-0.22 (1.314)	-0.4 (-0.9, 0.8)	-2.1, 1.6						
Percent change from baseline	3	-6.34 (13.558)	-9.8 (-17.8, 8.6)	-17.8, 8.6			6	-1.61 (22.900)	-5.1 (-14.1, 15.4)	-32.8, 32.0						
24h																
Absolute value	1	5.80 (NC)	5.8 (5.8, 5.8)	5.8, 5.8			3	5.03 (1.305)	4.6 (4.0, 6.5)	4.0, 6.5						
Change from baseline	1	-1.50 (NC)	-1.5 (-1.5, -1.5)	-1.5, -1.5			3	-1.30 (1.229)	-1.8 (-2.2, 0.1)	-2.2, 0.1						
Percent change from baseline	1	-20.55 (NC)	-20.6 (-20.6, -20.6)	-20.6, -20.6			3	-20.68 (19.611)	-28.1 (-35.5, 1.6)	-35.5, 1.6						
EOT																
Absolute value	15	5.87 (0.486)	5.8 (5.6, 6.4)	5.0, 6.7			10	5.45 (0.807)	5.6 (5.1, 5.7)	4.0, 6.7						
Change from baseline	15	-0.37 (0.779)	-0.2 (-0.9, 0.1)	-2.3, 0.6			10	-0.89 (0.808)	-0.8 (-1.7, -0.1)	-2.2, 0.1						
Percent change from baseline	15	-5.13 (11.164)	-3.2 (-13.9, 2.0)	-31.5, 9.8			10	-13.84 (12.598)	-12.5 (-25.0, -1.9)	-35.5, 1.6						

CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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26/02/2021

Lokelma

Table 7.1.1.1 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)

	Placebo (N=37)						Lokelma 10g QD (N=33)									
Subgroup / Category / Timepoint / Statistic	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	n	Mean (SD)	Median (Q1, Q3)	Min, Max	Adjusted mean (SE)	95% CI of adj. mean	Diff. vs Placebo (95% CI)	Diff. p-value	Effect size (Hedge's g) (95% CI)	Interaction p-value
Region *(contd.)*																
Rest of world																
Baseline																
Absolute value	17	6.82 (0.735)	6.8 (6.6, 7.1)	5.4, 8.9			14	6.38 (0.570)	6.2 (6.0, 6.8)	5.3, 7.3						
1h																
Absolute value	17	6.21 (0.872)	6.5 (5.7, 6.8)	4.8, 7.5			14	6.06 (0.742)	6.0 (5.9, 6.6)	4.6, 7.3						
Change from baseline	17	-0.61 (1.086)	-0.5 (-0.7, 0.0)	-4.0, 0.6	-0.56 (0.193)	(-0.96, -0.17)	14	-0.31 (0.384)	-0.3 (-0.5, -0.1)	-1.1, 0.5	-0.38 (0.213)	(-0.81, 0.06)	0.19 (-0.41, 0.78)	0.5228	0.35 (-0.36, 1.06)	
Percent change from baseline	17	-8.28 (13.438)	-6.9 (-11.1, 0.0)	-44.9, 8.7			14	-5.07 (6.137)	-4.1 (-7.7, -1.7)	-18.0, 7.4						
2h																
Absolute value	17	6.59 (0.828)	6.5 (5.9, 7.0)	5.3, 8.8			14	6.00 (0.706)	5.9 (5.6, 6.6)	4.9, 7.3						
Change from baseline	17	-0.23 (0.440)	-0.3 (-0.5, -0.1)	-0.9, 0.7	-0.18 (0.121)	(-0.43, 0.07)	14	-0.38 (0.518)	-0.3 (-0.6, -0.1)	-1.4, 0.6	-0.44 (0.134)	(-0.72, -0.17)	-0.26 (-0.64, 0.12)	0.1704	-0.31 (-1.02, 0.40)	
Percent change from baseline	17	-3.34 (6.456)	-4.3 (-8.2, -1.1)	-12.3, 10.6			14	-5.87 (7.985)	-4.9 (-9.2, -1.9)	-19.2, 10.0						
4h																
Absolute value	17	6.57 (0.864)	6.5 (6.0, 7.1)	5.4, 8.9			14	6.14 (0.506)	6.1 (5.7, 6.5)	5.4, 7.3						
Change from baseline	17	-0.25 (0.618)	-0.1 (-0.6, 0.0)	-1.5, 1.1	-0.20 (0.126)	(-0.46, 0.05)	14	-0.24 (0.391)	-0.3 (-0.5, 0.0)	-0.9, 0.7	-0.30 (0.140)	(-0.58, -0.01)	-0.09 (-0.48, 0.30)	0.6312	0.03 (-0.67, 0.74)	
Percent change from baseline	17	-3.50 (9.565)	-1.6 (-9.0, 0.0)	-20.6, 20.4			14	-3.47 (6.022)	-5.0 (-7.1, 0.0)	-12.3, 11.7						
6h																
Absolute value	16	6.47 (0.704)	6.7 (5.9, 6.8)	4.8, 7.3			14	6.01 (0.696)	5.9 (5.7, 6.4)	4.9, 7.3						
Change from baseline	16	-0.34 (1.160)	0.0 (-0.7, 0.2)	-4.1, 1.1	-0.27 (0.220)	(-0.73, 0.18)	14	-0.37 (0.722)	-0.3 (-1.0, 0.0)	-1.6, 1.0	-0.43 (0.236)	(-0.92, 0.05)	-0.16 (-0.83, 0.51)	0.6240	-0.03 (-0.75, 0.69)	
Percent change from baseline	16	-3.82 (14.607)	0.0 (-10.3, 2.9)	-46.1, 20.4			14	-5.43 (11.448)	-4.8 (-15.4, 0.0)	-21.9, 16.7						
8h																
Absolute value	14	6.61 (0.703)	6.6 (5.9, 7.3)	5.6, 7.6			14	5.97 (0.577)	5.8 (5.7, 6.1)	5.3, 7.3						
Change from baseline	14	-0.30 (0.625)	-0.3 (-0.9, 0.2)	-1.3, 0.6	-0.09 (0.168)	(-0.43, 0.26)	14	-0.41 (0.687)	-0.3 (-1.0, 0.0)	-1.4, 1.0	-0.47 (0.174)	(-0.83, -0.11)	-0.38 (-0.89, 0.12)	0.1306	-0.16 (-0.91, 0.58)	
Percent change from baseline	14	-4.06 (8.655)	-4.0 (-12.3, 2.8)	-14.9, 9.1			14	-5.88 (10.530)	-4.7 (-15.9, 0.0)	-19.2, 16.7						
10h																
Absolute value	14	6.77 (0.593)	6.9 (6.3, 7.3)	5.4, 7.6			14	5.89 (0.749)	6.0 (5.5, 6.3)	4.1, 7.3						
Change from baseline	14	-0.14 (0.648)	-0.0 (-0.6, 0.3)	-1.3, 0.8	0.03 (0.154)	(-0.28, 0.35)	14	-0.49 (0.629)	-0.4 (-0.8, 0.0)	-1.9, 0.4	-0.55 (0.163)	(-0.89, -0.22)	-0.59 (-1.06, -0.12)	0.0156	-0.55 (-1.30, 0.21)	
Percent change from baseline	14	-1.59 (9.220)	-0.8 (-8.7, 4.5)	-15.6, 13.1			14	-7.58 (10.088)	-7.0 (-13.3, 0.0)	-31.7, 6.7						
12h																
Absolute value	15	6.67 (0.675)	6.8 (6.3, 7.3)	5.5, 7.3			14	5.81 (0.703)	5.8 (5.3, 6.2)	4.6, 7.3						
Change from baseline	15	-0.15 (1.144)	0.2 (-0.5, 0.3)	-3.4, 1.9	-0.06 (0.209)	(-0.49, 0.37)	14	-0.57 (0.639)	-0.5 (-0.7, -0.1)	-2.0, 0.2	-0.63 (0.222)	(-1.09, -0.17)	-0.58 (-1.21, 0.06)	0.0726	-0.45 (-1.19, 0.28)	
Percent change from baseline	15	-0.80 (15.801)	2.8 (-6.9, 4.5)	-38.2, 35.2			14	-8.77 (9.343)	-8.5 (-13.2, -1.7)	-27.4, 3.3						
24h																
Absolute value	11	5.95 (0.926)	6.1 (5.6, 6.4)	3.6, 7.3			13	5.52 (0.546)	5.3 (5.2, 5.6)	4.8, 6.7						
Change from baseline	11	-1.02 (1.499)	-0.7 (-1.0, -0.6)	-5.3, 0.7	-0.82 (0.243)	(-1.32, -0.32)	13	-0.89 (0.598)	-0.7 (-1.3, -0.5)	-2.0, -0.1	-0.86 (0.253)	(-1.38, -0.34)	-0.04 (-0.77, 0.69)	0.9110	0.11 (-0.69, 0.92)	
Percent change from baseline	11	-13.22 (16.911)	-9.9 (-14.3, -8.5)	-59.6, 10.6			13	-13.57 (8.426)	-11.7 (-21.2, -7.4)	-27.4, -1.6						
EOT																
Absolute value	15	6.03 (0.833)	6.2 (5.6, 6.5)	3.6, 7.3			14	5.51 (0.525)	5.3 (5.2, 5.6)	4.8, 6.7						
Change from baseline	15	-0.79 (1.401)	-0.6 (-0.9, -0.6)	-5.3, 1.3			14	-0.86 (0.584)	-0.7 (-1.3, -0.5)	-2.0, -0.1						
Percent change from baseline	15	-9.97 (17.188)	-9.6 (-13.0, -8.5)	-59.6, 24.1			14	-13.20 (8.215)	-10.8 (-21.2, -7.4)	-27.4, -1.6						

