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Dossier zur Nutzenbewertung gemäß § 35a SGB V

Relugolix (Orgovyx®)

Accord Healthcare GmbH

Modul 4A – Anhang 4-G

Behandlung von erwachsenen Patienten mit fortgeschrittenem hormonsensitivem Prostatakarzinom

Medizinischer Nutzen und
medizinischer Zusatznutzen,
Patientengruppen mit therapeutisch
bedeutsamem Zusatznutzen

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4 Weitere Ergebnisse der nutzenbewertungsrelevanten Teilpopulation b) der Studie HERO

4.1 Subgruppenergebnisse

4.1.1 Mortalität

4.1.1.1 Gesamtüberleben

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.OS.KM.MITTM0.S1: Time to Overall Survival, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: NC							
<= 75 years old							
Relugolix	304	3 (1.0)	301 (99.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	153	1 (0.7)	152 (99.3)	NC [NC;NC]			
> 75 years old							
Relugolix	123	0	123 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	60	3 (5.0)	57 (95.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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Table MOR.OS.KM.MITTM0.S2: Time to Overall Survival, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region I, Interaction p-value: NC							
North and South America							
Relugolix	161	2 (1.2)	159 (98.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	80	1 (1.3)	79 (98.8)	NC [NC;NC]			
Europe							
Relugolix	155	1 (0.6)	154 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	78	3 (3.8)	75 (96.2)	NC [NC;NC]			
Asia and Rest of World							
Relugolix	111	0	111 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	55	0	55 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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Table MOR.OS.KM.MITTM0.S3: Time to Overall Survival, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: NC							
Not Hispanic or Latino							
Relugolix	381	3 (0.8)	378 (99.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	188	4 (2.1)	184 (97.9)	NC [NC;NC]			
Hispanic or Latino							
Relugolix	37	0	37 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	22	0	22 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	9	0	9 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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Table MOR.OS.KM.MITTM0.S4: Time to Overall Survival, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: NC							
Asian							
Relugolix	94	0	94 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	51	0	51 (100.0)	NC [NC;NC]			
Black or African American							
Relugolix	21	0	21 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	12	1 (8.3)	11 (91.7)	NC [NC;NC]			
White							
Relugolix	292	3 (1.0)	289 (99.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	139	3 (2.2)	136 (97.8)	NC [NC;NC]			
Others							
Relugolix	14	0	14 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	7	0	7 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	6	0	6 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

Table MOR.OS.KM.MITTM0.S5: Time to Overall Survival, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Gleason Score at Study Entry, Interaction p-value: NC							
< 8							
Relugolix	252	2 (0.8)	250 (99.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	136	2 (1.5)	134 (98.5)	NC [NC;NC]			
>= 8							
Relugolix	163	1 (0.6)	162 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	74	2 (2.7)	72 (97.3)	NC [NC;NC]			
Missing							
Relugolix	12	0	12 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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Table MOR.OS.KM.MITTM0.S6: Time to Overall Survival, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: NC							
< 250 ng/dL							
Relugolix	37	0	37 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	20	0	20 (100.0)	NC [NC;NC]			
>= 250 ng/dL							
Relugolix	383	3 (0.8)	380 (99.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	185	4 (2.2)	181 (97.8)	NC [NC;NC]			
Missing							
Relugolix	7	0	7 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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Table MOR.OS.KM.MITTM0.S7: Time to Overall Survival, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: NC							
< 20 ng/mL							
Relugolix	320	3 (0.9)	317 (99.1)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	169	2 (1.2)	167 (98.8)	NC [NC;NC]			
>= 20 ng/mL							
Relugolix	107	0	107 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	44	2 (4.5)	42 (95.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.OS.KM.MITTM0.S8: Time to Overall Survival, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: NC							
Asia (Excl. Korea)							
Relugolix	70	0	70 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	36	0	36 (100.0)	NC [NC;NC]			
Rest of World							
Relugolix	357	3 (0.8)	354 (99.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	177	4 (2.3)	173 (97.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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4.1.2 Mortalität/ Morbidität

4.1.2.1 Major Adverse Cardiovascular Events

4.1.2.1.1 Hauptanalyse des kombinierten Endpunkts

Myovant Sciences, Inc.: HERO AMNOG

Table MC.T2MACE1.KM.SAFM0.S5: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Gleason Score at Study Entry, Interaction p-value: 0.2703							
< 8							
Relugolix	252	4 (1.6)	248 (98.4)	NE [NE;NE]	NE	0.360 [0.101;1.274]	0.1130
Leuprolide	136	6 (4.4)	130 (95.6)	NE [NE;NE]			
>= 8							
Relugolix	163	1 (0.6)	162 (99.4)	NE [NE;NE]	NE	0.089 [0.010;0.758]	0.0269
Leuprolide	74	5 (6.8)	69 (93.2)	NE [NE;NE]			
Missing							
Relugolix	12	0	12 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAFM0.S1: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.3048							
<= 75 years old							
Relugolix	304	4 (1.3)	300 (98.7)	NE [NE;NE]	NE	0.336 [0.095;1.191]	0.0912
Leuprolide	153	6 (3.9)	147 (96.1)	NE [NE;NE]			
> 75 years old							
Relugolix	123	1 (0.8)	122 (99.2)	NE [NE;NE]	NE	0.091 [0.011;0.780]	0.0288
Leuprolide	60	5 (8.3)	55 (91.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAFM0.S4: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.4054							
Asian							
Relugolix	94	2 (2.1)	92 (97.9)	NE [NE;NE]	NE	0.546 [0.077;3.877]	0.5453
Leuprolide	51	2 (3.9)	49 (96.1)	NE [NE;NE]			
Black or African American							
Relugolix	21	0	21 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	12	2 (16.7)	10 (83.3)	NC [NC;NC]			
White							
Relugolix	292	3 (1.0)	289 (99.0)	NE [NE;NE]	NE	0.199 [0.051;0.769]	0.0192
Leuprolide	139	7 (5.0)	132 (95.0)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAFM0.S4: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4054							
Others							
Relugolix	14	0	14 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	7	0	7 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	6	0	6 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAFM0.S7: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.6157							
< 20 ng/mL							
Relugolix	320	4 (1.3)	316 (98.8)	NE [NE;NE]	NE	0.259 [0.078;0.861]	0.0275
Leuprolide	169	8 (4.7)	161 (95.3)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	107	1 (0.9)	106 (99.1)	NE [NE;NE]	NE	0.135 [0.014;1.294]	0.0824
Leuprolide	44	3 (6.8)	41 (93.2)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAFM0.S8: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.8934							
Asia (Excl. Korea)							
Relugolix	70	1 (1.4)	69 (98.6)	NE [NE;NE]	NE	0.259 [0.023;2.853]	0.2695
Leuprolide	36	2 (5.6)	34 (94.4)	NE [NE;NE]			
Rest of World							
Relugolix	357	4 (1.1)	353 (98.9)	NE [NE;NE]	NE	0.215 [0.066;0.700]	0.0106
Leuprolide	177	9 (5.1)	168 (94.9)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAFM0.S2: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: NC							
North and South America							
Relugolix	161	2 (1.2)	159 (98.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	80	3 (3.8)	77 (96.3)	NC [NC;NC]			
Europe							
Relugolix	155	1 (0.6)	154 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	78	6 (7.7)	72 (92.3)	NC [NC;NC]			
Asia and Rest of World							
Relugolix	111	2 (1.8)	109 (98.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	55	2 (3.6)	53 (96.4)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAFM0.S3: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: NC							
Not Hispanic or Latino							
Relugolix	381	4 (1.0)	377 (99.0)	NE [NE;NE]	NE	0.175 [0.056;0.551]	0.0029
Leuprolide	188	11 (5.9)	177 (94.1)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	37	1 (2.7)	36 (97.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	22	0	22 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	9	0	9 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAFM0.S6: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: NC							
< 250 ng/dL							
Relugolix	37	1 (2.7)	36 (97.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	20	0	20 (100.0)	NC [NC;NC]			
>= 250 ng/dL							
Relugolix	383	4 (1.0)	379 (99.0)	NE [NE;NE]	NE	0.172 [0.055;0.539]	0.0025
Leuprolide	185	11 (5.9)	174 (94.1)	NE [NE;NE]			
Missing							
Relugolix	7	0	7 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

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4.1.2.1.2 Sensitivitätsanalyse des kombinierten Endpunkts

Myovant Sciences, Inc.: HERO AMNOG

Table MC.T2MACE2.KM.SAFM0.S8: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.7971							
Asia (Excl. Korea)							
Relugolix	70	1 (1.4)	69 (98.6)	NE [NE;NE]	NE	0.260 [0.024;2.867]	0.2714
Leuprolide	36	2 (5.6)	34 (94.4)	NE [NE;NE]			
Rest of World							
Relugolix	357	3 (0.8)	354 (99.2)	NE [NE;NE]	NE	0.181 [0.048;0.684]	0.0117
Leuprolide	177	8 (4.5)	169 (95.5)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE2.KM.SAFM0.S7: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.9799							
< 20 ng/mL							
Relugolix	320	3 (0.9)	317 (99.1)	NE [NE;NE]	NE	0.194 [0.052;0.733]	0.0156
Leuprolide	169	8 (4.7)	161 (95.3)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	107	1 (0.9)	106 (99.1)	NE [NE;NE]	NE	0.201 [0.018;2.221]	0.1908
Leuprolide	44	2 (4.5)	42 (95.5)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

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Table MC.T2MACE2.KM.SAFM0.S1: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: NC							
<= 75 years old							
Relugolix	304	3 (1.0)	301 (99.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	153	5 (3.3)	148 (96.7)	NC [NC;NC]			
> 75 years old							
Relugolix	123	1 (0.8)	122 (99.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	60	5 (8.3)	55 (91.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE2.KM.SAFM0.S2: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: NC							
North and South America							
Relugolix	161	1 (0.6)	160 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	80	2 (2.5)	78 (97.5)	NC [NC;NC]			
Europe							
Relugolix	155	1 (0.6)	154 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	78	6 (7.7)	72 (92.3)	NC [NC;NC]			
Asia and Rest of World							
Relugolix	111	2 (1.8)	109 (98.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	55	2 (3.6)	53 (96.4)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2MACE2.KM.SAFM0.S3: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: NC							
Not Hispanic or Latino							
Relugolix	381	3 (0.8)	378 (99.2)	NE [NE;NE]	NE	0.144 [0.040;0.525]	0.0033
Leuprolide	188	10 (5.3)	178 (94.7)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	37	1 (2.7)	36 (97.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	22	0	22 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	9	0	9 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

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Table MC.T2MACE2.KM.SAFM0.S4: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: NC							
Asian							
Relugolix	94	2 (2.1)	92 (97.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	51	2 (3.9)	49 (96.1)	NC [NC;NC]			
Black or African American							
Relugolix	21	0	21 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	12	1 (8.3)	11 (91.7)	NC [NC;NC]			
White							
Relugolix	292	2 (0.7)	290 (99.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	139	7 (5.0)	132 (95.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2MACE2.KM.SAFM0.S4: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: NC							
Others							
Relugolix	14	0	14 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	7	0	7 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	6	0	6 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2MACE2.KM.SAFM0.S5: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: NC							
< 8							
Relugolix	252	3 (1.2)	249 (98.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	136	6 (4.4)	130 (95.6)	NC [NC;NC]			
>= 8							
Relugolix	163	1 (0.6)	162 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	74	4 (5.4)	70 (94.6)	NC [NC;NC]			
Missing							
Relugolix	12	0	12 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2MACE2.KM.SAFM0.S6: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: NC							
< 250 ng/dL							
Relugolix	37	1 (2.7)	36 (97.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	20	0	20 (100.0)	NC [NC;NC]			
>= 250 ng/dL							
Relugolix	383	3 (0.8)	380 (99.2)	NE [NE;NE]	NE	0.142 [0.039;0.514]	0.0030
Leuprolide	185	10 (5.4)	175 (94.6)	NE [NE;NE]			
Missing							
Relugolix	7	0	7 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