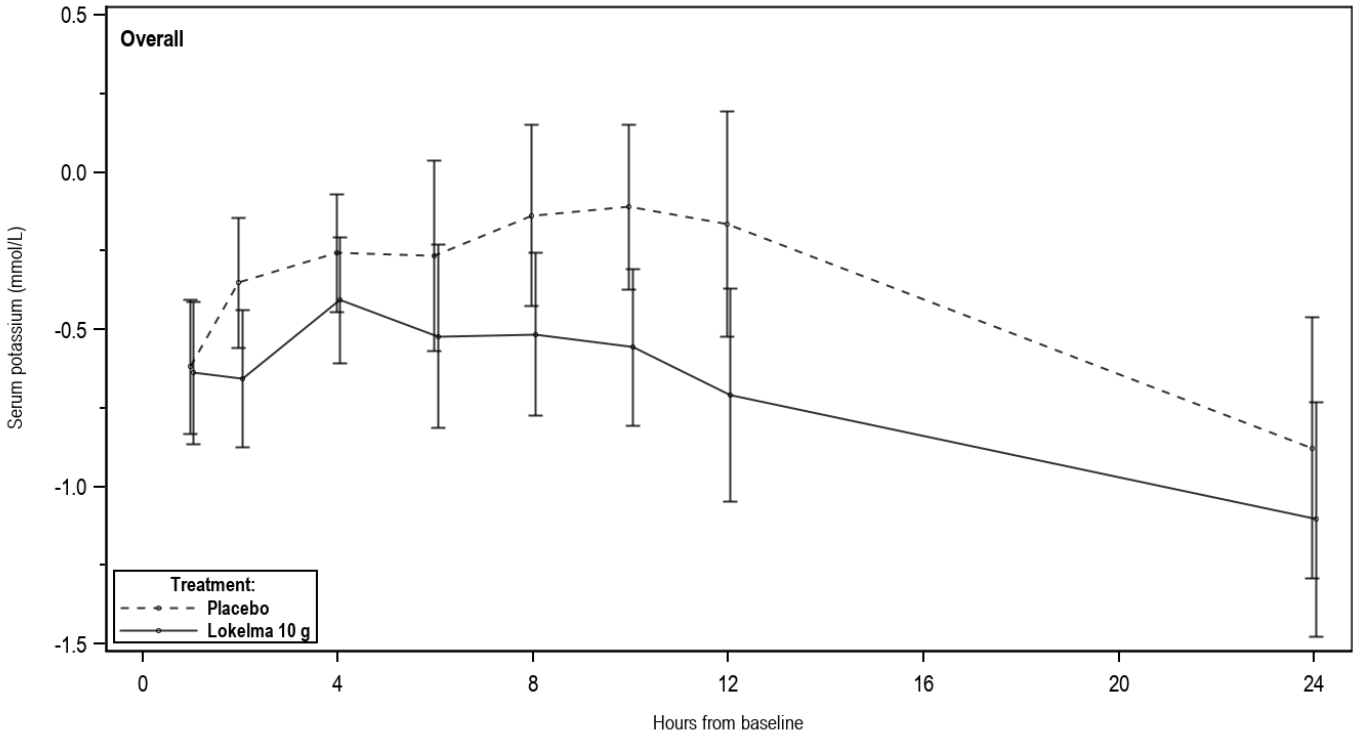
CI: Confidence Interval. Max: maximum. Min:minimum. N: number of subjects in treatment group. n: number of subjects included in analysis. Q1: First Quartile. Q3: Third Quartile. SD: Standard deviation. SE: Standard error.
Adjusted mean change from baseline estimated using a mixed methods repeated measures (MMRM) model including treatment, time, and treatment*time as covariates.
Modelled results for subgroup categories are omitted if there are fewer than 10 patients total, or if the model failed to converge.

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Figure 7.1.1.2 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)



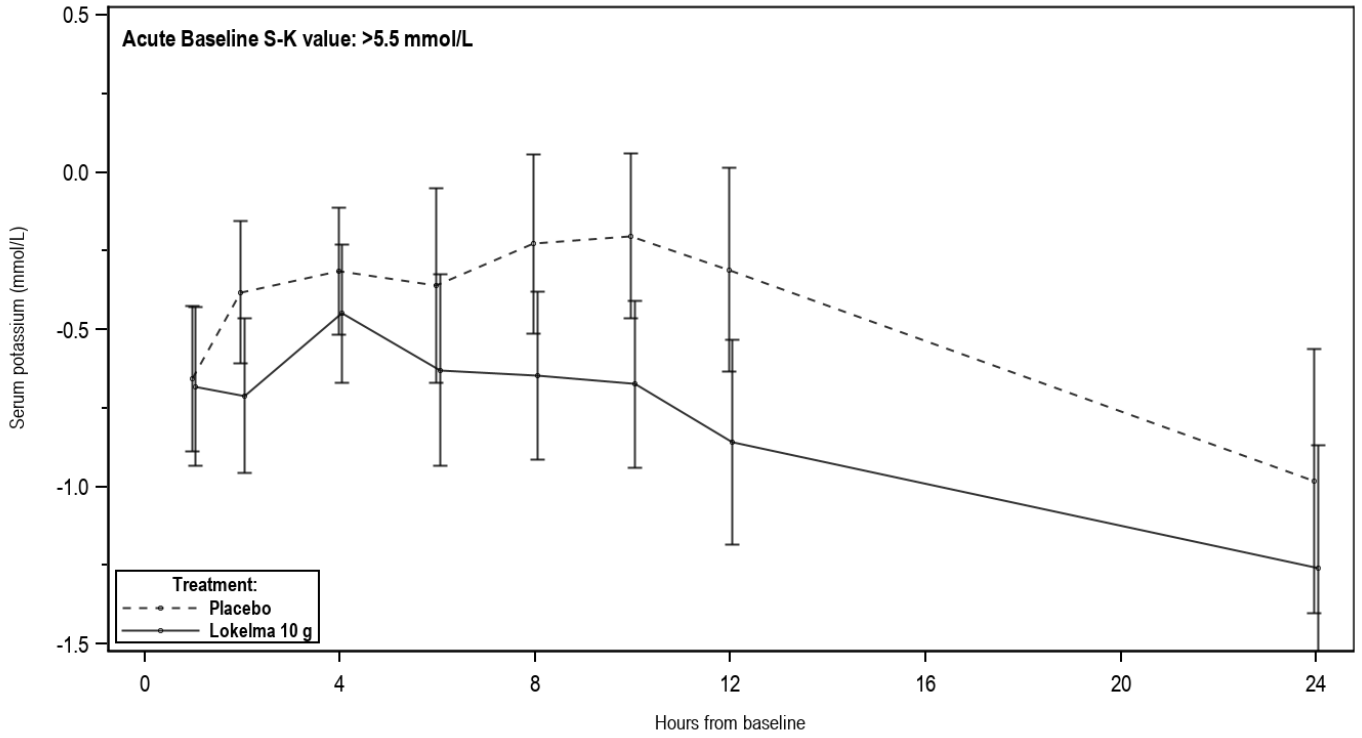
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Results are adjusted using an MMRM model including terms for treatment, time and treatment*time.
Categories where the model failed to converge have been omitted.

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Figure 7.1.1.2 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)



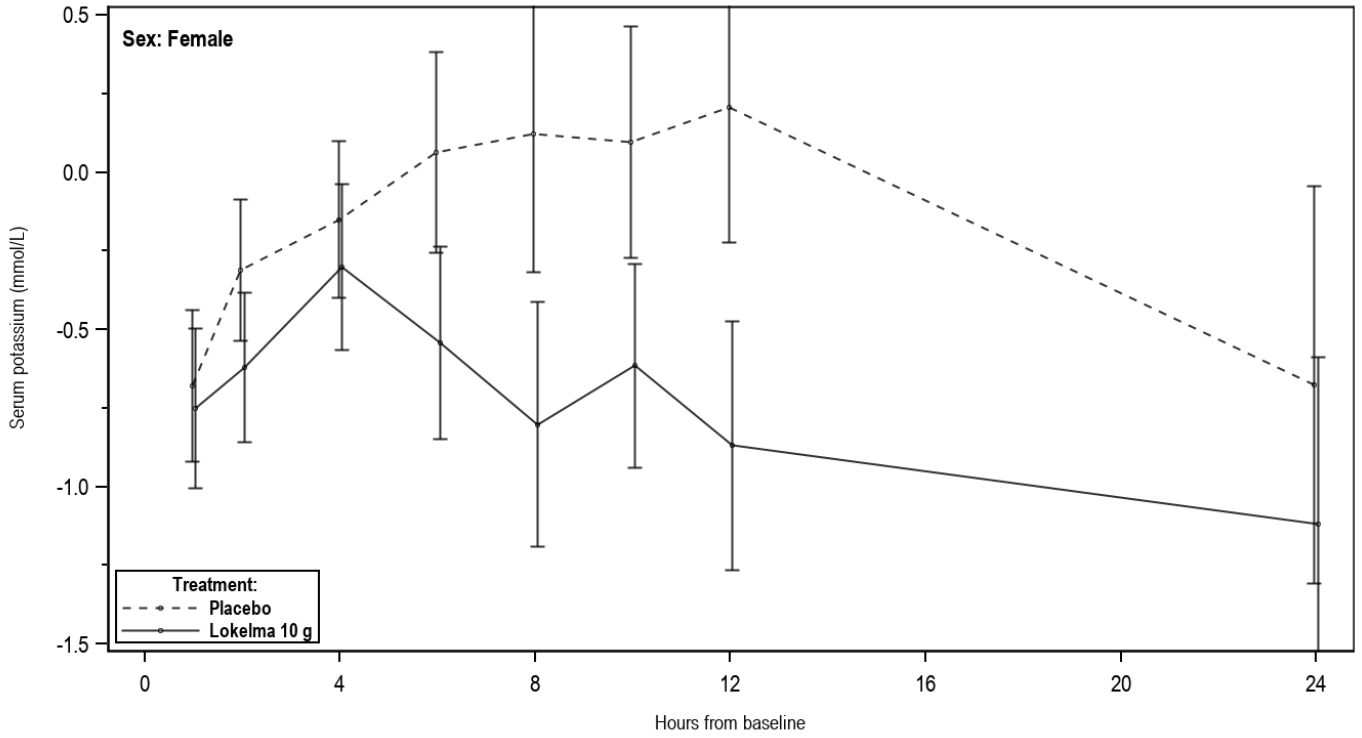
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Results are adjusted using an MMRM model including terms for treatment, time and treatment*time.
Categories where the model failed to converge have been omitted.

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Figure 7.1.1.2 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)



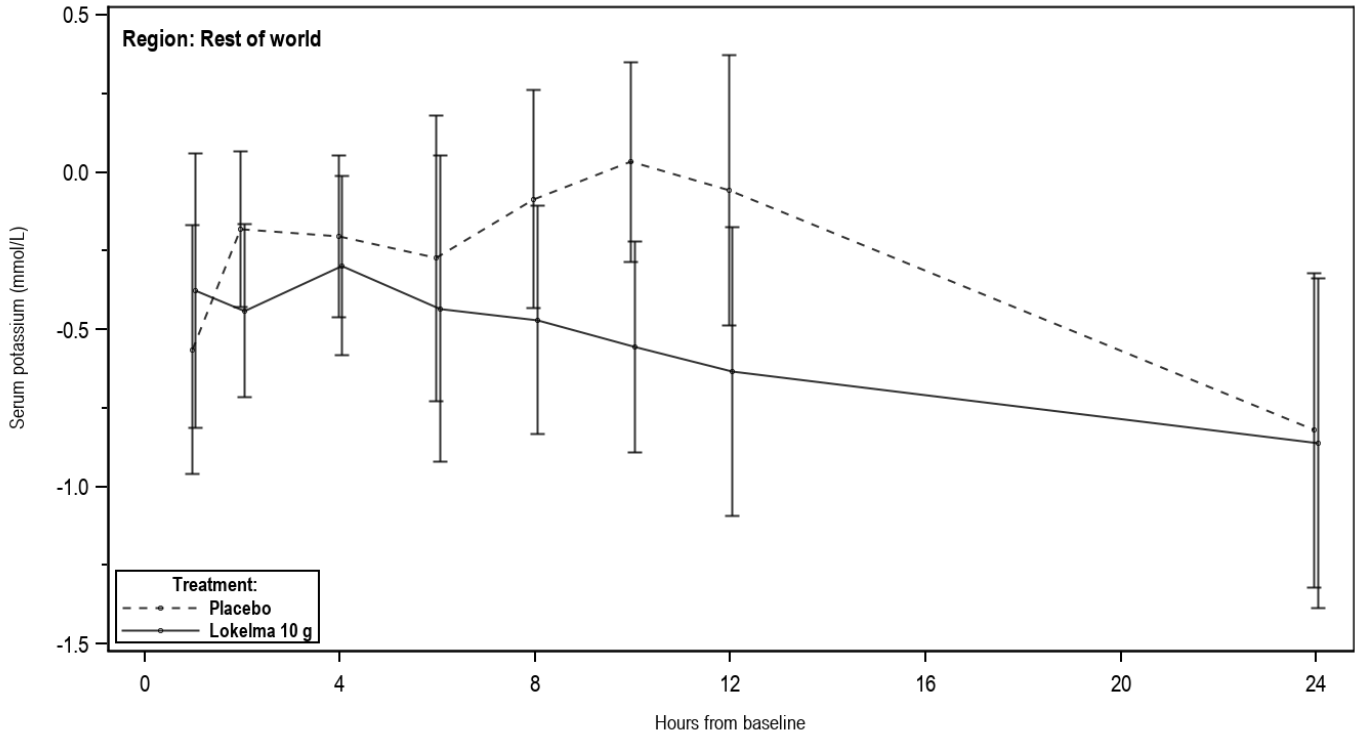
Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Results are adjusted using an MMRM model including terms for treatment, time and treatment*time.
Categories where the model failed to converge have been omitted.

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Figure 7.1.1.2 - Study ENERGIZE: Change from baseline in serum potassium by timepoint, SZC 10g TID vs. placebo, overall and by subgroups (full population)



Excludes timepoints where serum potassium was measured conditionally based on levels from a previous measurement.
Excludes subgroup categories with fewer than 10 subjects total across [both/all] treatment arms.
Results are adjusted using an MMRM model including terms for treatment, time and treatment*time.
Categories where the model failed to converge have been omitted.

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Table 7.1.2.1 - Study ENERGIZE: Proportion of responders (subjects who maintained serum potassium <6.0 mmol/L from 1h to 4h post-dose, had serum potassium <5.0 mmol/L at 4h post-dose, and had no additional hyperkalemia therapy administered from 0h to 4h post-dose apart from initial insulin treatment), SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Overall	36	2 (5.6%)	32	2 (6.3%)	8.78 (0.08, 979.29)	0.3665	7.50 (0.12, 457.35)	0.3365	NC	NC	
Baseline S-K											-
<=5.3 mmol/L	2	1 (50.0%)	4	1 (25.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	33	1 (3.0%)	28	1 (3.6%)	-	-	-	-	-	-	
Sex											-
Male	18	2 (11.1%)	16	2 (12.5%)	-	-	-	-	-	-	
Female	18	0 (0.0%)	16	0 (0.0%)	-	-	-	-	-	-	
Age (years)											-
<65 years	28	1 (3.6%)	16	1 (6.3%)	-	-	-	-	-	-	
>=65 years	8	1 (12.5%)	16	1 (6.3%)	-	-	-	-	-	-	
Region											-
USA	19	2 (10.5%)	18	2 (11.1%)	-	-	-	-	-	-	
Rest of world	17	0 (0.0%)	14	0 (0.0%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

t_energize_prop_response.pdf generated by energize_prop.sas at 15:34:18 on 19 January 2021

26/02/2021

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Table 7.1.3.1 - Study ENERGIZE: Proportion of subjects with serum potassium in normal range by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Overall											
1h	36	5 (13.9%)	32	5 (15.6%)	1.07 (0.23, 4.87)	0.9340	1.06 (0.26, 4.30)	0.9384	-4.6 (-37.4, 28.2)	0.7836	
2h	36	2 (5.6%)	32	4 (12.5%)	3.87 (0.33, 45.32)	0.2808	3.50 (0.32, 37.73)	0.3017	NC	NC	
4h	36	2 (5.6%)	32	2 (6.3%)	8.78 (0.08, 979.29)	0.3665	7.50 (0.12, 457.35)	0.3365	NC	NC	
6h	21	1 (4.8%)	23	4 (17.4%)	4.71 (0.43, 51.50)	0.2044	NC	NC	NC	NC	
8h	17	0 (0.0%)	22	0 (0.0%)	n/a	n/a	n/a	n/a	NC	NC	
10h	18	0 (0.0%)	21	1 (4.8%)	n/a	n/a	n/a	n/a	NC	NC	
12h	18	0 (0.0%)	20	2 (10.0%)	n/a	n/a	n/a	n/a	NC	NC	
24h	12	1 (8.3%)	16	3 (18.8%)	6.46 (0.29, 146.15)	0.2414	4.60 (0.28, 74.90)	0.2837	NC	NC	
EOT	30	2 (6.7%)	24	3 (12.5%)	2.96 (0.32, 27.62)	0.3420	2.57 (0.33, 19.93)	0.3665	6.0 (-326.8, 338.7)	0.9720	
Baseline S-K											
1h											-
<=5.3 mmol/L	2	1 (50.0%)	4	3 (75.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	1 (100.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	33	3 (9.1%)	28	2 (7.1%)	-	-	-	-	-	-	
2h											-
<=5.3 mmol/L	2	1 (50.0%)	4	2 (50.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	33	1 (3.0%)	28	2 (7.1%)	-	-	-	-	-	-	
4h											-
<=5.3 mmol/L	2	1 (50.0%)	4	1 (25.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	33	1 (3.0%)	28	1 (3.6%)	-	-	-	-	-	-	
6h											-
<=5.3 mmol/L	0	0 (0.0%)	2	1 (50.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	20	1 (5.0%)	21	3 (14.3%)	-	-	-	-	-	-	
8h											-
<=5.3 mmol/L	0	0 (0.0%)	2	0 (0.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	0	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	17	0 (0.0%)	20	0 (0.0%)	-	-	-	-	-	-	
10h											-
<=5.3 mmol/L	0	0 (0.0%)	3	0 (0.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	0	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	18	0 (0.0%)	18	1 (5.6%)	-	-	-	-	-	-	
12h											-
<=5.3 mmol/L	0	0 (0.0%)	3	1 (33.3%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	17	0 (0.0%)	17	1 (5.9%)	-	-	-	-	-	-	
24h											-

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

t_energize_prop_norm.pdf generated by energize_prop.sas at 15:34:12 on 19 January 2021

Lokelma

Table 7.1.3.1 - Study ENERGIZE: Proportion of subjects with serum potassium in normal range by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
<=5.3 mmol/L	0	0 (0.0%)	1	0 (0.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	0	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	12	1 (8.3%)	15	3 (20.0%)	-	-	-	-	-	-	
EOT											-
<=5.3 mmol/L	1	0 (0.0%)	2	0 (0.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	28	2 (7.1%)	22	3 (13.6%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Lokelma

Table 7.1.3.1 - Study ENERGIZE: Proportion of subjects with serum potassium in normal range by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