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4.1.2.1.3 Einzelkomponenten

Myovant Sciences, Inc.: HERO AMNOG

Table MC.T2DTHALL.KM.SAFM0.S1: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: NC							
<= 75 years old							
Relugolix	304	1 (0.3)	303 (99.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	153	1 (0.7)	152 (99.3)	NC [NC;NC]			
> 75 years old							
Relugolix	123	0	123 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	60	3 (5.0)	57 (95.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHALL.KM.SAFM0.S2: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: NC							
North and South America							
Relugolix	161	1 (0.6)	160 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	80	1 (1.3)	79 (98.8)	NC [NC;NC]			
Europe							
Relugolix	155	0	155 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	78	3 (3.8)	75 (96.2)	NC [NC;NC]			
Asia and Rest of World							
Relugolix	111	0	111 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	55	0	55 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2DTHALL.KM.SAFM0.S3: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: NC							
Not Hispanic or Latino							
Relugolix	381	1 (0.3)	380 (99.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	188	4 (2.1)	184 (97.9)	NC [NC;NC]			
Hispanic or Latino							
Relugolix	37	0	37 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	22	0	22 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	9	0	9 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2DTHALL.KM.SAFM0.S4: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: NC							
Asian							
Relugolix	94	0	94 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	51	0	51 (100.0)	NC [NC;NC]			
Black or African American							
Relugolix	21	0	21 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	12	1 (8.3)	11 (91.7)	NC [NC;NC]			
White							
Relugolix	292	1 (0.3)	291 (99.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	139	3 (2.2)	136 (97.8)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHALL.KM.SAFM0.S4: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: NC							
Others							
Relugolix	14	0	14 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	7	0	7 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	6	0	6 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHALL.KM.SAFM0.S5: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: NC							
< 8							
Relugolix	252	1 (0.4)	251 (99.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	136	2 (1.5)	134 (98.5)	NC [NC;NC]			
>= 8							
Relugolix	163	0	163 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	74	2 (2.7)	72 (97.3)	NC [NC;NC]			
Missing							
Relugolix	12	0	12 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHALL.KM.SAFM0.S6: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: NC							
< 250 ng/dL							
Relugolix	37	0	37 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	20	0	20 (100.0)	NC [NC;NC]			
>= 250 ng/dL							
Relugolix	383	1 (0.3)	382 (99.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	185	4 (2.2)	181 (97.8)	NC [NC;NC]			
Missing							
Relugolix	7	0	7 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHALL.KM.SAFM0.S7: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: NC							
< 20 ng/mL							
Relugolix	320	1 (0.3)	319 (99.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	169	2 (1.2)	167 (98.8)	NC [NC;NC]			
>= 20 ng/mL							
Relugolix	107	0	107 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	44	2 (4.5)	42 (95.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHALL.KM.SAFM0.S8: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: NC							
Asia (Excl. Korea)							
Relugolix	70	0	70 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	36	0	36 (100.0)	NC [NC;NC]			
Rest of World							
Relugolix	357	1 (0.3)	356 (99.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	177	4 (2.3)	173 (97.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHCV.KM.SAFM0.S1: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: NC							
<= 75 years old							
Relugolix	304	0	304 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	153	0	153 (100.0)	NC [NC;NC]			
> 75 years old							
Relugolix	123	0	123 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	60	3 (5.0)	57 (95.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHCV.KM.SAFM0.S2: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: NC							
North and South America							
Relugolix	161	0	161 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	80	0	80 (100.0)	NC [NC;NC]			
Europe							
Relugolix	155	0	155 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	78	3 (3.8)	75 (96.2)	NC [NC;NC]			
Asia and Rest of World							
Relugolix	111	0	111 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	55	0	55 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHCV.KM.SAFM0.S3: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: NC							
Not Hispanic or Latino							
Relugolix	381	0	381 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	188	3 (1.6)	185 (98.4)	NC [NC;NC]			
Hispanic or Latino							
Relugolix	37	0	37 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	22	0	22 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	9	0	9 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHCV.KM.SAFM0.S4: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: NC							
Asian							
Relugolix	94	0	94 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	51	0	51 (100.0)	NC [NC;NC]			
Black or African American							
Relugolix	21	0	21 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	12	0	12 (100.0)	NC [NC;NC]			
White							
Relugolix	292	0	292 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	139	3 (2.2)	136 (97.8)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHCV.KM.SAFM0.S4: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: NC							
Others							
Relugolix	14	0	14 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	7	0	7 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	6	0	6 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHCV.KM.SAFM0.S5: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: NC							
< 8							
Relugolix	252	0	252 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	136	2 (1.5)	134 (98.5)	NC [NC;NC]			
>= 8							
Relugolix	163	0	163 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	74	1 (1.4)	73 (98.6)	NC [NC;NC]			
Missing							
Relugolix	12	0	12 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHCV.KM.SAFM0.S6: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: NC							
< 250 ng/dL							
Relugolix	37	0	37 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	20	0	20 (100.0)	NC [NC;NC]			
>= 250 ng/dL							
Relugolix	383	0	383 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	185	3 (1.6)	182 (98.4)	NC [NC;NC]			
Missing							
Relugolix	7	0	7 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2DTHCV.KM.SAFM0.S7: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: NC							
< 20 ng/mL							
Relugolix	320	0	320 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	169	2 (1.2)	167 (98.8)	NC [NC;NC]			
>= 20 ng/mL							
Relugolix	107	0	107 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	44	1 (2.3)	43 (97.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2DTHCV.KM.SAFM0.S8: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: NC							
Asia (Excl. Korea)							
Relugolix	70	0	70 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	36	0	36 (100.0)	NC [NC;NC]			
Rest of World							
Relugolix	357	0	357 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	177	3 (1.7)	174 (98.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDMI.KM.SAFM0.S1: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: NC							
<= 75 years old							
Relugolix	304	3 (1.0)	301 (99.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	153	0	153 (100.0)	NC [NC;NC]			
> 75 years old							
Relugolix	123	0	123 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	60	1 (1.7)	59 (98.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDMI.KM.SAFM0.S2: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: NC							
North and South America							
Relugolix	161	0	161 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	80	1 (1.3)	79 (98.8)	NC [NC;NC]			
Europe							
Relugolix	155	1 (0.6)	154 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	78	0	78 (100.0)	NC [NC;NC]			
Asia and Rest of World							
Relugolix	111	2 (1.8)	109 (98.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	55	0	55 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2NDMI.KM.SAFM0.S3: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: NC							
Not Hispanic or Latino							
Relugolix	381	3 (0.8)	378 (99.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	188	1 (0.5)	187 (99.5)	NC [NC;NC]			
Hispanic or Latino							
Relugolix	37	0	37 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	22	0	22 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	9	0	9 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDMI.KM.SAFM0.S4: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: NC							
Asian							
Relugolix	94	2 (2.1)	92 (97.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	51	0	51 (100.0)	NC [NC;NC]			
Black or African American							
Relugolix	21	0	21 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	12	1 (8.3)	11 (91.7)	NC [NC;NC]			
White							
Relugolix	292	1 (0.3)	291 (99.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	139	0	139 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDMI.KM.SAFM0.S4: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: NC							
Others							
Relugolix	14	0	14 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	7	0	7 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	6	0	6 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDMI.KM.SAFM0.S5: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: NC							
< 8							
Relugolix	252	2 (0.8)	250 (99.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	136	0	136 (100.0)	NC [NC;NC]			
>= 8							
Relugolix	163	1 (0.6)	162 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	74	1 (1.4)	73 (98.6)	NC [NC;NC]			
Missing							
Relugolix	12	0	12 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2NDMI.KM.SAFM0.S6: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: NC							
< 250 ng/dL							
Relugolix	37	1 (2.7)	36 (97.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	20	0	20 (100.0)	NC [NC;NC]			
>= 250 ng/dL							
Relugolix	383	2 (0.5)	381 (99.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	185	1 (0.5)	184 (99.5)	NC [NC;NC]			
Missing							
Relugolix	7	0	7 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2NDMI.KM.SAFM0.S7: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: NC							
< 20 ng/mL							
Relugolix	320	2 (0.6)	318 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	169	1 (0.6)	168 (99.4)	NC [NC;NC]			
>= 20 ng/mL							
Relugolix	107	1 (0.9)	106 (99.1)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	44	0	44 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2NDMI.KM.SAFM0.S8: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: NC							
Asia (Excl. Korea)							
Relugolix	70	1 (1.4)	69 (98.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	36	0	36 (100.0)	NC [NC;NC]			
Rest of World							
Relugolix	357	2 (0.6)	355 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	177	1 (0.6)	176 (99.4)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Myovant Sciences, Inc.: HERO AMNOG

Table MC.T2NDSTRK.KM.SAFM0.S1: Time to Non-deadly Stroke, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: NC							
<= 75 years old							
Relugolix	304	0	304 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	153	5 (3.3)	148 (96.7)	NC [NC;NC]			
> 75 years old							
Relugolix	123	1 (0.8)	122 (99.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	60	2 (3.3)	58 (96.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDSTRK.KM.SAFM0.S2: Time to Non-deadly Stroke, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: NC							
North and South America							
Relugolix	161	1 (0.6)	160 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	80	2 (2.5)	78 (97.5)	NC [NC;NC]			
Europe							
Relugolix	155	0	155 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	78	3 (3.8)	75 (96.2)	NC [NC;NC]			
Asia and Rest of World							
Relugolix	111	0	111 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	55	2 (3.6)	53 (96.4)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2NDSTRK.KM.SAFM0.S3: Time to Non-deadly Stroke, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: NC							
Not Hispanic or Latino							
Relugolix	381	0	381 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	188	7 (3.7)	181 (96.3)	NC [NC;NC]			
Hispanic or Latino							
Relugolix	37	1 (2.7)	36 (97.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	22	0	22 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	9	0	9 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2NDSTRK.KM.SAFM0.S4: Time to Non-deadly Stroke, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: NC							
Asian							
Relugolix	94	0	94 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	51	2 (3.9)	49 (96.1)	NC [NC;NC]			
Black or African American							
Relugolix	21	0	21 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	12	1 (8.3)	11 (91.7)	NC [NC;NC]			
White							
Relugolix	292	1 (0.3)	291 (99.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	139	4 (2.9)	135 (97.1)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2NDSTRK.KM.SAFM0.S4: Time to Non-deadly Stroke, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: NC							
Others							
Relugolix	14	0	14 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	7	0	7 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	6	0	6 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDSTRK.KM.SAFM0.S5: Time to Non-deadly Stroke, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: NC							
< 8							
Relugolix	252	1 (0.4)	251 (99.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	136	4 (2.9)	132 (97.1)	NC [NC;NC]			
>= 8							
Relugolix	163	0	163 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	74	3 (4.1)	71 (95.9)	NC [NC;NC]			
Missing							
Relugolix	12	0	12 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2NDSTRK.KM.SAFM0.S6: Time to Non-deadly Stroke, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: NC							
< 250 ng/dL							
Relugolix	37	0	37 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	20	0	20 (100.0)	NC [NC;NC]			
>= 250 ng/dL							
Relugolix	383	1 (0.3)	382 (99.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	185	7 (3.8)	178 (96.2)	NC [NC;NC]			
Missing							
Relugolix	7	0	7 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDSTRK.KM.SAFM0.S7: Time to Non-deadly Stroke, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: NC							
< 20 ng/mL							
Relugolix	320	1 (0.3)	319 (99.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	169	6 (3.6)	163 (96.4)	NC [NC;NC]			
>= 20 ng/mL							
Relugolix	107	0	107 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	44	1 (2.3)	43 (97.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDSTRK.KM.SAFM0.S8: Time to Non-deadly Stroke, by subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: NC							
Asia (Excl. Korea)							
Relugolix	70	0	70 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	36	2 (5.6)	34 (94.4)	NC [NC;NC]			
Rest of World							
Relugolix	357	1 (0.3)	356 (99.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	177	5 (2.8)	172 (97.2)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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4.1.3 Morbidität