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	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Sex											
1h											-
Male	18	4 (22.2%)	16	3 (18.8%)	-	-	-	-	-	-	
Female	18	1 (5.6%)	16	2 (12.5%)	-	-	-	-	-	-	
2h											-
Male	18	2 (11.1%)	16	4 (25.0%)	-	-	-	-	-	-	
Female	18	0 (0.0%)	16	0 (0.0%)	-	-	-	-	-	-	
4h											-
Male	18	2 (11.1%)	16	2 (12.5%)	-	-	-	-	-	-	
Female	18	0 (0.0%)	16	0 (0.0%)	-	-	-	-	-	-	
6h											-
Male	10	1 (10.0%)	11	4 (36.4%)	-	-	-	-	-	-	
Female	11	0 (0.0%)	12	0 (0.0%)	-	-	-	-	-	-	
8h											-
Male	9	0 (0.0%)	10	0 (0.0%)	-	-	-	-	-	-	
Female	8	0 (0.0%)	12	0 (0.0%)	-	-	-	-	-	-	
10h											-
Male	10	0 (0.0%)	11	1 (9.1%)	-	-	-	-	-	-	
Female	8	0 (0.0%)	10	0 (0.0%)	-	-	-	-	-	-	
12h											-
Male	9	0 (0.0%)	10	2 (20.0%)	-	-	-	-	-	-	
Female	9	0 (0.0%)	10	0 (0.0%)	-	-	-	-	-	-	
24h											-
Male	7	1 (14.3%)	7	1 (14.3%)	-	-	-	-	-	-	
Female	5	0 (0.0%)	9	2 (22.2%)	-	-	-	-	-	-	
EOT											-
Male	16	2 (12.5%)	10	1 (10.0%)	-	-	-	-	-	-	
Female	14	0 (0.0%)	14	2 (14.3%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
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ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 7.1.3.1 - Study ENERGIZE: Proportion of subjects with serum potassium in normal range by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Age (years)											
1h											-
<65 years	28	4 (14.3%)	16	4 (25.0%)	-	-	-	-	-	-	
>=65 years	8	1 (12.5%)	16	1 (6.3%)	-	-	-	-	-	-	
2h											-
<65 years	28	1 (3.6%)	16	2 (12.5%)	-	-	-	-	-	-	
>=65 years	8	1 (12.5%)	16	2 (12.5%)	-	-	-	-	-	-	
4h											-
<65 years	28	1 (3.6%)	16	1 (6.3%)	-	-	-	-	-	-	
>=65 years	8	1 (12.5%)	16	1 (6.3%)	-	-	-	-	-	-	
6h											-
<65 years	16	1 (6.3%)	12	3 (25.0%)	-	-	-	-	-	-	
>=65 years	5	0 (0.0%)	11	1 (9.1%)	-	-	-	-	-	-	
8h											-
<65 years	13	0 (0.0%)	11	0 (0.0%)	-	-	-	-	-	-	
>=65 years	4	0 (0.0%)	11	0 (0.0%)	-	-	-	-	-	-	
10h											-
<65 years	13	0 (0.0%)	10	1 (10.0%)	-	-	-	-	-	-	
>=65 years	5	0 (0.0%)	11	0 (0.0%)	-	-	-	-	-	-	
12h											-
<65 years	14	0 (0.0%)	9	1 (11.1%)	-	-	-	-	-	-	
>=65 years	4	0 (0.0%)	11	1 (9.1%)	-	-	-	-	-	-	
24h											-
<65 years	8	1 (12.5%)	6	1 (16.7%)	-	-	-	-	-	-	
>=65 years	4	0 (0.0%)	10	2 (20.0%)	-	-	-	-	-	-	
EOT											-
<65 years	24	2 (8.3%)	11	1 (9.1%)	-	-	-	-	-	-	
>=65 years	6	0 (0.0%)	13	2 (15.4%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 7.1.3.1 - Study ENERGIZE: Proportion of subjects with serum potassium in normal range by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Region											
1h											-
USA	19	3 (15.8%)	18	3 (16.7%)	-	-	-	-	-	-	
Rest of world	17	2 (11.8%)	14	2 (14.3%)	-	-	-	-	-	-	
2h											-
USA	19	2 (10.5%)	18	3 (16.7%)	-	-	-	-	-	-	
Rest of world	17	0 (0.0%)	14	1 (7.1%)	-	-	-	-	-	-	
4h											-
USA	19	2 (10.5%)	18	2 (11.1%)	-	-	-	-	-	-	
Rest of world	17	0 (0.0%)	14	0 (0.0%)	-	-	-	-	-	-	
6h											-
USA	5	0 (0.0%)	9	2 (22.2%)	-	-	-	-	-	-	
Rest of world	16	1 (6.3%)	14	2 (14.3%)	-	-	-	-	-	-	
8h											-
USA	3	0 (0.0%)	8	0 (0.0%)	-	-	-	-	-	-	
Rest of world	14	0 (0.0%)	14	0 (0.0%)	-	-	-	-	-	-	
10h											-
USA	4	0 (0.0%)	7	0 (0.0%)	-	-	-	-	-	-	
Rest of world	14	0 (0.0%)	14	1 (7.1%)	-	-	-	-	-	-	
12h											-
USA	3	0 (0.0%)	6	1 (16.7%)	-	-	-	-	-	-	
Rest of world	15	0 (0.0%)	14	1 (7.1%)	-	-	-	-	-	-	
24h											-
USA	1	0 (0.0%)	3	2 (66.7%)	-	-	-	-	-	-	
Rest of world	11	1 (9.1%)	13	1 (7.7%)	-	-	-	-	-	-	
EOT											-
USA	15	1 (6.7%)	10	2 (20.0%)	-	-	-	-	-	-	
Rest of world	15	1 (6.7%)	14	1 (7.1%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 7.1.3.2 - Study ENERGIZE: Proportion of subjects with serum potassium <5.5 mmol/L by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Overall											
1h	36	11 (30.6%)	32	10 (31.3%)	0.77 (0.23, 2.59)	0.6684	0.87 (0.33, 2.25)	0.7668	-5.5 (-60.6, 49.6)	0.8444	
2h	36	6 (16.7%)	32	12 (37.5%)	3.39 (0.83, 13.75)	0.0881	2.01 (0.69, 5.87)	0.2001	14.5 (-55.1, 84.2)	0.6830	
4h	36	5 (13.9%)	32	5 (15.6%)	0.93 (0.14, 6.17)	0.9413	0.91 (0.22, 3.82)	0.8985	-1.5 (-79.9, 77.0)	0.9708	
6h	21	1 (4.8%)	23	4 (17.4%)	4.71 (0.43, 51.50)	0.2044	NC	NC	NC	NC	
8h	17	0 (0.0%)	22	3 (13.6%)	n/a	n/a	n/a	n/a	NC	NC	
10h	18	2 (11.1%)	21	4 (19.0%)	1.43 (0.14, 14.60)	0.7635	1.43 (0.22, 9.21)	0.7039	5.9 (-2000.0, 2011.7)	0.9954	
12h	18	0 (0.0%)	20	6 (30.0%)	n/a	n/a	n/a	n/a	NC	NC	
24h	12	2 (16.7%)	16	11 (68.8%)	48.63 (1.90, >999.99)	0.0188	4.45 (0.85, 23.34)	0.0773	61.3 (-122.3, 244.9)	0.5128	
EOT	30	4 (13.3%)	24	13 (54.2%)	10.46 (2.36, 46.45)	0.0020	4.54 (1.43, 14.42)	0.0103	44.3 (10.6, 77.9)	0.0099	
Baseline S-K											
1h											-
<=5.3 mmol/L	2	2 (100.0%)	4	4 (100.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	1 (100.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	33	8 (24.2%)	28	6 (21.4%)	-	-	-	-	-	-	
2h											-
<=5.3 mmol/L	2	2 (100.0%)	4	4 (100.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	1 (100.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	33	3 (9.1%)	28	8 (28.6%)	-	-	-	-	-	-	
4h											-
<=5.3 mmol/L	2	2 (100.0%)	4	4 (100.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	33	3 (9.1%)	28	1 (3.6%)	-	-	-	-	-	-	
6h											-
<=5.3 mmol/L	0	0 (0.0%)	2	1 (50.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	20	1 (5.0%)	21	3 (14.3%)	-	-	-	-	-	-	
8h											-
<=5.3 mmol/L	0	0 (0.0%)	2	0 (0.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	0	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	17	0 (0.0%)	20	3 (15.0%)	-	-	-	-	-	-	
10h											-
<=5.3 mmol/L	0	0 (0.0%)	3	1 (33.3%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	0	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	18	2 (11.1%)	18	3 (16.7%)	-	-	-	-	-	-	
12h											-
<=5.3 mmol/L	0	0 (0.0%)	3	1 (33.3%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	17	0 (0.0%)	17	5 (29.4%)	-	-	-	-	-	-	
24h											-

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 7.1.3.2 - Study ENERGIZE: Proportion of subjects with serum potassium <5.5 mmol/L by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
<=5.3 mmol/L	0	0 (0.0%)	1	1 (100.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	0	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	12	2 (16.7%)	15	10 (66.7%)	-	-	-	-	-	-	
EOT											-
<=5.3 mmol/L	1	1 (100.0%)	2	2 (100.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	28	3 (10.7%)	22	11 (50.0%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Lokelma