4.1.3.1 Gesundheitszustand (EuroQol-5-Dimension Visual Analog Scale)

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2EQ5D15.KM.MITTM0.S7: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.0397							
< 20 ng/mL							
Relugolix	320	84 (26.3)	236 (73.8)	NE [NE;NE]	NE	1.044 [0.723;1.508]	0.8176
Leuprolide	169	43 (25.4)	126 (74.6)	351.0 [NE;NE]			
>= 20 ng/mL							
Relugolix	107	23 (21.5)	84 (78.5)	NE [NE;NE]	NE	0.487 [0.260;0.912]	0.0246
Leuprolide	44	17 (38.6)	27 (61.4)	340.0 [258.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2EQ5D15.KM.MITTM0.S3: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.1709							
Not Hispanic or Latino							
Relugolix	381	91 (23.9)	290 (76.1)	NE [NE;NE]	NE	0.853 [0.605;1.202]	0.3634
Leuprolide	188	51 (27.1)	137 (72.9)	NE [344.0;NE]			
Hispanic or Latino							
Relugolix	37	15 (40.5)	22 (59.5)	NE [253.0;NE]	NE	1.724 [0.669;4.446]	0.2595
Leuprolide	22	6 (27.3)	16 (72.7)	NE [338.0;NE]			
Not Reported							
Relugolix	9	1 (11.1)	8 (88.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	3 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2EQ5D15.KM.MITTM0.S5: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.1711							
< 8							
Relugolix	252	65 (25.8)	187 (74.2)	NE [NE;NE]	NE	1.039 [0.689;1.567]	0.8553
Leuprolide	136	35 (25.7)	101 (74.3)	351.0 [344.0;NE]			
>= 8							
Relugolix	163	36 (22.1)	127 (77.9)	NE [NE;NE]	NE	0.653 [0.386;1.102]	0.1103
Leuprolide	74	23 (31.1)	51 (68.9)	NE [340.0;NE]			
Missing							
Relugolix	12	6 (50.0)	6 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2EQ5D15.KM.MITTM0.S8: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.3762							
Asia (Excl. Korea)							
Relugolix	70	17 (24.3)	53 (75.7)	NE [NE;NE]	NE	0.650 [0.316;1.339]	0.2427
Leuprolide	36	13 (36.1)	23 (63.9)	344.0 [337.0;NE]			
Rest of World							
Relugolix	357	90 (25.2)	267 (74.8)	NE [NE;NE]	NE	0.935 [0.657;1.330]	0.7069
Leuprolide	177	47 (26.6)	130 (73.4)	351.0 [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EQ5D15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4956							
Asian							
Relugolix	94	23 (24.5)	71 (75.5)	NE [NE;NE]	NE	0.684 [0.369;1.268]	0.2283
Leuprolide	51	18 (35.3)	33 (64.7)	344.0 [337.0;NE]			
Black or African American							
Relugolix	21	6 (28.6)	15 (71.4)	NE [173.0;NE]	NE	1.517 [0.306;7.517]	0.6101
Leuprolide	12	2 (16.7)	10 (83.3)	NE [94.0;NE]			
White							
Relugolix	292	74 (25.3)	218 (74.7)	NE [NE;NE]	NE	1.031 [0.687;1.548]	0.8818
Leuprolide	139	34 (24.5)	105 (75.5)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EQ5D15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4956							
Others							
Relugolix	14	4 (28.6)	10 (71.4)	NE [169.0;NE]	NE	0.476 [0.117;1.939]	0.3002
Leuprolide	7	4 (57.1)	3 (42.9)	351.0 [29.0;NE]			
Not Reported							
Relugolix	6	0	6 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	2 (50.0)	2 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2EQ5D15.KM.MITTM0.S2: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region I, Interaction p-value: 0.6680							
North and South America							
Relugolix	161	44 (27.3)	117 (72.7)	NE [NE;NE]	NE	1.037 [0.611;1.760]	0.8921
Leuprolide	80	20 (25.0)	60 (75.0)	NE [340.0;NE]			
Europe							
Relugolix	155	35 (22.6)	120 (77.4)	NE [NE;NE]	NE	0.843 [0.490;1.447]	0.5350
Leuprolide	78	21 (26.9)	57 (73.1)	351.0 [NE;NE]			
Asia and Rest of World							
Relugolix	111	28 (25.2)	83 (74.8)	NE [NE;NE]	NE	0.726 [0.405;1.301]	0.2823
Leuprolide	55	19 (34.5)	36 (65.5)	344.0 [337.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EQ5D15.KM.MITTM0.S6: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.7822							
< 250 ng/dL							
Relugolix	37	9 (24.3)	28 (75.7)	NE [339.0;NE]	NE	0.777 [0.276;2.185]	0.6321
Leuprolide	20	6 (30.0)	14 (70.0)	NE [336.0;NE]			
>= 250 ng/dL							
Relugolix	383	93 (24.3)	290 (75.7)	NE [NE;NE]	NE	0.906 [0.641;1.281]	0.5758
Leuprolide	185	49 (26.5)	136 (73.5)	351.0 [NE;NE]			
Missing							
Relugolix	7	5 (71.4)	2 (28.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	5 (62.5)	3 (37.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2EQ5D15.KM.MITTM0.S1: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.9344							
<= 75 years old							
Relugolix	304	70 (23.0)	234 (77.0)	NE [NE;NE]	NE	0.878 [0.595;1.295]	0.5105
Leuprolide	153	40 (26.1)	113 (73.9)	NE [344.0;NE]			
> 75 years old							
Relugolix	123	37 (30.1)	86 (69.9)	NE [NE;NE]	NE	0.853 [0.495;1.470]	0.5678
Leuprolide	60	20 (33.3)	40 (66.7)	351.0 [339.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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4.1.3.2 Symptomatik (European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire C30)

4.1.3.2.1 Skala: Fatigue

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2FAT15.KM.MITTM0.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.0821							
< 8							
Relugolix	252	110 (43.7)	142 (56.3)	355.0 [335.0;NE]	NE	1.344 [0.958;1.887]	0.0874
Leuprolide	136	48 (35.3)	88 (64.7)	NE [338.0;NE]			
>= 8							
Relugolix	163	72 (44.2)	91 (55.8)	343.0 [337.0;NE]	6.0	0.846 [0.569;1.258]	0.4088
Leuprolide	74	37 (50.0)	37 (50.0)	337.0 [254.0;NE]			
Missing							
Relugolix	12	5 (41.7)	7 (58.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITTM0.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.1950							
<= 75 years old							
Relugolix	304	131 (43.1)	173 (56.9)	NE [337.0;NE]	NE	1.005 [0.749;1.349]	0.9739
Leuprolide	153	67 (43.8)	86 (56.2)	340.0 [337.0;NE]			
> 75 years old							
Relugolix	123	56 (45.5)	67 (54.5)	343.0 [255.0;NE]	-14.0	1.492 [0.887;2.512]	0.1317
Leuprolide	60	19 (31.7)	41 (68.3)	357.0 [338.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.2460							
Asian							
Relugolix	94	36 (38.3)	58 (61.7)	NE [337.0;NE]	NE	1.136 [0.645;2.002]	0.6581
Leuprolide	51	18 (35.3)	33 (64.7)	NE [337.0;NE]			
Black or African American							
Relugolix	21	15 (71.4)	6 (28.6)	166.0 [36.0;335.0]	-164.0	1.751 [0.679;4.515]	0.2465
Leuprolide	12	6 (50.0)	6 (50.0)	330.0 [85.0;NE]			
White							
Relugolix	292	125 (42.8)	167 (57.2)	355.0 [339.0;NE]	-2.0	1.121 [0.816;1.540]	0.4799
Leuprolide	139	55 (39.6)	84 (60.4)	357.0 [338.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.2460							
Others							
Relugolix	14	7 (50.0)	7 (50.0)	339.0 [176.0;NE]	168.0	0.406 [0.136;1.211]	0.1060
Leuprolide	7	6 (85.7)	1 (14.3)	171.0 [29.0;NE]			
Not Reported							
Relugolix	6	4 (66.7)	2 (33.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	1 (25.0)	3 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITTM0.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.5093							
< 20 ng/mL							
Relugolix	320	142 (44.4)	178 (55.6)	343.0 [337.0;NE]	-14.0	1.173 [0.878;1.566]	0.2808
Leuprolide	169	68 (40.2)	101 (59.8)	357.0 [338.0;NE]			
>= 20 ng/mL							
Relugolix	107	45 (42.1)	62 (57.9)	NE [335.0;NE]	NE	0.952 [0.550;1.646]	0.8591
Leuprolide	44	18 (40.9)	26 (59.1)	NE [248.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITTM0.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.5622							
Not Hispanic or Latino							
Relugolix	381	163 (42.8)	218 (57.2)	355.0 [339.0;NE]	-2.0	1.096 [0.834;1.441]	0.5113
Leuprolide	188	75 (39.9)	113 (60.1)	357.0 [338.0;NE]			
Hispanic or Latino							
Relugolix	37	18 (48.6)	19 (51.4)	337.0 [176.0;NE]	NE	1.421 [0.617;3.269]	0.4089
Leuprolide	22	8 (36.4)	14 (63.6)	NE [171.0;NE]			
Not Reported							
Relugolix	9	6 (66.7)	3 (33.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	3 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITTM0.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.6167							
< 250 ng/dL							
Relugolix	37	20 (54.1)	17 (45.9)	253.0 [173.0;NE]	-85.0	1.375 [0.626;3.021]	0.4280
Leuprolide	20	9 (45.0)	11 (55.0)	338.0 [91.0;NE]			
>= 250 ng/dL							
Relugolix	383	164 (42.8)	219 (57.2)	355.0 [339.0;NE]	-2.0	1.111 [0.843;1.464]	0.4541
Leuprolide	185	73 (39.5)	112 (60.5)	357.0 [338.0;NE]			
Missing							
Relugolix	7	3 (42.9)	4 (57.1)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2FAT15.KM.MITTM0.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.8031							
North and South America							
Relugolix	161	87 (54.0)	74 (46.0)	257.0 [175.0;339.0]	-81.0	1.239 [0.849;1.808]	0.2664
Leuprolide	80	39 (48.8)	41 (51.3)	338.0 [251.0;NE]			
Europe							
Relugolix	155	58 (37.4)	97 (62.6)	355.0 [NE;NE]	NE	1.053 [0.667;1.663]	0.8243
Leuprolide	78	27 (34.6)	51 (65.4)	NE [338.0;NE]			
Asia and Rest of World							
Relugolix	111	42 (37.8)	69 (62.2)	NE [340.0;NE]	NE	1.029 [0.604;1.752]	0.9172
Leuprolide	55	20 (36.4)	35 (63.6)	NE [337.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITTM0.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.8287							
Asia (Excl. Korea)							
Relugolix	70	28 (40.0)	42 (60.0)	NE [260.0;NE]	NE	1.187 [0.615;2.293]	0.6095
Leuprolide	36	13 (36.1)	23 (63.9)	NE [337.0;NE]			
Rest of World							
Relugolix	357	159 (44.5)	198 (55.5)	343.0 [337.0;NE]	-14.0	1.097 [0.832;1.448]	0.5120
Leuprolide	177	73 (41.2)	104 (58.8)	357.0 [338.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITTM0.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.1563							
<= 75 years old							
Relugolix	304	148 (48.7)	156 (51.3)	339.0 [258.0;344.0]	NE	1.261 [0.939;1.693]	0.1239
Leuprolide	153	63 (41.2)	90 (58.8)	NE [336.0;NE]			
> 75 years old							
Relugolix	123	63 (51.2)	60 (48.8)	337.0 [170.0;NE]	84.0	0.869 [0.570;1.325]	0.5134
Leuprolide	60	33 (55.0)	27 (45.0)	253.0 [169.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITTM0.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.3202							
< 20 ng/mL							
Relugolix	320	158 (49.4)	162 (50.6)	337.0 [253.0;344.0]	NE	1.204 [0.913;1.587]	0.1889
Leuprolide	169	74 (43.8)	95 (56.2)	NE [329.0;NE]			
>= 20 ng/mL							
Relugolix	107	53 (49.5)	54 (50.5)	339.0 [175.0;NE]	2.0	0.902 [0.549;1.483]	0.6841
Leuprolide	44	22 (50.0)	22 (50.0)	337.0 [248.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITTM0.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: 0.3229							
< 250 ng/dL							
Relugolix	37	21 (56.8)	16 (43.2)	170.0 [85.0;NE]	NE	1.664 [0.737;3.757]	0.2205
Leuprolide	20	8 (40.0)	12 (60.0)	NE [91.0;NE]			
>= 250 ng/dL							
Relugolix	383	186 (48.6)	197 (51.4)	338.0 [260.0;344.0]	-2.0	1.081 [0.836;1.399]	0.5518
Leuprolide	185	84 (45.4)	101 (54.6)	340.0 [255.0;NE]			
Missing							
Relugolix	7	4 (57.1)	3 (42.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4285							
Asian							
Relugolix	94	40 (42.6)	54 (57.4)	344.0 [253.0;NE]	4.0	1.216 [0.711;2.081]	0.4744
Leuprolide	51	20 (39.2)	31 (60.8)	340.0 [330.0;NE]			
Black or African American							
Relugolix	21	15 (71.4)	6 (28.6)	166.0 [30.0;338.0]	0.0	1.077 [0.439;2.645]	0.8711
Leuprolide	12	7 (58.3)	5 (41.7)	166.0 [29.0;NE]			
White							
Relugolix	292	144 (49.3)	148 (50.7)	337.0 [257.0;344.0]	NE	1.163 [0.862;1.569]	0.3235
Leuprolide	139	61 (43.9)	78 (56.1)	NE [256.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.4285							
Others							
Relugolix	14	8 (57.1)	6 (42.9)	297.0 [78.0;NE]	207.0	0.467 [0.162;1.348]	0.1594
Leuprolide	7	6 (85.7)	1 (14.3)	90.0 [29.0;338.0]			
Not Reported							
Relugolix	6	4 (66.7)	2 (33.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	2 (50.0)	2 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITTM0.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.4539							
Asia (Excl. Korea)							
Relugolix	70	30 (42.9)	40 (57.1)	344.0 [169.0;NE]	NE	1.408 [0.734;2.700]	0.3026
Leuprolide	36	13 (36.1)	23 (63.9)	NE [330.0;NE]			
Rest of World							
Relugolix	357	181 (50.7)	176 (49.3)	337.0 [255.0;341.0]	-1.0	1.077 [0.831;1.397]	0.5746
Leuprolide	177	83 (46.9)	94 (53.1)	338.0 [254.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITTM0.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.5609							
< 8							
Relugolix	252	126 (50.0)	126 (50.0)	337.0 [252.0;342.0]	-3.0	1.212 [0.891;1.649]	0.2201
Leuprolide	136	60 (44.1)	76 (55.9)	340.0 [330.0;NE]			
>= 8							
Relugolix	163	79 (48.5)	84 (51.5)	341.0 [332.0;344.0]	3.0	1.043 [0.698;1.560]	0.8369
Leuprolide	74	34 (45.9)	40 (54.1)	338.0 [252.0;NE]			
Missing							
Relugolix	12	6 (50.0)	6 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2PAIN15.KM.MITTM0.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.7854							
North and South America							
Relugolix	161	93 (57.8)	68 (42.2)	252.0 [169.0;338.0]	-77.0	1.216 [0.842;1.757]	0.2964
Leuprolide	80	41 (51.3)	39 (48.8)	329.0 [169.0;NE]			
Europe							
Relugolix	155	74 (47.7)	81 (52.3)	340.0 [254.0;NE]	2.0	1.008 [0.674;1.508]	0.9682
Leuprolide	78	35 (44.9)	43 (55.1)	338.0 [248.0;NE]			
Asia and Rest of World							
Relugolix	111	44 (39.6)	67 (60.4)	344.0 [339.0;NE]	4.0	1.176 [0.693;1.994]	0.5487
Leuprolide	55	20 (36.4)	35 (63.6)	340.0 [334.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITTM0.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.8340							
Not Hispanic or Latino							
Relugolix	381	181 (47.5)	200 (52.5)	340.0 [333.0;344.0]	NE	1.120 [0.862;1.454]	0.3965
Leuprolide	188	82 (43.6)	106 (56.4)	NE [330.0;NE]			
Hispanic or Latino							
Relugolix	37	23 (62.2)	14 (37.8)	255.0 [86.0;344.0]	2.0	1.215 [0.592;2.494]	0.5955
Leuprolide	22	11 (50.0)	11 (50.0)	253.0 [35.0;NE]			
Not Reported							
Relugolix	9	7 (77.8)	2 (22.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	3 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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4.1.3.2.3 Skala: Übelkeit und Erbrechen

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2NAUS15.KM.MITTM0.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.1132							
Not Hispanic or Latino							
Relugolix	381	75 (19.7)	306 (80.3)	NE [NE;NE]	NE	0.818 [0.562;1.191]	0.2948
Leuprolide	188	43 (22.9)	145 (77.1)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	37	13 (35.1)	24 (64.9)	NE [183.0;NE]	NE	2.127 [0.693;6.525]	0.1869
Leuprolide	22	4 (18.2)	18 (81.8)	NE [NE;NE]			
Not Reported							
Relugolix	9	2 (22.2)	7 (77.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITTM0.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.1227							
< 20 ng/mL							
Relugolix	320	68 (21.3)	252 (78.8)	NE [NE;NE]	NE	1.077 [0.710;1.633]	0.7267
Leuprolide	169	33 (19.5)	136 (80.5)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	107	22 (20.6)	85 (79.4)	NE [NE;NE]	NE	0.579 [0.296;1.131]	0.1098
Leuprolide	44	14 (31.8)	30 (68.2)	NE [339.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITTM0.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.5854							
North and South America							
Relugolix	161	46 (28.6)	115 (71.4)	NE [NE;NE]	NE	1.114 [0.659;1.883]	0.6877
Leuprolide	80	20 (25.0)	60 (75.0)	NE [NE;NE]			
Europe							
Relugolix	155	26 (16.8)	129 (83.2)	NE [NE;NE]	NE	0.849 [0.450;1.603]	0.6133
Leuprolide	78	15 (19.2)	63 (80.8)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	111	18 (16.2)	93 (83.8)	NE [NE;NE]	NE	0.707 [0.340;1.467]	0.3518
Leuprolide	55	12 (21.8)	43 (78.2)	NE [339.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITTM0.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.5977							
<= 75 years old							
Relugolix	304	70 (23.0)	234 (77.0)	NE [NE;NE]	NE	0.889 [0.601;1.316]	0.5569
Leuprolide	153	39 (25.5)	114 (74.5)	NE [NE;NE]			
> 75 years old							
Relugolix	123	20 (16.3)	103 (83.7)	NE [NE;NE]	NE	1.136 [0.500;2.578]	0.7610
Leuprolide	60	8 (13.3)	52 (86.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITTM0.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.6135							
< 250 ng/dL							
Relugolix	37	6 (16.2)	31 (83.8)	NE [NE;NE]	NE	0.654 [0.200;2.142]	0.4828
Leuprolide	20	5 (25.0)	15 (75.0)	NE [336.0;NE]			
>= 250 ng/dL							
Relugolix	383	82 (21.4)	301 (78.6)	NE [NE;NE]	NE	0.901 [0.621;1.307]	0.5826
Leuprolide	185	42 (22.7)	143 (77.3)	NE [NE;NE]			
Missing							
Relugolix	7	2 (28.6)	5 (71.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITTM0.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.6539							
< 8							
Relugolix	252	53 (21.0)	199 (79.0)	NE [NE;NE]	NE	0.983 [0.625;1.546]	0.9405
Leuprolide	136	29 (21.3)	107 (78.7)	NE [NE;NE]			
>= 8							
Relugolix	163	33 (20.2)	130 (79.8)	NE [NE;NE]	NE	0.830 [0.462;1.490]	0.5324
Leuprolide	74	17 (23.0)	57 (77.0)	NE [NE;NE]			
Missing							
Relugolix	12	4 (33.3)	8 (66.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITTM0.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.8888							
Asia (Excl. Korea)							
Relugolix	70	10 (14.3)	60 (85.7)	NE [NE;NE]	NE	0.860 [0.313;2.366]	0.7702
Leuprolide	36	6 (16.7)	30 (83.3)	NE [339.0;NE]			
Rest of World							
Relugolix	357	80 (22.4)	277 (77.6)	NE [NE;NE]	NE	0.929 [0.637;1.354]	0.7007
Leuprolide	177	41 (23.2)	136 (76.8)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.9418							
Asian							
Relugolix	94	14 (14.9)	80 (85.1)	NE [NE;NE]	NE	0.764 [0.339;1.720]	0.5157
Leuprolide	51	10 (19.6)	41 (80.4)	NE [339.0;NE]			
Black or African American							
Relugolix	21	8 (38.1)	13 (61.9)	NE [171.0;NE]	NE	0.860 [0.281;2.631]	0.7921
Leuprolide	12	5 (41.7)	7 (58.3)	NE [94.0;NE]			
White							
Relugolix	292	64 (21.9)	228 (78.1)	NE [NE;NE]	NE	0.940 [0.612;1.444]	0.7784
Leuprolide	139	31 (22.3)	108 (77.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.9418							
Others							
Relugolix	14	3 (21.4)	11 (78.6)	NE [253.0;NE]	NE	1.491 [0.155;14.337]	0.7295
Leuprolide	7	1 (14.3)	6 (85.7)	NE [29.0;NE]			
Not Reported							
Relugolix	6	1 (16.7)	5 (83.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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4.1.3.2.4 Skala: Atemnot