Table 7.1.3.2 - Study ENERGIZE: Proportion of subjects with serum potassium <5.5 mmol/L by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Sex											
1h											0.9654
Male	18	5 (27.8%)	16	5 (31.3%)	1.08 (0.17, 6.75)	0.9324	1.05 (0.23, 4.80)	0.9547	6.6 (-136.7, 149.9)	0.9278	
Female	18	6 (33.3%)	16	5 (31.3%)	0.75 (0.13, 4.35)	0.7517	0.98 (0.24, 3.90)	0.9740	-1.2 (-99.4, 96.9)	0.9805	
2h											0.7935
Male	18	3 (16.7%)	16	8 (50.0%)	5.88 (0.81, 42.72)	0.0801	3.06 (0.57, 16.45)	0.1925	39.9 (-159.1, 238.9)	0.6944	
Female	18	3 (16.7%)	16	4 (25.0%)	3.06 (0.30, 31.71)	0.3484	2.46 (0.40, 15.31)	0.3333	8.9 (-216.5, 234.3)	0.9383	
4h											-
Male	18	4 (22.2%)	16	5 (31.3%)	-	-	-	-	-	-	
Female	18	1 (5.6%)	16	0 (0.0%)	-	-	-	-	-	-	
6h											-
Male	10	1 (10.0%)	11	4 (36.4%)	-	-	-	-	-	-	
Female	11	0 (0.0%)	12	0 (0.0%)	-	-	-	-	-	-	
8h											-
Male	9	0 (0.0%)	10	0 (0.0%)	-	-	-	-	-	-	
Female	8	0 (0.0%)	12	3 (25.0%)	-	-	-	-	-	-	
10h											-
Male	10	2 (20.0%)	11	3 (27.3%)	-	-	-	-	-	-	
Female	8	0 (0.0%)	10	1 (10.0%)	-	-	-	-	-	-	
12h											-
Male	9	0 (0.0%)	10	4 (40.0%)	-	-	-	-	-	-	
Female	9	0 (0.0%)	10	2 (20.0%)	-	-	-	-	-	-	
24h											-
Male	7	2 (28.6%)	7	5 (71.4%)	-	-	-	-	-	-	
Female	5	0 (0.0%)	9	6 (66.7%)	-	-	-	-	-	-	
EOT											-
Male	16	3 (18.8%)	10	6 (60.0%)	-	-	-	-	-	-	
Female	14	1 (7.1%)	14	7 (50.0%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 7.1.3.2 - Study ENERGIZE: Proportion of subjects with serum potassium <5.5 mmol/L by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Age (years)											
1h											0.3658
<65 years	28	8 (28.6%)	16	6 (37.5%)	1.72 (0.40, 7.33)	0.4617	1.40 (0.46, 4.28)	0.5593	11.3 (-35.7, 58.4)	0.6368	
>=65 years	8	3 (37.5%)	16	4 (25.0%)	0.14 (<0.01, 83.92)	0.5454	0.42 (<0.01, 38.69)	0.7082	NC	NC	
2h											0.0278
<65 years	28	3 (10.7%)	16	9 (56.3%)	16.79 (2.23, 126.75)	0.0062	4.20 (1.12, 15.71)	0.0328	34.6 (-65.3, 134.6)	0.4970	
>=65 years	8	3 (37.5%)	16	3 (18.8%)	0.14 (<0.01, 83.92)	0.5454	0.42 (<0.01, 38.69)	0.7082	NC	NC	
4h											-
<65 years	28	3 (10.7%)	16	3 (18.8%)	-	-	-	-	-	-	
>=65 years	8	2 (25.0%)	16	2 (12.5%)	-	-	-	-	-	-	
6h											-
<65 years	16	1 (6.3%)	12	3 (25.0%)	-	-	-	-	-	-	
>=65 years	5	0 (0.0%)	11	1 (9.1%)	-	-	-	-	-	-	
8h											-
<65 years	13	0 (0.0%)	11	1 (9.1%)	-	-	-	-	-	-	
>=65 years	4	0 (0.0%)	11	2 (18.2%)	-	-	-	-	-	-	
10h											-
<65 years	13	0 (0.0%)	10	1 (10.0%)	-	-	-	-	-	-	
>=65 years	5	2 (40.0%)	11	3 (27.3%)	-	-	-	-	-	-	
12h											-
<65 years	14	0 (0.0%)	9	3 (33.3%)	-	-	-	-	-	-	
>=65 years	4	0 (0.0%)	11	3 (27.3%)	-	-	-	-	-	-	
24h											-
<65 years	8	1 (12.5%)	6	3 (50.0%)	-	-	-	-	-	-	
>=65 years	4	1 (25.0%)	10	8 (80.0%)	-	-	-	-	-	-	
EOT											0.6915
<65 years	24	3 (12.5%)	11	3 (27.3%)	6.54 (0.61, 70.56)	0.1215	4.92 (0.59, 41.35)	0.1424	10.2 (-106.2, 126.6)	0.8636	
>=65 years	6	1 (16.7%)	13	10 (76.9%)	>999.99 (<0.01, >999.99)	0.7613	3.89 (0.45, 33.51)	0.2161	55.1 (-132.0, 242.2)	0.5640	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 7.1.3.2 - Study ENERGIZE: Proportion of subjects with serum potassium <5.5 mmol/L by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Region											
1h											0.2369
USA	19	7 (36.8%)	18	8 (44.4%)	2.70 (0.32, 22.54)	0.3600	1.43 (0.40, 5.12)	0.5804	11.2 (-99.9, 122.3)	0.8429	
Rest of world	17	4 (23.5%)	14	2 (14.3%)	0.44 (0.06, 3.32)	0.4230	0.52 (0.09, 3.16)	0.4801	-15.4 (-63.0, 32.2)	0.5265	
2h											0.8971
USA	19	5 (26.3%)	18	9 (50.0%)	5.46 (0.82, 36.39)	0.0792	2.17 (0.62, 7.59)	0.2273	24.2 (-76.5, 125.0)	0.6374	
Rest of world	17	1 (5.9%)	14	3 (21.4%)	>999.99 (<0.01, >999.99)	0.3609	NC	NC	NC	NC	
4h											-
USA	19	4 (21.1%)	18	4 (22.2%)	-	-	-	-	-	-	
Rest of world	17	1 (5.9%)	14	1 (7.1%)	-	-	-	-	-	-	
6h											-
USA	5	0 (0.0%)	9	2 (22.2%)	-	-	-	-	-	-	
Rest of world	16	1 (6.3%)	14	2 (14.3%)	-	-	-	-	-	-	
8h											-
USA	3	0 (0.0%)	8	2 (25.0%)	-	-	-	-	-	-	
Rest of world	14	0 (0.0%)	14	1 (7.1%)	-	-	-	-	-	-	
10h											-
USA	4	1 (25.0%)	7	2 (28.6%)	-	-	-	-	-	-	
Rest of world	14	1 (7.1%)	14	2 (14.3%)	-	-	-	-	-	-	
12h											-
USA	3	0 (0.0%)	6	1 (16.7%)	-	-	-	-	-	-	
Rest of world	15	0 (0.0%)	14	5 (35.7%)	-	-	-	-	-	-	
24h											
USA	1	0 (0.0%)	3	2 (66.7%)	n/a	n/a	n/a	n/a	NC	NC	
Rest of world	11	2 (18.2%)	13	9 (69.2%)	32.49 (1.32, 798.78)	0.0331	3.92 (0.72, 21.40)	0.1147	55.0 (-125.2, 235.2)	0.5498	
EOT											0.8235
USA	15	2 (13.3%)	10	4 (40.0%)	5.96 (0.51, 69.52)	0.1545	3.15 (0.46, 21.85)	0.2448	19.0 (-141.1, 179.1)	0.8161	
Rest of world	15	2 (13.3%)	14	9 (64.3%)	39.67 (2.03, 773.63)	0.0152	5.92 (1.09, 32.07)	0.0390	58.9 (-106.6, 224.4)	0.4857	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 7.1.3.3 - Study ENERGIZE: Proportion of subjects with serum potassium <6.0 mmol/L by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Overall											
1h	36	22 (61.1%)	32	21 (65.6%)	1.08 (0.33, 3.58)	0.8940	1.05 (0.56, 1.97)	0.8832	-0.5 (-45.0, 44.1)	0.9835	
2h	36	17 (47.2%)	32	20 (62.5%)	2.57 (0.73, 9.03)	0.1418	1.34 (0.68, 2.64)	0.4017	12.0 (-37.7, 61.6)	0.6367	
4h	36	13 (36.1%)	32	15 (46.9%)	1.38 (0.45, 4.27)	0.5712	1.19 (0.53, 2.64)	0.6771	1.0 (-44.5, 46.5)	0.9651	
6h	21	7 (33.3%)	23	15 (65.2%)	3.15 (0.86, 11.53)	0.0834	1.75 (0.70, 4.38)	0.2311	28.7 (-14.7, 72.1)	0.1950	
8h	17	5 (29.4%)	22	15 (68.2%)	6.80 (1.34, 34.44)	0.0205	2.54 (0.81, 7.92)	0.1093	43.8 (-5.8, 93.4)	0.0832	
10h	18	3 (16.7%)	21	11 (52.4%)	4.05 (0.77, 21.22)	0.0982	2.31 (0.62, 8.69)	0.2139	24.3 (-532.4, 581.0)	0.9318	
12h	18	4 (22.2%)	20	11 (55.0%)	4.09 (0.80, 21.07)	0.0917	2.15 (0.63, 7.33)	0.2202	38.8 (-35.3, 113.0)	0.3048	
24h	12	4 (33.3%)	16	12 (75.0%)	7.58 (0.89, 64.21)	0.0633	1.94 (0.56, 6.70)	0.2944	48.7 (-12.3, 109.6)	0.1177	
EOT	30	13 (43.3%)	24	19 (79.2%)	5.76 (1.48, 22.53)	0.0118	1.82 (0.88, 3.76)	0.1055	35.7 (-10.4, 81.8)	0.1289	
Baseline S-K											
1h											-
<=5.3 mmol/L	2	2 (100.0%)	4	4 (100.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	1 (100.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	33	19 (57.6%)	28	17 (60.7%)	-	-	-	-	-	-	
2h											-
<=5.3 mmol/L	2	2 (100.0%)	4	4 (100.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	1 (100.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	33	14 (42.4%)	28	16 (57.1%)	-	-	-	-	-	-	
4h											-
<=5.3 mmol/L	2	2 (100.0%)	4	4 (100.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	33	11 (33.3%)	28	11 (39.3%)	-	-	-	-	-	-	
6h											-
<=5.3 mmol/L	0	0 (0.0%)	2	2 (100.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	20	7 (35.0%)	21	13 (61.9%)	-	-	-	-	-	-	
8h											-
<=5.3 mmol/L	0	0 (0.0%)	2	1 (50.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	0	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	17	5 (29.4%)	20	14 (70.0%)	-	-	-	-	-	-	
10h											-
<=5.3 mmol/L	0	0 (0.0%)	3	2 (66.7%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	0	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	18	3 (16.7%)	18	9 (50.0%)	-	-	-	-	-	-	
12h											-
<=5.3 mmol/L	0	0 (0.0%)	3	1 (33.3%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	17	4 (23.5%)	17	10 (58.8%)	-	-	-	-	-	-	
24h											-