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2DYSP15.KM.MITTM0.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.1783							
<= 75 years old							
Relugolix	304	102 (33.6)	202 (66.4)	NE [342.0;NE]	NE	0.932 [0.670;1.297]	0.6772
Leuprolide	153	54 (35.3)	99 (64.7)	344.0 [340.0;NE]			
> 75 years old							
Relugolix	123	36 (29.3)	87 (70.7)	350.0 [350.0;NE]	6.0	0.612 [0.365;1.026]	0.0625
Leuprolide	60	24 (40.0)	36 (60.0)	344.0 [330.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITTM0.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.2018							
< 250 ng/dL							
Relugolix	37	12 (32.4)	25 (67.6)	NE [342.0;NE]	NE	0.489 [0.216;1.108]	0.0866
Leuprolide	20	11 (55.0)	9 (45.0)	295.0 [92.0;NE]			
>= 250 ng/dL							
Relugolix	383	123 (32.1)	260 (67.9)	350.0 [344.0;NE]	6.0	0.863 [0.639;1.165]	0.3357
Leuprolide	185	65 (35.1)	120 (64.9)	344.0 [340.0;NE]			
Missing							
Relugolix	7	3 (42.9)	4 (57.1)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	2 (25.0)	6 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITTM0.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.3419							
< 20 ng/mL							
Relugolix	320	109 (34.1)	211 (65.9)	NE [342.0;NE]	NE	0.895 [0.656;1.220]	0.4818
Leuprolide	169	63 (37.3)	106 (62.7)	344.0 [340.0;NE]			
>= 20 ng/mL							
Relugolix	107	29 (27.1)	78 (72.9)	350.0 [350.0;NE]	NE	0.638 [0.341;1.192]	0.1584
Leuprolide	44	15 (34.1)	29 (65.9)	NE [340.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITTM0.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.4884							
< 8							
Relugolix	252	77 (30.6)	175 (69.4)	NE [342.0;NE]	NE	0.763 [0.535;1.087]	0.1340
Leuprolide	136	51 (37.5)	85 (62.5)	344.0 [341.0;NE]			
>= 8							
Relugolix	163	56 (34.4)	107 (65.6)	350.0 [350.0;NE]	NE	0.938 [0.589;1.495]	0.7887
Leuprolide	74	26 (35.1)	48 (64.9)	NE [340.0;NE]			
Missing							
Relugolix	12	5 (41.7)	7 (58.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITTM0.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.7715							
Not Hispanic or Latino							
Relugolix	381	124 (32.5)	257 (67.5)	350.0 [344.0;NE]	6.0	0.798 [0.595;1.071]	0.1333
Leuprolide	188	70 (37.2)	118 (62.8)	344.0 [340.0;NE]			
Hispanic or Latino							
Relugolix	37	7 (18.9)	30 (81.1)	NE [NE;NE]	NE	0.675 [0.227;2.010]	0.4806
Leuprolide	22	6 (27.3)	16 (72.7)	NE [337.0;NE]			
Not Reported							
Relugolix	9	7 (77.8)	2 (22.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITTM0.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.7931							
Asia (Excl. Korea)							
Relugolix	70	20 (28.6)	50 (71.4)	NE [340.0;NE]	NE	0.903 [0.432;1.885]	0.7852
Leuprolide	36	11 (30.6)	25 (69.4)	344.0 [344.0;NE]			
Rest of World							
Relugolix	357	118 (33.1)	239 (66.9)	350.0 [344.0;NE]	6.0	0.812 [0.601;1.096]	0.1726
Leuprolide	177	67 (37.9)	110 (62.1)	344.0 [340.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.7992							
Asian							
Relugolix	94	28 (29.8)	66 (70.2)	NE [340.0;NE]	NE	0.921 [0.498;1.704]	0.7942
Leuprolide	51	16 (31.4)	35 (68.6)	NE [344.0;NE]			
Black or African American							
Relugolix	21	6 (28.6)	15 (71.4)	NE [335.0;NE]	NE	1.445 [0.291;7.161]	0.6524
Leuprolide	12	2 (16.7)	10 (83.3)	NE [258.0;NE]			
White							
Relugolix	292	97 (33.2)	195 (66.8)	350.0 [342.0;NE]	9.0	0.737 [0.531;1.023]	0.0681
Leuprolide	139	57 (41.0)	82 (59.0)	341.0 [338.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.7992							
Others							
Relugolix	14	3 (21.4)	11 (78.6)	NE [99.0;NE]	NE	0.656 [0.130;3.302]	0.6094
Leuprolide	7	3 (42.9)	4 (57.1)	351.0 [165.0;NE]			
Not Reported							
Relugolix	6	4 (66.7)	2 (33.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITTM0.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region I, Interaction p-value: 0.8100							
North and South America							
Relugolix	161	50 (31.1)	111 (68.9)	NE [342.0;NE]	NE	0.765 [0.486;1.203]	0.2461
Leuprolide	80	30 (37.5)	50 (62.5)	341.0 [337.0;NE]			
Europe							
Relugolix	155	55 (35.5)	100 (64.5)	350.0 [342.0;NE]	6.0	0.809 [0.523;1.251]	0.3408
Leuprolide	78	32 (41.0)	46 (59.0)	344.0 [337.0;NE]			
Asia and Rest of World							
Relugolix	111	33 (29.7)	78 (70.3)	NE [NE;NE]	NE	0.976 [0.537;1.775]	0.9377
Leuprolide	55	16 (29.1)	39 (70.9)	NE [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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4.1.3.2.5 Skala: Appetitlosigkeit

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2APPT15.KM.MITTM0.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.1438							
Asia (Excl. Korea)							
Relugolix	70	17 (24.3)	53 (75.7)	NE [344.0;NE]	NE	2.349 [0.790;6.980]	0.1244
Leuprolide	36	4 (11.1)	32 (88.9)	NE [344.0;NE]			
Rest of World							
Relugolix	357	82 (23.0)	275 (77.0)	NE [NE;NE]	NE	0.994 [0.681;1.451]	0.9751
Leuprolide	177	40 (22.6)	137 (77.4)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2APPT15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.2128							
Asian							
Relugolix	94	19 (20.2)	75 (79.8)	NE [NE;NE]	NE	1.507 [0.633;3.585]	0.3538
Leuprolide	51	7 (13.7)	44 (86.3)	NE [344.0;NE]			
Black or African American							
Relugolix	21	4 (19.0)	17 (81.0)	NE [NE;NE]	NE	0.429 [0.107;1.717]	0.2316
Leuprolide	12	4 (33.3)	8 (66.7)	NE [166.0;NE]			
White							
Relugolix	292	72 (24.7)	220 (75.3)	NE [345.0;NE]	NE	1.193 [0.775;1.836]	0.4230
Leuprolide	139	29 (20.9)	110 (79.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2APPT15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.2128							
Others							
Relugolix	14	3 (21.4)	11 (78.6)	NE [253.0;NE]	NE	0.364 [0.081;1.630]	0.1863
Leuprolide	7	4 (57.1)	3 (42.9)	338.0 [92.0;NE]			
Not Reported							
Relugolix	6	1 (16.7)	5 (83.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2APPT15.KM.MITTM0.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.3757							
<= 75 years old							
Relugolix	304	67 (22.0)	237 (78.0)	NE [345.0;NE]	NE	1.242 [0.799;1.931]	0.3360
Leuprolide	153	28 (18.3)	125 (81.7)	NE [NE;NE]			
> 75 years old							
Relugolix	123	32 (26.0)	91 (74.0)	NE [NE;NE]	NE	0.887 [0.487;1.616]	0.6951
Leuprolide	60	16 (26.7)	44 (73.3)	NE [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2APPT15.KM.MITTM0.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.3935							
< 20 ng/mL							
Relugolix	320	74 (23.1)	246 (76.9)	NE [345.0;NE]	NE	1.210 [0.803;1.824]	0.3628
Leuprolide	169	33 (19.5)	136 (80.5)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	107	25 (23.4)	82 (76.6)	NE [NE;NE]	NE	0.847 [0.417;1.722]	0.6461
Leuprolide	44	11 (25.0)	33 (75.0)	NE [338.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2APPT15.KM.MITTM0.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.4792							
< 8							
Relugolix	252	56 (22.2)	196 (77.8)	NE [345.0;NE]	NE	1.294 [0.802;2.088]	0.2905
Leuprolide	136	24 (17.6)	112 (82.4)	NE [NE;NE]			
>= 8							
Relugolix	163	40 (24.5)	123 (75.5)	NE [NE;NE]	NE	0.993 [0.569;1.733]	0.9806
Leuprolide	74	18 (24.3)	56 (75.7)	NE [344.0;NE]			
Missing							
Relugolix	12	3 (25.0)	9 (75.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2APPT15.KM.MITTM0.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.6182							
Not Hispanic or Latino							
Relugolix	381	83 (21.8)	298 (78.2)	NE [345.0;NE]	NE	1.085 [0.736;1.600]	0.6789
Leuprolide	188	37 (19.7)	151 (80.3)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	37	13 (35.1)	24 (64.9)	NE [253.0;NE]	NE	1.415 [0.538;3.723]	0.4821
Leuprolide	22	6 (27.3)	16 (72.7)	NE [335.0;NE]			
Not Reported							
Relugolix	9	3 (33.3)	6 (66.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2APPT15.KM.MITTM0.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.7031							
North and South America							
Relugolix	161	45 (28.0)	116 (72.0)	NE [345.0;NE]	NE	1.048 [0.629;1.746]	0.8559
Leuprolide	80	22 (27.5)	58 (72.5)	NE [NE;NE]			
Europe							
Relugolix	155	32 (20.6)	123 (79.4)	NE [NE;NE]	NE	1.029 [0.557;1.901]	0.9267
Leuprolide	78	15 (19.2)	63 (80.8)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	111	22 (19.8)	89 (80.2)	NE [NE;NE]	NE	1.553 [0.663;3.636]	0.3104
Leuprolide	55	7 (12.7)	48 (87.3)	NE [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2APPT15.KM.MITTM0.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.7376							
< 250 ng/dL							
Relugolix	37	10 (27.0)	27 (73.0)	NE [NE;NE]	NE	1.394 [0.437;4.448]	0.5743
Leuprolide	20	4 (20.0)	16 (80.0)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	383	87 (22.7)	296 (77.3)	NE [345.0;NE]	NE	1.131 [0.770;1.663]	0.5293
Leuprolide	185	37 (20.0)	148 (80.0)	NE [NE;NE]			
Missing							
Relugolix	7	2 (28.6)	5 (71.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	3 (37.5)	5 (62.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITTM0.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.3487							
Asia (Excl. Korea)							
Relugolix	70	32 (45.7)	38 (54.3)	344.0 [169.0;NE]	NE	1.375 [0.721;2.622]	0.3335
Leuprolide	36	13 (36.1)	23 (63.9)	NE [253.0;NE]			
Rest of World							
Relugolix	357	188 (52.7)	169 (47.3)	256.0 [251.0;338.0]	3.0	0.988 [0.772;1.265]	0.9230
Leuprolide	177	95 (53.7)	82 (46.3)	253.0 [176.0;341.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITTM0.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.4146							
< 8							
Relugolix	252	129 (51.2)	123 (48.8)	257.0 [176.0;344.0]	-81.0	1.104 [0.820;1.485]	0.5144
Leuprolide	136	66 (48.5)	70 (51.5)	338.0 [198.0;NE]			
>= 8							
Relugolix	163	83 (50.9)	80 (49.1)	337.0 [253.0;NE]	84.0	0.905 [0.622;1.316]	0.6000
Leuprolide	74	41 (55.4)	33 (44.6)	253.0 [169.0;NE]			
Missing							
Relugolix	12	8 (66.7)	4 (33.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITTM0.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.4618							
<= 75 years old							
Relugolix	304	162 (53.3)	142 (46.7)	254.0 [176.0;339.0]	-13.0	1.099 [0.839;1.440]	0.4943
Leuprolide	153	78 (51.0)	75 (49.0)	267.0 [176.0;NE]			
> 75 years old							
Relugolix	123	58 (47.2)	65 (52.8)	NE [254.0;NE]	NE	0.905 [0.582;1.407]	0.6569
Leuprolide	60	30 (50.0)	30 (50.0)	337.0 [198.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITTM0.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.6256							
< 250 ng/dL							
Relugolix	37	25 (67.6)	12 (32.4)	169.0 [36.0;253.0]	-2.0	1.188 [0.608;2.323]	0.6144
Leuprolide	20	13 (65.0)	7 (35.0)	171.0 [84.0;NE]			
>= 250 ng/dL							
Relugolix	383	189 (49.3)	194 (50.7)	337.0 [254.0;NE]	70.0	0.994 [0.775;1.276]	0.9642
Leuprolide	185	92 (49.7)	93 (50.3)	267.0 [251.0;NE]			
Missing							
Relugolix	7	6 (85.7)	1 (14.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	3 (37.5)	5 (62.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.6858							
Asian							
Relugolix	94	39 (41.5)	55 (58.5)	NE [337.0;NE]	NE	0.885 [0.528;1.483]	0.6430
Leuprolide	51	23 (45.1)	28 (54.9)	NE [175.0;NE]			
Black or African American							
Relugolix	21	11 (52.4)	10 (47.6)	335.0 [85.0;NE]	NE	1.727 [0.550;5.426]	0.3493
Leuprolide	12	4 (33.3)	8 (66.7)	NE [90.0;NE]			
White							
Relugolix	292	160 (54.8)	132 (45.2)	253.0 [171.0;336.0]	-1.0	1.061 [0.806;1.397]	0.6707
Leuprolide	139	75 (54.0)	64 (46.0)	254.0 [173.0;341.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.6858							
Others							
Relugolix	14	8 (57.1)	6 (42.9)	295.0 [90.0;NE]	119.0	0.745 [0.243;2.276]	0.6049
Leuprolide	7	5 (71.4)	2 (28.6)	176.0 [78.0;NE]			
Not Reported							
Relugolix	6	2 (33.3)	4 (66.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	1 (25.0)	3 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITTM0.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.7731							
North and South America							
Relugolix	161	87 (54.0)	74 (46.0)	251.0 [169.0;338.0]	-2.0	1.095 [0.759;1.579]	0.6287
Leuprolide	80	43 (53.8)	37 (46.3)	253.0 [169.0;NE]			
Europe							
Relugolix	155	83 (53.5)	72 (46.5)	259.0 [176.0;NE]	-79.0	1.095 [0.748;1.602]	0.6416
Leuprolide	78	39 (50.0)	39 (50.0)	338.0 [176.0;NE]			
Asia and Rest of World							
Relugolix	111	50 (45.0)	61 (55.0)	344.0 [254.0;NE]	NE	0.897 [0.558;1.442]	0.6541
Leuprolide	55	26 (47.3)	29 (52.7)	NE [169.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITTM0.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.8737							
< 20 ng/mL							
Relugolix	320	165 (51.6)	155 (48.4)	257.0 [176.0;344.0]	-10.0	1.031 [0.795;1.337]	0.8178
Leuprolide	169	87 (51.5)	82 (48.5)	267.0 [176.0;NE]			
>= 20 ng/mL							
Relugolix	107	55 (51.4)	52 (48.6)	337.0 [251.0;NE]	-1.0	1.080 [0.653;1.786]	0.7656
Leuprolide	44	21 (47.7)	23 (52.3)	338.0 [251.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITTM0.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.9597							
Not Hispanic or Latino							
Relugolix	381	199 (52.2)	182 (47.8)	259.0 [253.0;340.0]	-8.0	1.033 [0.810;1.319]	0.7920
Leuprolide	188	96 (51.1)	92 (48.9)	267.0 [198.0;NE]			
Hispanic or Latino							
Relugolix	37	16 (43.2)	21 (56.8)	339.0 [173.0;NE]	NE	1.012 [0.459;2.229]	0.9773
Leuprolide	22	10 (45.5)	12 (54.5)	NE [173.0;NE]			
Not Reported							
Relugolix	9	5 (55.6)	4 (44.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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4.1.3.2.7 Skala: Diarrhoe