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 7.1.3.3 - Study ENERGIZE: Proportion of subjects with serum potassium <6.0 mmol/L by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
<=5.3 mmol/L	0	0 (0.0%)	1	1 (100.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	0	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	12	4 (33.3%)	15	11 (73.3%)	-	-	-	-	-	-	
EOT											-
<=5.3 mmol/L	1	1 (100.0%)	2	2 (100.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	28	12 (42.9%)	22	17 (77.3%)	-	-	-	-	-	-	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 7.1.3.3 - Study ENERGIZE: Proportion of subjects with serum potassium <6.0 mmol/L by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Sex											
1h											0.9991
Male	18	10 (55.6%)	16	10 (62.5%)	1.31 (0.24, 7.25)	0.7564	1.10 (0.41, 2.93)	0.8485	6.6 (-63.6, 76.7)	0.8548	
Female	18	12 (66.7%)	16	11 (68.8%)	0.86 (0.11, 6.96)	0.8865	1.15 (0.48, 2.77)	0.7566	7.7 (-47.5, 62.9)	0.7855	
2h											0.9916
Male	18	9 (50.0%)	16	12 (75.0%)	5.85 (0.66, 52.26)	0.1136	1.55 (0.59, 4.04)	0.3745	24.9 (-49.3, 99.0)	0.5107	
Female	18	8 (44.4%)	16	8 (50.0%)	1.41 (0.24, 8.41)	0.7045	1.40 (0.48, 4.05)	0.5353	12.3 (-70.1, 94.7)	0.7701	
4h											0.9293
Male	18	8 (44.4%)	16	10 (62.5%)	2.25 (0.40, 12.56)	0.3536	1.32 (0.46, 3.80)	0.6125	21.9 (-69.1, 113.0)	0.6368	
Female	18	5 (27.8%)	16	5 (31.3%)	1.24 (0.20, 7.71)	0.8166	1.33 (0.29, 6.14)	0.7106	1.9 (-93.3, 97.1)	0.9688	
6h											0.2345
Male	10	5 (50.0%)	11	8 (72.7%)	1.51 (0.18, 12.32)	0.7031	1.19 (0.37, 3.87)	0.7736	12.8 (-65.2, 90.8)	0.7483	
Female	11	2 (18.2%)	12	7 (58.3%)	26.11 (1.22, 558.28)	0.0368	7.20 (0.73, 70.69)	0.0901	40.5 (-137.9, 218.9)	0.6564	
8h											0.2602
Male	9	4 (44.4%)	10	6 (60.0%)	2.30 (0.24, 22.15)	0.4714	1.37 (0.32, 5.92)	0.6750	19.2 (-57.0, 95.4)	0.6216	
Female	8	1 (12.5%)	12	9 (75.0%)	38.60 (1.88, 793.42)	0.0179	6.33 (0.78, 51.49)	0.0846	63.6 (-298.5, 425.7)	0.7308	
10h											-
Male	10	2 (20.0%)	11	6 (54.5%)	-	-	-	-	-	-	
Female	8	1 (12.5%)	10	5 (50.0%)	-	-	-	-	-	-	
12h											-
Male	9	3 (33.3%)	10	5 (50.0%)	-	-	-	-	-	-	
Female	9	1 (11.1%)	10	6 (60.0%)	-	-	-	-	-	-	
24h											
Male	7	4 (57.1%)	7	6 (85.7%)	6.54 (0.16, 264.61)	0.3199	1.34 (0.33, 5.44)	0.6791	28.4 (-82.0, 138.7)	0.6145	
Female	5	0 (0.0%)	9	6 (66.7%)	n/a	n/a	n/a	n/a	NC	NC	
EOT											0.3129
Male	16	9 (56.3%)	10	9 (90.0%)	6.18 (0.50, 75.94)	0.1548	1.49 (0.55, 4.02)	0.4358	30.2 (-48.2, 108.7)	0.4500	
Female	14	4 (28.6%)	14	10 (71.4%)	21.55 (1.73, 269.19)	0.0171	3.44 (0.98, 12.11)	0.0546	48.2 (-49.7, 146.1)	0.3347	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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Table 7.1.3.3 - Study ENERGIZE: Proportion of subjects with serum potassium <6.0 mmol/L by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Age (years)											
1h											0.9978
<65 years	28	18 (64.3%)	16	10 (62.5%)	1.67 (0.36, 7.86)	0.5157	1.20 (0.52, 2.76)	0.6640	7.4 (-49.6, 64.4)	0.7996	
>=65 years	8	4 (50.0%)	16	11 (68.8%)	<0.01 (<0.01, >999.99)	0.5182	0.63 (0.12, 3.45)	0.5965	-17.0 (-306.3, 272.3)	0.9082	
2h											0.4872
<65 years	28	13 (46.4%)	16	11 (68.8%)	5.08 (0.91, 28.42)	0.0642	1.63 (0.69, 3.86)	0.2645	24.7 (-38.3, 87.7)	0.4422	
>=65 years	8	4 (50.0%)	16	9 (56.3%)	0.50 (0.01, 20.16)	0.7153	1.10 (0.22, 5.51)	0.9110	-3.8 (-141.1, 133.5)	0.9569	
4h											0.3091
<65 years	28	9 (32.1%)	16	7 (43.8%)	1.87 (0.42, 8.30)	0.4113	1.36 (0.48, 3.82)	0.5620	7.0 (-54.6, 68.6)	0.8232	
>=65 years	8	4 (50.0%)	16	8 (50.0%)	0.06 (<0.01, 2.38)	0.1365	0.28 (0.04, 2.07)	0.2099	-38.3 (-216.8, 140.2)	0.6739	
6h											0.4766
<65 years	16	5 (31.3%)	12	9 (75.0%)	6.08 (1.07, 34.44)	0.0413	2.26 (0.74, 6.96)	0.1546	41.8 (-21.0, 104.6)	0.1919	
>=65 years	5	2 (40.0%)	11	6 (54.5%)	>999.99 (<0.01, >999.99)	0.8641	1.67 (0.18, 15.85)	0.6542	9.8 (-158.1, 177.7)	0.9089	
8h											0.7097
<65 years	13	3 (23.1%)	11	8 (72.7%)	10.98 (1.22, 99.04)	0.0327	3.26 (0.82, 12.95)	0.0933	50.7 (-15.7, 117.0)	0.1346	
>=65 years	4	2 (50.0%)	11	7 (63.6%)	3.60 (0.11, 113.21)	0.4671	1.64 (0.16, 16.60)	0.6739	44.8 (-152.3, 241.9)	0.6559	
10h											-
<65 years	13	1 (7.7%)	10	5 (50.0%)	-	-	-	-	-	-	
>=65 years	5	2 (40.0%)	11	6 (54.5%)	-	-	-	-	-	-	
12h											-
<65 years	14	3 (21.4%)	9	5 (55.6%)	-	-	-	-	-	-	
>=65 years	4	1 (25.0%)	11	6 (54.5%)	-	-	-	-	-	-	
24h											-
<65 years	8	3 (37.5%)	6	4 (66.7%)	-	-	-	-	-	-	
>=65 years	4	1 (25.0%)	10	8 (80.0%)	-	-	-	-	-	-	
EOT											0.6147
<65 years	24	11 (45.8%)	11	8 (72.7%)	2.33 (0.44, 12.24)	0.3179	1.38 (0.53, 3.56)	0.5082	16.8 (-45.5, 79.2)	0.5965	
>=65 years	6	2 (33.3%)	13	11 (84.6%)	>999.99 (<0.01, >999.99)	0.8372	2.07 (0.40, 10.86)	0.3879	46.8 (-132.4, 226.0)	0.6089	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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26/02/2021

Lokelma

Table 7.1.3.3 - Study ENERGIZE: Proportion of subjects with serum potassium <6.0 mmol/L by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Region											
1h											0.6804
USA	19	15 (78.9%)	18	14 (77.8%)	2.94 (0.29, 30.34)	0.3643	1.16 (0.51, 2.63)	0.7293	13.8 (-53.7, 81.3)	0.6884	
Rest of world	17	7 (41.2%)	14	7 (50.0%)	0.77 (0.14, 4.38)	0.7686	0.88 (0.29, 2.66)	0.8178	-10.3 (-77.9, 57.2)	0.7646	
2h											0.9862
USA	19	12 (63.2%)	18	12 (66.7%)	3.33 (0.49, 22.59)	0.2180	1.30 (0.54, 3.17)	0.5603	17.6 (-48.8, 83.9)	0.6037	
Rest of world	17	5 (29.4%)	14	8 (57.1%)	0.76 (0.07, 7.80)	0.8199	1.08 (0.34, 3.38)	0.8967	4.4 (-85.3, 94.1)	0.9229	
4h											0.8498
USA	19	9 (47.4%)	18	10 (55.6%)	1.76 (0.33, 9.36)	0.5055	1.27 (0.45, 3.61)	0.6541	1.8 (-54.4, 58.0)	0.9498	
Rest of world	17	4 (23.5%)	14	5 (35.7%)	0.63 (0.08, 4.64)	0.6487	0.85 (0.22, 3.28)	0.8102	-6.9 (-125.8, 111.9)	0.9092	
6h											0.7363
USA	5	3 (60.0%)	9	7 (77.8%)	2.45 (0.13, 47.97)	0.5552	1.21 (0.30, 4.93)	0.7905	42.7 (-72.6, 158.0)	0.4679	
Rest of world	16	4 (25.0%)	14	8 (57.1%)	3.00 (0.56, 16.04)	0.1983	1.84 (0.51, 6.59)	0.3508	30.3 (-19.2, 79.9)	0.2304	
8h											0.9085
USA	3	1 (33.3%)	8	5 (62.5%)	>999.99 (<0.01, >999.99)	0.6018	3.13 (0.20, 48.24)	0.4140	53.4 (-841.9, 948.7)	0.9069	
Rest of world	14	4 (28.6%)	14	10 (71.4%)	5.67 (0.52, 62.24)	0.1556	1.67 (0.41, 6.87)	0.4771	21.6 (-69.3, 112.5)	0.6413	
10h											-
USA	4	2 (50.0%)	7	4 (57.1%)	-	-	-	-	-	-	
Rest of world	14	1 (7.1%)	14	7 (50.0%)	-	-	-	-	-	-	
12h											0.4209
USA	3	1 (33.3%)	6	2 (33.3%)	0.68 (<0.01, 74.57)	0.8742	0.83 (0.02, 44.47)	0.9267	NC	NC	
Rest of world	15	3 (20.0%)	14	9 (64.3%)	6.13 (0.93, 40.41)	0.0596	2.59 (0.64, 10.49)	0.1831	41.9 (-49.7, 133.5)	0.3701	
24h											0.5504
USA	1	1 (100.0%)	3	2 (66.7%)	n/a	n/a	1.00 (<0.01, >999.99)	1.0000	0.0 (-1406.5, 1406.5)	1.0000	
Rest of world	11	3 (27.3%)	13	10 (76.9%)	NC	NC	2.24 (0.55, 9.05)	0.2583	50.6 (-9.8, 111.1)	0.1007	
EOT											0.5686
USA	15	9 (60.0%)	10	8 (80.0%)	5.18 (0.40, 67.49)	0.2095	1.49 (0.52, 4.32)	0.4606	26.8 (-53.2, 106.7)	0.5118	
Rest of world	15	4 (26.7%)	14	11 (78.6%)	12.69 (1.55, 103.97)	0.0179	2.74 (0.80, 9.43)	0.1095	61.1 (5.4, 116.8)	0.0316	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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26/02/2021

Lokelma

Table 7.1.4.1 - Study ENERGIZE: Proportion of subjects receiving additional potassium lowering therapy by timepoint, SZC 10g TID vs. Placebo, overall and by subgroups (full population)