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2DIAR15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.1951							
Asian							
Relugolix	94	26 (27.7)	68 (72.3)	NE [344.0;NE]	NE	1.646 [0.771;3.512]	0.1979
Leuprolide	51	9 (17.6)	42 (82.4)	NE [NE;NE]			
Black or African American							
Relugolix	21	7 (33.3)	14 (66.7)	NE [172.0;NE]	NE	0.463 [0.155;1.379]	0.1668
Leuprolide	12	6 (50.0)	6 (50.0)	274.0 [30.0;NE]			
White							
Relugolix	292	96 (32.9)	196 (67.1)	NE [NE;NE]	NE	1.522 [1.020;2.270]	0.0398
Leuprolide	139	32 (23.0)	107 (77.0)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.1951							
Others							
Relugolix	14	7 (50.0)	7 (50.0)	NE [32.0;NE]	NE	2.348 [0.488;11.309]	0.2871
Leuprolide	7	2 (28.6)	5 (71.4)	NE [169.0;NE]			
Not Reported							
Relugolix	6	3 (50.0)	3 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	1 (25.0)	3 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITTM0.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.2262							
Not Hispanic or Latino							
Relugolix	381	120 (31.5)	261 (68.5)	NE [NE;NE]	NE	1.338 [0.950;1.886]	0.0956
Leuprolide	188	45 (23.9)	143 (76.1)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	37	14 (37.8)	23 (62.2)	NE [172.0;NE]	NE	2.745 [0.903;8.343]	0.0750
Leuprolide	22	4 (18.2)	18 (81.8)	NE [339.0;NE]			
Not Reported							
Relugolix	9	5 (55.6)	4 (44.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITTM0.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.3342							
North and South America							
Relugolix	161	60 (37.3)	101 (62.7)	NE [339.0;NE]	NE	1.141 [0.724;1.797]	0.5697
Leuprolide	80	27 (33.8)	53 (66.3)	NE [339.0;NE]			
Europe							
Relugolix	155	48 (31.0)	107 (69.0)	NE [NE;NE]	NE	2.010 [1.089;3.710]	0.0256
Leuprolide	78	13 (16.7)	65 (83.3)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	111	31 (27.9)	80 (72.1)	NE [344.0;NE]	NE	1.559 [0.764;3.180]	0.2223
Leuprolide	55	10 (18.2)	45 (81.8)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITTM0.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.4009							
< 8							
Relugolix	252	74 (29.4)	178 (70.6)	NE [NE;NE]	NE	1.664 [1.064;2.602]	0.0255
Leuprolide	136	26 (19.1)	110 (80.9)	NE [NE;NE]			
>= 8							
Relugolix	163	63 (38.7)	100 (61.3)	NE [338.0;NE]	NE	1.257 [0.780;2.027]	0.3474
Leuprolide	74	23 (31.1)	51 (68.9)	NE [339.0;NE]			
Missing							
Relugolix	12	2 (16.7)	10 (83.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITTM0.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.5522							
< 20 ng/mL							
Relugolix	320	96 (30.0)	224 (70.0)	NE [NE;NE]	NE	1.514 [1.028;2.229]	0.0358
Leuprolide	169	35 (20.7)	134 (79.3)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	107	43 (40.2)	64 (59.8)	NE [337.0;NE]	NE	1.223 [0.679;2.201]	0.5027
Leuprolide	44	15 (34.1)	29 (65.9)	NE [339.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITTM0.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.6945							
<= 75 years old							
Relugolix	304	100 (32.9)	204 (67.1)	NE [NE;NE]	NE	1.398 [0.962;2.032]	0.0786
Leuprolide	153	38 (24.8)	115 (75.2)	NE [NE;NE]			
> 75 years old							
Relugolix	123	39 (31.7)	84 (68.3)	NE [344.0;NE]	NE	1.624 [0.850;3.102]	0.1418
Leuprolide	60	12 (20.0)	48 (80.0)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITTM0.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.9094							
Asia (Excl. Korea)							
Relugolix	70	18 (25.7)	52 (74.3)	NE [344.0;NE]	NE	1.382 [0.577;3.309]	0.4674
Leuprolide	36	7 (19.4)	29 (80.6)	NE [NE;NE]			
Rest of World							
Relugolix	357	121 (33.9)	236 (66.1)	NE [NE;NE]	NE	1.460 [1.031;2.068]	0.0332
Leuprolide	177	43 (24.3)	134 (75.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITTM0.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.9510							
< 250 ng/dL							
Relugolix	37	15 (40.5)	22 (59.5)	NE [171.0;NE]	NE	1.433 [0.556;3.694]	0.4567
Leuprolide	20	6 (30.0)	14 (70.0)	NE [250.0;NE]			
>= 250 ng/dL							
Relugolix	383	123 (32.1)	260 (67.9)	NE [NE;NE]	NE	1.479 [1.042;2.099]	0.0286
Leuprolide	185	42 (22.7)	143 (77.3)	NE [NE;NE]			
Missing							
Relugolix	7	1 (14.3)	6 (85.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	2 (25.0)	6 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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4.1.3.2.8 Skala: Obstipation

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2CONS15.KM.MITTM0.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.0921							
<= 75 years old							
Relugolix	304	103 (33.9)	201 (66.1)	NE [344.0;NE]	NE	1.371 [0.951;1.975]	0.0905
Leuprolide	153	40 (26.1)	113 (73.9)	NE [NE;NE]			
> 75 years old							
Relugolix	123	43 (35.0)	80 (65.0)	350.0 [350.0;NE]	NE	0.796 [0.474;1.335]	0.3865
Leuprolide	60	22 (36.7)	38 (63.3)	NE [329.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITTM0.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.2487							
< 20 ng/mL							
Relugolix	320	113 (35.3)	207 (64.7)	NE [NE;NE]	NE	1.282 [0.915;1.798]	0.1493
Leuprolide	169	48 (28.4)	121 (71.6)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	107	33 (30.8)	74 (69.2)	350.0 [350.0;NE]	10.0	0.842 [0.449;1.580]	0.5934
Leuprolide	44	14 (31.8)	30 (68.2)	340.0 [339.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITTM0.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.2648							
Asia (Excl. Korea)							
Relugolix	70	27 (38.6)	43 (61.4)	NE [337.0;NE]	NE	1.718 [0.808;3.653]	0.1597
Leuprolide	36	9 (25.0)	27 (75.0)	NE [339.0;NE]			
Rest of World							
Relugolix	357	119 (33.3)	238 (66.7)	350.0 [350.0;NE]	NE	1.077 [0.779;1.490]	0.6543
Leuprolide	177	53 (29.9)	124 (70.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.2806							
Asian							
Relugolix	94	38 (40.4)	56 (59.6)	NE [259.0;NE]	NE	1.525 [0.839;2.773]	0.1667
Leuprolide	51	15 (29.4)	36 (70.6)	NE [339.0;NE]			
Black or African American							
Relugolix	21	9 (42.9)	12 (57.1)	NE [169.0;NE]	NE	2.474 [0.535;11.453]	0.2466
Leuprolide	12	2 (16.7)	10 (83.3)	NE [162.0;NE]			
White							
Relugolix	292	96 (32.9)	196 (67.1)	350.0 [350.0;NE]	NE	1.089 [0.755;1.571]	0.6488
Leuprolide	139	41 (29.5)	98 (70.5)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.2806							
Others							
Relugolix	14	1 (7.1)	13 (92.9)	NE [NE;NE]	NE	0.205 [0.019;2.257]	0.1952
Leuprolide	7	2 (28.6)	5 (71.4)	NE [29.0;NE]			
Not Reported							
Relugolix	6	2 (33.3)	4 (66.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	2 (50.0)	2 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITTM0.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.3233							
< 250 ng/dL							
Relugolix	37	11 (29.7)	26 (70.3)	NE [342.0;NE]	NE	0.729 [0.283;1.882]	0.5142
Leuprolide	20	7 (35.0)	13 (65.0)	NE [84.0;NE]			
>= 250 ng/dL							
Relugolix	383	132 (34.5)	251 (65.5)	350.0 [350.0;NE]	NE	1.207 [0.877;1.662]	0.2477
Leuprolide	185	53 (28.6)	132 (71.4)	NE [NE;NE]			
Missing							
Relugolix	7	3 (42.9)	4 (57.1)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	2 (25.0)	6 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITTM0.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.3315							
Not Hispanic or Latino							
Relugolix	381	131 (34.4)	250 (65.6)	350.0 [350.0;NE]	NE	1.225 [0.888;1.691]	0.2162
Leuprolide	188	52 (27.7)	136 (72.3)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	37	10 (27.0)	27 (73.0)	NE [338.0;NE]	NE	0.752 [0.297;1.907]	0.5489
Leuprolide	22	8 (36.4)	14 (63.6)	340.0 [176.0;NE]			
Not Reported							
Relugolix	9	5 (55.6)	4 (44.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITTM0.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.4937							
North and South America							
Relugolix	161	59 (36.6)	102 (63.4)	360.0 [342.0;NE]	NE	1.188 [0.738;1.912]	0.4780
Leuprolide	80	24 (30.0)	56 (70.0)	NE [340.0;NE]			
Europe							
Relugolix	155	45 (29.0)	110 (71.0)	350.0 [350.0;NE]	NE	0.938 [0.567;1.551]	0.8017
Leuprolide	78	23 (29.5)	55 (70.5)	NE [340.0;NE]			
Asia and Rest of World							
Relugolix	111	42 (37.8)	69 (62.2)	NE [NE;NE]	NE	1.495 [0.829;2.697]	0.1811
Leuprolide	55	15 (27.3)	40 (72.7)	NE [339.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITTM0.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.6760							
< 8							
Relugolix	252	79 (31.3)	173 (68.7)	NE [NE;NE]	NE	1.202 [0.810;1.783]	0.3606
Leuprolide	136	36 (26.5)	100 (73.5)	NE [NE;NE]			
>= 8							
Relugolix	163	60 (36.8)	103 (63.2)	350.0 [350.0;NE]	NE	1.055 [0.660;1.686]	0.8234
Leuprolide	74	25 (33.8)	49 (66.2)	NE [339.0;NE]			
Missing							
Relugolix	12	7 (58.3)	5 (41.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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4.1.3.3 Symptomatik (European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire PR25)