	Placebo (N=37)		Lokelma 10g QD (N=33)								
Subgroup / Analysis Visit / Category	N	Patients meeting criteria [n (%)]	N	Patients meeting criteria [n (%)]	Odds ratio (95% CI)	OR p-value	Relative risk (95% CI)	RR p-value	Absolute risk reduction (95% CI)	ARR p-value	p-value for interaction (RR)
Overall											
From 0 to 4 hrs	36	11 (30.6%)	32	5 (15.6%)	0.40 (0.09, 1.77)	0.2281	0.49 (0.13, 1.85)	0.2914	-11.3 (-32.9, 10.2)	0.3028	
From 4 to 24 hrs	36	16 (44.4%)	32	13 (40.6%)	0.84 (0.30, 2.36)	0.7410	0.92 (0.44, 1.92)	0.8160	-4.0 (-40.7, 32.7)	0.8317	
Baseline S-K											
From 0 to 4 hrs											-
<=5.3 mmol/L	2	1 (50.0%)	4	0 (0.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	33	10 (30.3%)	28	5 (17.9%)	-	-	-	-	-	-	
From 4 to 24 hrs											-
<=5.3 mmol/L	2	0 (0.0%)	4	2 (50.0%)	-	-	-	-	-	-	
5.4-5.5 mmol/L	1	0 (0.0%)	0	0 (0.0%)	-	-	-	-	-	-	
>5.5 mmol/L	33	16 (48.5%)	28	11 (39.3%)	-	-	-	-	-	-	
Sex											
From 0 to 4 hrs											0.6069
Male	18	6 (33.3%)	16	4 (25.0%)	0.98 (0.11, 8.56)	0.9882	1.03 (0.15, 7.02)	0.9756	1.1 (-253.2, 255.5)	0.9931	
Female	18	5 (27.8%)	16	1 (6.3%)	0.40 (0.02, 9.52)	0.5682	0.55 (0.06, 5.02)	0.5930	-2.2 (-259.7, 255.3)	0.9867	
From 4 to 24 hrs											0.6456
Male	18	7 (38.9%)	16	7 (43.8%)	1.01 (0.20, 5.07)	0.9881	1.02 (0.34, 3.05)	0.9777	-0.7 (-60.1, 58.8)	0.9826	
Female	18	9 (50.0%)	16	6 (37.5%)	0.57 (0.14, 2.44)	0.4521	0.75 (0.26, 2.16)	0.5995	-14.1 (-67.2, 39.1)	0.6037	
Age (years)											
From 0 to 4 hrs											
<65 years	28	9 (32.1%)	16	3 (18.8%)	0.27 (0.03, 2.58)	0.2530	0.33 (0.04, 2.79)	0.3053	-15.6 (-40.1, 9.0)	0.2144	
>=65 years	8	2 (25.0%)	16	2 (12.5%)	>999.99 (<0.01, >999.99)	0.9466	>999.99 (>999.99, >999.99)	NC	NC	NC	
From 4 to 24 hrs											0.8249
<65 years	28	14 (50.0%)	16	8 (50.0%)	1.35 (0.35, 5.24)	0.6668	1.15 (0.46, 2.87)	0.7664	7.4 (-41.3, 56.1)	0.7657	
>=65 years	8	2 (25.0%)	16	5 (31.3%)	0.28 (0.02, 4.84)	0.3836	0.43 (0.05, 3.85)	0.4540	-35.3 (-340.4, 269.7)	0.8204	
Region											
From 0 to 4 hrs											
USA	19	7 (36.8%)	18	5 (27.8%)	0.74 (0.12, 4.71)	0.7527	0.84 (0.18, 4.01)	0.8287	-1.2 (-36.1, 33.6)	0.9451	
Rest of world	17	4 (23.5%)	14	0 (0.0%)	n/a	n/a	NC	NC	NC	NC	
From 4 to 24 hrs											0.1217
USA	19	11 (57.9%)	18	12 (66.7%)	2.02 (0.26, 15.62)	0.4989	1.18 (0.51, 2.76)	0.7007	15.7 (-51.4, 82.8)	0.6470	
Rest of world	17	5 (29.4%)	14	1 (7.1%)	0.10 (<0.01, 1.56)	0.1005	0.21 (0.02, 1.94)	0.1681	-37.6 (-956.7, 881.6)	0.9362	

OR, RR and ARR derived from model with the following effects:
Treatment group, baseline S-K, time from the start of dosing insulin to the start of dosing SZC/placebo and the dose (units/kg) of the first course of insulin.
For subgroup interaction analysis, the subgroup variable (if not already present), an interaction term for subgroup*treatment group were added and the continuous version of the subgroup variable (if present) was removed.
OR is calculated from logistic regression. RR and ARR are calculated from a poisson regression using a generalized linear model procedure. RR and ARR confidence intervals are wider as robust error variance was not applied (i.e by using the repeated statement with subject identifier). Generally, applying robust error variance while matching model covariates used in CSRs increased likelihood of model not converging, so conservative method was used.
'-' denotes value not calculated because summed across treatment groups there are fewer than 10 subjects in at least one subgroup level or there are fewer than 10 events for the subgroup level
'n/a' denotes odds ratio not calculated because there were 0% or 100% of subjects with events in one arm, or relative risk not calculated because there were of 0% subjects with events in one arm. Using a regression method, it is not possible to apply an offset for zero counts (Haldane-Anscombe correction) to allow an estimate to be calculated.
ARR: absolute risk reduction, NC: model did not converge, OR: odds ratio, RR: relative risk

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26/02/2021

Lokelma

Table 7.2.1.1 - Study ENERGIZE: Subjects experiencing any adverse event (AE), SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	11 (33.3%)	29	9 (31.0%)	0.90 (0.31 , 2.62)	0.8468	0.93 (0.45 , 1.92)	0.8470	-2.30 (-25.58 , 20.99)	0.8466	
Baseline S-K											0.4977
<=5.3 mmol/L	1	0 (0.0%)	3	1 (33.3%)	1.80 (0.04 , 79.42)	0.7610	1.50 (0.10 , 22.62)	0.7696	33.33 (-20.01 , 86.68)	0.2207	
5.4-5.5 mmol/L	1	1 (100.0%)	0	0 (%)							
>5.5 mmol/L	31	10 (32.3%)	26	8 (30.8%)	0.93 (0.30 , 2.87)	0.9041	0.95 (0.44 , 2.06)	0.9042	-1.49 (-25.69 , 22.71)	0.9040	
Sex											0.7239
Male	16	6 (37.5%)	13	4 (30.8%)	0.74 (0.16 , 3.50)	0.7049	0.82 (0.29 , 2.30)	0.7071	-6.73 (-41.26 , 27.80)	0.7024	
Female	17	5 (29.4%)	16	5 (31.3%)	1.09 (0.25 , 4.82)	0.9086	1.06 (0.38 , 2.99)	0.9086	1.84 (-29.55 , 33.22)	0.9086	
Age (years)											0.7347
<65 years	27	9 (33.3%)	14	5 (35.7%)	1.11 (0.29 , 4.31)	0.8788	1.07 (0.44 , 2.59)	0.8782	2.38 (-28.38 , 33.14)	0.8794	
>=65 years	6	2 (33.3%)	15	4 (26.7%)	0.73 (0.09 , 5.63)	0.7604	0.80 (0.20 , 3.27)	0.7562	-6.67 (-50.53 , 37.19)	0.7658	
Region											0.0168
USA	17	5 (29.4%)	15	8 (53.3%)	2.74 (0.64 , 11.75)	0.1741	1.81 (0.76 , 4.35)	0.1827	23.92 (-9.34 , 57.19)	0.1587	
Rest of world	16	6 (37.5%)	14	1 (7.1%)	0.13 (0.01 , 1.24)	0.0764	0.19 (0.03 , 1.40)	0.1027	-30.36 (-57.65 , -3.07)	0.0292	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_ae_any.pdf generated by energize_ae_soc_pt.sas at 16:42:00 on 25 February 2021

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Table 7.2.1.2 - Study ENERGIZE: Subjects experiencing any serious adverse event (SAE), SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	4 (12.1%)	29	2 (6.9%)	0.54 (0.09 , 3.17)	0.4928	0.57 (0.11 , 2.88)	0.4957	-5.22 (-19.68 , 9.23)	0.4788	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_ae_sae.pdf generated by energize_ae_soc_pt.sas at 16:42:07 on 25 February 2021

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Table 7.2.1.3 - Study ENERGIZE: Subjects experiencing any AE leading to discontinuation of study medication (DAE), SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	1 (3.0%)	29	0 (0.0%)	0.37 (0.01 , 9.37)	0.5444	0.38 (0.02 , 8.93)	0.5463	-3.03 (-8.88 , 2.82)	0.3099	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_ae_dae.pdf generated by energize_ae_soc_pt.sas at 16:42:11 on 25 February 2021

Lokelma

Table 7.2.1.4 - Study ENERGIZE: Subjects experiencing any AE graded as severe, SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	4 (12.1%)	29	2 (6.9%)	0.54 (0.09 , 3.17)	0.4928	0.57 (0.11 , 2.88)	0.4957	-5.22 (-19.68 , 9.23)	0.4788	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_ae_sev.pdf generated by energize_ae_soc_pt.sas at 16:42:16 on 25 February 2021

Lokelma

Table 7.2.1.5 - Study ENERGIZE: Subjects experiencing any AE graded as non-severe, SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	8 (24.2%)	29	9 (31.0%)	1.41 (0.46 , 4.31)	0.5505	1.28 (0.57 , 2.88)	0.5507	6.79 (-15.51 , 29.09)	0.5505	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_ae_rsev.pdf generated by energize_ae_soc_pt.sas at 16:42:21 on 25 February 2021

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Lokelma

Table 7.2.1.6 - Study ENERGIZE: Subjects experiencing any AE resulting in death, SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	1 (3.0%)	29	0 (0.0%)	0.37 (0.01 , 9.37)	0.5444	0.38 (0.02 , 8.93)	0.5463	-3.03 (-8.88 , 2.82)	0.3099	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_ae_death.pdf generated by energize_ae_soc_pt.sas at 16:42:26 on 25 February 2021

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Table 7.2.1.7 - Study ENERGIZE: Adverse events leading to discontinuation (DAE) by SOC and PT, SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		10g ZS (N=29)	
Subgroup / Category / SOC / PT	**N**	**n (%)**	**N**	**n (%)**
Overall				
Any AE	33	1 (3.0%)	29	0 (0.0%)
Investigations	33	1 (3.0%)	29	0 (0.0%)
Electrocardiogram QT shortened	33	1 (3.0%)	29	0 (0.0%)
Nervous system disorders	33	1 (3.0%)	29	0 (0.0%)
Clonic convulsion	33	1 (3.0%)	29	0 (0.0%)
Baseline S-K				
<=5.3 mmol/L				
Any AE	1	0 (0.0%)	3	0 (0.0%)
5.4-5.5 mmol/L				
Any AE	1	1 (100.0%)	0	0 (0.0%)
Investigations	1	1 (100.0%)	0	0 (0.0%)
Electrocardiogram QT shortened	1	1 (100.0%)	0	0 (0.0%)
Nervous system disorders	1	1 (100.0%)	0	0 (0.0%)
Clonic convulsion	1	1 (100.0%)	0	0 (0.0%)
>5.5 mmol/L				
Any AE	31	0 (0.0%)	26	0 (0.0%)
Sex				
Male				
Any AE	16	0 (0.0%)	13	0 (0.0%)
Female				
Any AE	17	1 (5.9%)	16	0 (0.0%)
Investigations	17	1 (5.9%)	16	0 (0.0%)
Electrocardiogram QT shortened	17	1 (5.9%)	16	0 (0.0%)
Nervous system disorders	17	1 (5.9%)	16	0 (0.0%)
Clonic convulsion	17	1 (5.9%)	16	0 (0.0%)
Age (years)				
<65 years				
Any AE	27	1 (3.7%)	14	0 (0.0%)
Investigations	27	1 (3.7%)	14	0 (0.0%)
Electrocardiogram QT shortened	27	1 (3.7%)	14	0 (0.0%)
Nervous system disorders	27	1 (3.7%)	14	0 (0.0%)
Clonic convulsion	27	1 (3.7%)	14	0 (0.0%)
>=65 years				
Any AE	6	0 (0.0%)	15	0 (0.0%)
Region				
USA				
Any AE	17	0 (0.0%)	15	0 (0.0%)
Rest of world				
Any AE	16	1 (6.3%)	14	0 (0.0%)
Investigations	16	1 (6.3%)	14	0 (0.0%)
Electrocardiogram QT shortened	16	1 (6.3%)	14	0 (0.0%)
Nervous system disorders	16	1 (6.3%)	14	0 (0.0%)
Clonic convulsion	16	1 (6.3%)	14	0 (0.0%)

t_ener_ae_dae_socpt.pdf generated by energize_ae_soc_pt.sas at 16:43:37 on 25 February 2021

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Table 7.2.1.8 - Study ENERGIZE: Adverse events (AE) by SOC and PT occurring in at least 10% of subjects in any treatment group, SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		10g ZS (N=29)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	33	11 (33.3%)	29	9 (31.0%)	0.90 (0.31 , 2.62)	0.8468	0.93 (0.45 , 1.92)	0.8470	-2.30 (-25.58 , 20.99)	0.8466	
Gastrointestinal disorders: All	33	2 (6.1%)	29	4 (13.8%)	2.48 (0.42 , 14.67)	0.3165	2.28 (0.45 , 11.53)	0.3205	7.73 (-7.23 , 22.69)	0.3110	
Gastrointestinal disorders: Nausea	33	2 (6.1%)	29	3 (10.3%)	1.79 (0.28 , 11.53)	0.5409	1.71 (0.31 , 9.52)	0.5419	4.28 (-9.47 , 18.04)	0.5415	
Injury, poisoning and procedural complications: All	33	1 (3.0%)	29	3 (10.3%)	3.69 (0.36 , 37.63)	0.2701	3.41 (0.38 , 31.04)	0.2757	7.31 (-5.22 , 19.85)	0.2527	
Metabolism and nutrition disorders: All	33	5 (15.2%)	29	5 (17.2%)	1.17 (0.30 , 4.52)	0.8235	1.14 (0.37 , 3.54)	0.8234	2.09 (-16.31 , 20.49)	0.8239	
Metabolism and nutrition disorders: Hypoglycaemia	33	3 (9.1%)	29	4 (13.8%)	1.60 (0.33 , 7.83)	0.5619	1.52 (0.37 , 6.22)	0.5626	4.70 (-11.23 , 20.63)	0.5629	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

t_ener_ae_any_socpt.pdf generated by energize_ae_soc_pt.sas at 16:43:14 on 25 February 2021

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Table 7.2.1.9 - Study ENERGIZE: Serious adverse events (SAE) by SOC and PT occurring in at least 5% of subjects in any treatment group, SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		10g ZS (N=29)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	33	4 (12.1%)	29	2 (6.9%)	0.54 (0.09 , 3.17)	0.4928	0.57 (0.11 , 2.88)	0.4957	-5.22 (-19.68 , 9.23)	0.4788	
Metabolism and nutrition disorders: All	33	2 (6.1%)	29	0 (0.0%)	0.21 (0.01 , 4.64)	0.3255	0.23 (0.01 , 4.54)	0.3316	-6.06 (-14.20 , 2.08)	0.1445	
Metabolism and nutrition disorders: Hyperkalaemia	33	2 (6.1%)	29	0 (0.0%)	0.21 (0.01 , 4.64)	0.3255	0.23 (0.01 , 4.54)	0.3316	-6.06 (-14.20 , 2.08)	0.1445	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 7.2.1.10 - Study ENERGIZE: AEs graded as severe by SOC and PT occurring in at least 5% of subjects in any treatment group, SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		10g ZS (N=29)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	33	4 (12.1%)	29	2 (6.9%)	0.54 (0.09 , 3.17)	0.4928	0.57 (0.11 , 2.88)	0.4957	-5.22 (-19.68 , 9.23)	0.4788	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 7.2.1.11 - Study ENERGIZE: AEs graded as non-severe by SOC and PT occurring in at least 10% of subjects in any treatment group, SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		10g ZS (N=29)								
Subgroup / SOC :PT	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall											
Any AE	33	8 (24.2%)	29	9 (31.0%)	1.41 (0.46 , 4.31)	0.5505	1.28 (0.57 , 2.88)	0.5507	6.79 (-15.51 , 29.09)	0.5505	
Gastrointestinal disorders: All	33	2 (6.1%)	29	4 (13.8%)	2.48 (0.42 , 14.67)	0.3165	2.28 (0.45 , 11.53)	0.3205	7.73 (-7.23 , 22.69)	0.3110	
Gastrointestinal disorders: Nausea	33	2 (6.1%)	29	3 (10.3%)	1.79 (0.28 , 11.53)	0.5409	1.71 (0.31 , 9.52)	0.5419	4.28 (-9.47 , 18.04)	0.5415	
Metabolism and nutrition disorders: All	33	4 (12.1%)	29	4 (13.8%)	1.16 (0.26 , 5.12)	0.8448	1.14 (0.31 , 4.15)	0.8447	1.67 (-15.11 , 18.45)	0.8452	
Metabolism and nutrition disorders: Hypoglycaemia	33	3 (9.1%)	29	3 (10.3%)	1.15 (0.21 , 6.22)	0.8677	1.14 (0.25 , 5.21)	0.8677	1.25 (-13.55 , 16.05)	0.8681	

Overall adverse events by SOC/PT are shown if either i) in either treatment group at least 10% of subjects overall report events or ii) in either treatment group at least 10 subjects and at least 1% report events
Subgroup analysis is only shown if the overall odds ratio is significant (p <=0.05)
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)

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Table 7.2.2.1 - Study ENERGIZE: AEs of special interest: hypokalemia—subjects experiencing any adverse event (AE), SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	29	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_aesi_hypokal_ae.pdf generated by energize_ae_soc_pt.sas at 16:42:31 on 25 February 2021

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Table 7.2.2.2 - Study ENERGIZE: AEs of special interest: hypokalemia—subjects experiencing any serious adverse event (SAE), SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	29	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_aesi_hypokal_sae.pdf generated by energize_ae_soc_pt.sas at 16:42:36 on 25 February 2021

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Table 7.2.2.3 - Study ENERGIZE: AEs of special interest: hypokalemia—subjects experiencing any AE graded as severe, SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	29	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_aesi_hypokal_sev.pdf generated by energize_ae_soc_pt.sas at 16:42:40 on 25 February 2021

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Table 7.2.2.4 - Study ENERGIZE: AEs of special interest: hypokalemia—subjects experiencing any AE graded as non-severe, SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	29	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_aesi_hypokal_nsev.pdf generated by energize_ae_soc_pt.sas at 16:42:47 on 25 February 2021

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Table 7.2.2.5 - Study ENERGIZE: AEs of special interest: hypoglycaemia—subjects experiencing any adverse event (AE), SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	3 (9.1%)	29	4 (13.8%)	1.60 (0.33 , 7.83)	0.5619	1.52 (0.37 , 6.22)	0.5626	4.70 (-11.23 , 20.63)	0.5629	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_aesi_hypogly_ae.pdf generated by energize_ae_soc_pt.sas at 16:42:52 on 25 February 2021

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Table 7.2.2.6 - Study ENERGIZE: AEs of special interest: hypoglycaemia—subjects experiencing any serious adverse event (SAE), SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	29	0 (0.0%)							

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_aesi_hypogly_sae.pdf generated by energize_ae_soc_pt.sas at 16:42:57 on 25 February 2021

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Table 7.2.2.7 - Study ENERGIZE: AEs of special interest: hypoglycaemia—subjects experiencing any AE graded as severe, SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	0 (0.0%)	29	1 (3.4%)	3.53 (0.14 , 89.98)	0.4458	3.40 (0.14 , 80.36)	0.4482	3.45 (-3.19 , 10.09)	0.3088	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_aesi_hypogly_sev.pdf generated by energize_ae_soc_pt.sas at 16:43:03 on 25 February 2021

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Table 7.2.2.8 - Study ENERGIZE: AEs of special interest: hypoglycaemia—subjects experiencing any AE graded as non-severe, SZC 10g TID vs. placebo, overall and by subgroups (safety population)

	Placebo (N=33)		Lokelma 10g TID (N=29)								
Subgroup / Category	N	n (%)	N	n (%)	Odds Ratio (95% CI)	OR p-value	Risk Ratio (95% CI)	RR p-value	Absolute Risk Difference(%) (95% CI)	ARR p-value	Subgroup interaction test OR p-value
Overall	33	3 (9.1%)	29	3 (10.3%)	1.15 (0.21 , 6.22)	0.8677	1.14 (0.25 , 5.21)	0.8677	1.25 (-13.55 , 16.05)	0.8681	

Subgroups shown if at least 10 subjects overall in either treatment group report events
If counts are zero in one treatment group, 0.5 is added to the count for each group (Haldane-Anscombe correction)
t_ener_aesi_hypogly_nsev.pdf generated by energize_ae_soc_pt.sas at 16:43:09 on 25 February 2021