4.1.3.3.1 Skala: Miktionsbeschwerden

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2URIN15.KM.MITTM0.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.0193							
< 20 ng/mL							
Relugolix	320	113 (35.3)	207 (64.7)	NE [344.0;NE]	NE	1.605 [1.119;2.303]	0.0101
Leuprolide	169	40 (23.7)	129 (76.3)	345.0 [345.0;NE]			
>= 20 ng/mL							
Relugolix	107	30 (28.0)	77 (72.0)	NE [NE;NE]	NE	0.691 [0.377;1.269]	0.2333
Leuprolide	44	16 (36.4)	28 (63.6)	NE [258.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITTM0.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.0465							
Asia (Excl. Korea)							
Relugolix	70	27 (38.6)	43 (61.4)	344.0 [337.0;NE]	NE	3.174 [1.223;8.240]	0.0177
Leuprolide	36	5 (13.9)	31 (86.1)	NE [NE;NE]			
Rest of World							
Relugolix	357	116 (32.5)	241 (67.5)	NE [NE;NE]	NE	1.139 [0.819;1.583]	0.4402
Leuprolide	177	51 (28.8)	126 (71.2)	345.0 [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITTM0.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.0974							
North and South America							
Relugolix	161	59 (36.6)	102 (63.4)	NE [339.0;NE]	NE	1.520 [0.915;2.525]	0.1058
Leuprolide	80	20 (25.0)	60 (75.0)	NE [NE;NE]			
Europe							
Relugolix	155	46 (29.7)	109 (70.3)	NE [NE;NE]	NE	0.875 [0.541;1.416]	0.5870
Leuprolide	78	26 (33.3)	52 (66.7)	345.0 [344.0;NE]			
Asia and Rest of World							
Relugolix	111	38 (34.2)	73 (65.8)	NE [344.0;NE]	NE	2.067 [1.030;4.148]	0.0411
Leuprolide	55	10 (18.2)	45 (81.8)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITTM0.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.1505							
< 8							
Relugolix	252	90 (35.7)	162 (64.3)	NE [344.0;NE]	NE	1.576 [1.058;2.349]	0.0254
Leuprolide	136	33 (24.3)	103 (75.7)	345.0 [344.0;NE]			
>= 8							
Relugolix	163	48 (29.4)	115 (70.6)	NE [344.0;NE]	NE	0.983 [0.593;1.629]	0.9466
Leuprolide	74	22 (29.7)	52 (70.3)	NE [NE;NE]			
Missing							
Relugolix	12	5 (41.7)	7 (58.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITTM0.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.1760							
<= 75 years old							
Relugolix	304	101 (33.2)	203 (66.8)	NE [344.0;NE]	NE	1.160 [0.816;1.648]	0.4077
Leuprolide	153	45 (29.4)	108 (70.6)	345.0 [NE;NE]			
> 75 years old							
Relugolix	123	42 (34.1)	81 (65.9)	NE [NE;NE]	NE	1.949 [1.003;3.787]	0.0490
Leuprolide	60	11 (18.3)	49 (81.7)	NE [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.2611							
Asian							
Relugolix	94	36 (38.3)	58 (61.7)	344.0 [337.0;NE]	NE	2.225 [1.104;4.484]	0.0253
Leuprolide	51	10 (19.6)	41 (80.4)	NE [NE;NE]			
Black or African American							
Relugolix	21	9 (42.9)	12 (57.1)	NE [86.0;NE]	NE	0.911 [0.305;2.719]	0.8671
Leuprolide	12	5 (41.7)	7 (58.3)	NE [36.0;NE]			
White							
Relugolix	292	92 (31.5)	200 (68.5)	NE [NE;NE]	NE	1.173 [0.804;1.712]	0.4085
Leuprolide	139	38 (27.3)	101 (72.7)	345.0 [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.2611							
Others							
Relugolix	14	4 (28.6)	10 (71.4)	NE [169.0;NE]	NE	0.587 [0.131;2.625]	0.4861
Leuprolide	7	3 (42.9)	4 (57.1)	NE [86.0;NE]			
Not Reported							
Relugolix	6	2 (33.3)	4 (66.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITTM0.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.4934							
Not Hispanic or Latino							
Relugolix	381	129 (33.9)	252 (66.1)	NE [344.0;NE]	NE	1.307 [0.943;1.813]	0.1078
Leuprolide	188	50 (26.6)	138 (73.4)	345.0 [344.0;NE]			
Hispanic or Latino							
Relugolix	37	12 (32.4)	25 (67.6)	NE [338.0;NE]	NE	1.973 [0.636;6.121]	0.2391
Leuprolide	22	4 (18.2)	18 (81.8)	NE [NE;NE]			
Not Reported							
Relugolix	9	2 (22.2)	7 (77.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2URIN15.KM.MITTM0.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.7621							
< 250 ng/dL							
Relugolix	37	12 (32.4)	25 (67.6)	NE [255.0;NE]	NE	1.118 [0.420;2.981]	0.8231
Leuprolide	20	6 (30.0)	14 (70.0)	NE [173.0;NE]			
>= 250 ng/dL							
Relugolix	383	127 (33.2)	256 (66.8)	NE [344.0;NE]	NE	1.312 [0.941;1.829]	0.1090
Leuprolide	185	48 (25.9)	137 (74.1)	345.0 [345.0;NE]			
Missing							
Relugolix	7	4 (57.1)	3 (42.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	2 (25.0)	6 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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4.1.3.3.2 Skala: Darmfunktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2BOWE15.KM.MITTM0.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.1295							
< 20 ng/mL							
Relugolix	320	72 (22.5)	248 (77.5)	NE [NE;NE]	NE	1.535 [0.981;2.404]	0.0609
Leuprolide	169	26 (15.4)	143 (84.6)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	107	22 (20.6)	85 (79.4)	NE [NE;NE]	NE	0.782 [0.370;1.652]	0.5195
Leuprolide	44	10 (22.7)	34 (77.3)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2BOWE15.KM.MITTM0.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.2230							
< 250 ng/dL							
Relugolix	37	5 (13.5)	32 (86.5)	NE [NE;NE]	NE	0.625 [0.168;2.328]	0.4836
Leuprolide	20	4 (20.0)	16 (80.0)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	383	87 (22.7)	296 (77.3)	NE [NE;NE]	NE	1.474 [0.968;2.245]	0.0702
Leuprolide	185	29 (15.7)	156 (84.3)	NE [NE;NE]			
Missing							
Relugolix	7	2 (28.6)	5 (71.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	3 (37.5)	5 (62.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2BOWE15.KM.MITTM0.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.3948							
Not Hispanic or Latino							
Relugolix	381	80 (21.0)	301 (79.0)	NE [NE;NE]	NE	1.264 [0.835;1.914]	0.2685
Leuprolide	188	31 (16.5)	157 (83.5)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	37	10 (27.0)	27 (73.0)	NE [338.0;NE]	NE	2.277 [0.626;8.277]	0.2114
Leuprolide	22	3 (13.6)	19 (86.4)	NE [NE;NE]			
Not Reported							
Relugolix	9	4 (44.4)	5 (55.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2BOWE15.KM.MITTM0.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.4643							
Asia (Excl. Korea)							
Relugolix	70	14 (20.0)	56 (80.0)	NE [343.0;NE]	NE	1.917 [0.631;5.824]	0.2510
Leuprolide	36	4 (11.1)	32 (88.9)	NE [NE;NE]			
Rest of World							
Relugolix	357	80 (22.4)	277 (77.6)	NE [NE;NE]	NE	1.232 [0.818;1.857]	0.3186
Leuprolide	177	32 (18.1)	145 (81.9)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2BOWE15.KM.MITTM0.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.6422							
<= 75 years old							
Relugolix	304	70 (23.0)	234 (77.0)	NE [NE;NE]	NE	1.388 [0.885;2.178]	0.1531
Leuprolide	153	26 (17.0)	127 (83.0)	NE [NE;NE]			
> 75 years old							
Relugolix	123	24 (19.5)	99 (80.5)	NE [NE;NE]	NE	1.131 [0.541;2.366]	0.7433
Leuprolide	60	10 (16.7)	50 (83.3)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2BOWE15.KM.MITTM0.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.7644							
North and South America							
Relugolix	161	44 (27.3)	117 (72.7)	NE [343.0;NE]	NE	1.444 [0.803;2.595]	0.2194
Leuprolide	80	15 (18.8)	65 (81.3)	NE [NE;NE]			
Europe							
Relugolix	155	27 (17.4)	128 (82.6)	NE [NE;NE]	NE	1.064 [0.549;2.063]	0.8536
Leuprolide	78	13 (16.7)	65 (83.3)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	111	23 (20.7)	88 (79.3)	NE [NE;NE]	NE	1.441 [0.645;3.222]	0.3734
Leuprolide	55	8 (14.5)	47 (85.5)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2BOWE15.KM.MITTM0.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.7647							
< 8							
Relugolix	252	53 (21.0)	199 (79.0)	NE [NE;NE]	NE	1.285 [0.788;2.097]	0.3151
Leuprolide	136	23 (16.9)	113 (83.1)	NE [NE;NE]			
>= 8							
Relugolix	163	39 (23.9)	124 (76.1)	NE [NE;NE]	NE	1.455 [0.761;2.779]	0.2564
Leuprolide	74	12 (16.2)	62 (83.8)	NE [NE;NE]			
Missing							
Relugolix	12	2 (16.7)	10 (83.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2BOWE15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.8446							
Asian							
Relugolix	94	20 (21.3)	74 (78.7)	NE [343.0;NE]	NE	1.637 [0.692;3.872]	0.2616
Leuprolide	51	7 (13.7)	44 (86.3)	NE [NE;NE]			
Black or African American							
Relugolix	21	9 (42.9)	12 (57.1)	NE [170.0;NE]	NE	1.043 [0.321;3.390]	0.9442
Leuprolide	12	4 (33.3)	8 (66.7)	NE [87.0;NE]			
White							
Relugolix	292	61 (20.9)	231 (79.1)	NE [NE;NE]	NE	1.410 [0.858;2.315]	0.1748
Leuprolide	139	21 (15.1)	118 (84.9)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2BOWE15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.8446							
Others							
Relugolix	14	3 (21.4)	11 (78.6)	NE [339.0;NE]	NE	0.749 [0.125;4.483]	0.7512
Leuprolide	7	2 (28.6)	5 (71.4)	NE [165.0;NE]			
Not Reported							
Relugolix	6	1 (16.7)	5 (83.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	2 (50.0)	2 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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4.1.3.3.3 Skala: Nebenwirkungen der Hormontherapie

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2HRMN15.KM.MITTM0.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.2051							
Asia (Excl. Korea)							
Relugolix	70	22 (31.4)	48 (68.6)	NE [NE;NE]	NE	0.669 [0.351;1.273]	0.2205
Leuprolide	36	16 (44.4)	20 (55.6)	NE [172.0;NE]			
Rest of World							
Relugolix	357	192 (53.8)	165 (46.2)	256.0 [183.0;337.0]	-74.0	1.044 [0.816;1.335]	0.7312
Leuprolide	177	95 (53.7)	82 (46.3)	330.0 [251.0;341.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2HRMN15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.2756							
Asian							
Relugolix	94	30 (31.9)	64 (68.1)	NE [344.0;NE]	NE	0.685 [0.398;1.179]	0.1719
Leuprolide	51	23 (45.1)	28 (54.9)	NE [258.0;NE]			
Black or African American							
Relugolix	21	16 (76.2)	5 (23.8)	92.0 [36.0;176.0]	-166.0	1.907 [0.746;4.876]	0.1779
Leuprolide	12	6 (50.0)	6 (50.0)	258.0 [85.0;NE]			
White							
Relugolix	292	157 (53.8)	135 (46.2)	256.0 [183.0;337.0]	-3.0	1.023 [0.778;1.345]	0.8720
Leuprolide	139	76 (54.7)	63 (45.3)	259.0 [176.0;342.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2HRMN15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.2756							
Others							
Relugolix	14	8 (57.1)	6 (42.9)	135.0 [85.0;NE]	20.0	0.771 [0.252;2.357]	0.6478
Leuprolide	7	5 (71.4)	2 (28.6)	115.0 [80.0;NE]			
Not Reported							
Relugolix	6	3 (50.0)	3 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	1 (25.0)	3 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2HRMN15.KM.MITTM0.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.4413							
< 8							
Relugolix	252	127 (50.4)	125 (49.6)	330.0 [253.0;344.0]	-5.0	0.936 [0.703;1.247]	0.6535
Leuprolide	136	74 (54.4)	62 (45.6)	335.0 [176.0;342.0]			
>= 8							
Relugolix	163	82 (50.3)	81 (49.7)	337.0 [175.0;NE]	-2.0	1.135 [0.764;1.686]	0.5316
Leuprolide	74	35 (47.3)	39 (52.7)	339.0 [251.0;NE]			
Missing							
Relugolix	12	5 (41.7)	7 (58.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2HRMN15.KM.MITTM0.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.4841							
< 250 ng/dL							
Relugolix	37	20 (54.1)	17 (45.9)	330.0 [170.0;NE]	-12.0	1.245 [0.567;2.736]	0.5848
Leuprolide	20	9 (45.0)	11 (55.0)	342.0 [85.0;NE]			
>= 250 ng/dL							
Relugolix	383	188 (49.1)	195 (50.9)	337.0 [253.0;NE]	7.0	0.928 [0.727;1.184]	0.5474
Leuprolide	185	99 (53.5)	86 (46.5)	330.0 [248.0;341.0]			
Missing							
Relugolix	7	6 (85.7)	1 (14.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	3 (37.5)	5 (62.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2HRMN15.KM.MITTM0.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.5793							
North and South America							
Relugolix	161	81 (50.3)	80 (49.7)	253.0 [171.0;NE]	-1.0	0.978 [0.676;1.416]	0.9075
Leuprolide	80	43 (53.8)	37 (46.3)	254.0 [170.0;341.0]			
Europe							
Relugolix	155	94 (60.6)	61 (39.4)	252.0 [169.0;337.0]	-7.0	1.110 [0.776;1.588]	0.5685
Leuprolide	78	44 (56.4)	34 (43.6)	259.0 [169.0;344.0]			
Asia and Rest of World							
Relugolix	111	39 (35.1)	72 (64.9)	NE [344.0;NE]	NE	0.797 [0.479;1.326]	0.3822
Leuprolide	55	24 (43.6)	31 (56.4)	NE [258.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2HRMN15.KM.MITTM0.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.7393							
<= 75 years old							
Relugolix	304	154 (50.7)	150 (49.3)	330.0 [197.0;NE]	0.0	0.965 [0.740;1.259]	0.7929
Leuprolide	153	84 (54.9)	69 (45.1)	330.0 [248.0;342.0]			
> 75 years old							
Relugolix	123	60 (48.8)	63 (51.2)	337.0 [253.0;NE]	-4.0	1.055 [0.670;1.662]	0.8166
Leuprolide	60	27 (45.0)	33 (55.0)	341.0 [173.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2HRMN15.KM.MITTM0.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.7706							
< 20 ng/mL							
Relugolix	320	163 (50.9)	157 (49.1)	330.0 [250.0;342.0]	-5.0	0.976 [0.755;1.261]	0.8509
Leuprolide	169	91 (53.8)	78 (46.2)	335.0 [176.0;341.0]			
>= 20 ng/mL							
Relugolix	107	51 (47.7)	56 (52.3)	337.0 [252.0;NE]	NE	1.063 [0.634;1.783]	0.8163
Leuprolide	44	20 (45.5)	24 (54.5)	NE [248.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2HRMN15.KM.MITTM0.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.8131							
Not Hispanic or Latino							
Relugolix	381	191 (50.1)	190 (49.9)	337.0 [253.0;344.0]	2.0	0.962 [0.755;1.225]	0.7517
Leuprolide	188	100 (53.2)	88 (46.8)	335.0 [253.0;341.0]			
Hispanic or Latino							
Relugolix	37	16 (43.2)	21 (56.8)	NE [172.0;NE]	NE	1.066 [0.471;2.412]	0.8785
Leuprolide	22	9 (40.9)	13 (59.1)	NE [87.0;NE]			
Not Reported							
Relugolix	9	7 (77.8)	2 (22.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2INCT15.KM.MITTM0.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.0279							
< 20 ng/mL							
Relugolix	320	27 (8.4)	293 (91.6)	NE [NE;NE]	NE	0.854 [0.460;1.585]	0.6159
Leuprolide	169	16 (9.5)	153 (90.5)	344.0 [344.0;NE]			
>= 20 ng/mL							
Relugolix	107	3 (2.8)	104 (97.2)	357.0 [NE;NE]	20.0	0.131 [0.028;0.618]	0.0102
Leuprolide	44	8 (18.2)	36 (81.8)	337.0 [172.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INCT15.KM.MITTM0.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.1185							
<= 75 years old							
Relugolix	304	24 (7.9)	280 (92.1)	NE [NE;NE]	NE	0.828 [0.428;1.601]	0.5740
Leuprolide	153	14 (9.2)	139 (90.8)	NE [NE;NE]			
> 75 years old							
Relugolix	123	6 (4.9)	117 (95.1)	357.0 [NE;NE]	13.0	0.303 [0.103;0.889]	0.0296
Leuprolide	60	10 (16.7)	50 (83.3)	344.0 [258.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INCT15.KM.MITTM0.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.1257							
Not Hispanic or Latino							
Relugolix	381	25 (6.6)	356 (93.4)	357.0 [NE;NE]	13.0	0.515 [0.290;0.913]	0.0231
Leuprolide	188	23 (12.2)	165 (87.8)	344.0 [338.0;NE]			
Hispanic or Latino							
Relugolix	37	4 (10.8)	33 (89.2)	NE [32.0;NE]	NE	3.026 [0.338;27.116]	0.3224
Leuprolide	22	1 (4.5)	21 (95.5)	NE [169.0;NE]			
Not Reported							
Relugolix	9	1 (11.1)	8 (88.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2INCT15.KM.MITTM0.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.1411							
< 250 ng/dL							
Relugolix	37	1 (2.7)	36 (97.3)	NE [NE;NE]	NE	0.137 [0.016;1.176]	0.0700
Leuprolide	20	5 (25.0)	15 (75.0)	NE [87.0;NE]			
>= 250 ng/dL							
Relugolix	383	28 (7.3)	355 (92.7)	357.0 [NE;NE]	13.0	0.734 [0.400;1.347]	0.3178
Leuprolide	185	17 (9.2)	168 (90.8)	344.0 [338.0;NE]			
Missing							
Relugolix	7	1 (14.3)	6 (85.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	2 (25.0)	6 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2INCT15.KM.MITTM0.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.2091							
North and South America							
Relugolix	161	9 (5.6)	152 (94.4)	NE [NE;NE]	NE	0.328 [0.136;0.795]	0.0135
Leuprolide	80	11 (13.8)	69 (86.3)	338.0 [165.0;NE]			
Europe							
Relugolix	155	15 (9.7)	140 (90.3)	NE [NE;NE]	NE	0.936 [0.420;2.086]	0.8721
Leuprolide	78	10 (12.8)	68 (87.2)	344.0 [337.0;NE]			
Asia and Rest of World							
Relugolix	111	6 (5.4)	105 (94.6)	357.0 [NE;NE]	NE	0.800 [0.191;3.347]	0.7598
Leuprolide	55	3 (5.5)	52 (94.5)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2INCT15.KM.MITTM0.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.2546							
< 8							
Relugolix	252	23 (9.1)	229 (90.9)	NE [NE;NE]	NE	0.788 [0.421;1.477]	0.4577
Leuprolide	136	17 (12.5)	119 (87.5)	344.0 [337.0;NE]			
>= 8							
Relugolix	163	7 (4.3)	156 (95.7)	357.0 [NE;NE]	NE	0.379 [0.127;1.130]	0.0817
Leuprolide	74	7 (9.5)	67 (90.5)	NE [NE;NE]			
Missing							
Relugolix	12	0	12 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2INCT15.KM.MITTM0.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.3998							
Asia (Excl. Korea)							
Relugolix	70	4 (5.7)	66 (94.3)	357.0 [NE;NE]	NE	1.558 [0.162;14.990]	0.7009
Leuprolide	36	1 (2.8)	35 (97.2)	NE [NE;NE]			
Rest of World							
Relugolix	357	26 (7.3)	331 (92.7)	NE [NE;NE]	NE	0.572 [0.326;1.004]	0.0515
Leuprolide	177	23 (13.0)	154 (87.0)	344.0 [337.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INCT15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.5960							
Asian							
Relugolix	94	5 (5.3)	89 (94.7)	357.0 [NE;NE]	NE	0.672 [0.150;3.002]	0.6024
Leuprolide	51	3 (5.9)	48 (94.1)	NE [NE;NE]			
Black or African American							
Relugolix	21	3 (14.3)	18 (85.7)	NE [173.0;NE]	NE	0.236 [0.039;1.431]	0.1163
Leuprolide	12	2 (16.7)	10 (83.3)	100.0 [85.0;NE]			
White							
Relugolix	292	21 (7.2)	271 (92.8)	NE [NE;NE]	NE	0.619 [0.332;1.152]	0.1303
Leuprolide	139	19 (13.7)	120 (86.3)	344.0 [337.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INCT15.KM.MITTM0.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.5960							
Others							
Relugolix	14	1 (7.1)	13 (92.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	7	0	7 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	6	0	6 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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4.1.4 Morbidität – supportive Endpunkte

4.1.4.1 Testosteronkonzentration

4.1.4.1.1 Initiale Kastration

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.T2ITCAST.KM.MITTM0.S5: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Gleason Score at Study Entry, Interaction p-value: 0.0118							
< 8							
Relugolix	252	251 (99.6)	1 (0.4)	4.0 [4.0;5.0]	-23.0	14.167 [10.679;18.794]	<.0001
Leuprolide	136	134 (98.5)	2 (1.5)	27.0 [23.0;29.0]			
>= 8							
Relugolix	163	162 (99.4)	1 (0.6)	4.0 [NE;NE]	-24.0	8.930 [6.590;12.099]	<.0001
Leuprolide	74	74 (100.0)	0	28.0 [22.0;29.0]			
Missing							
Relugolix	12	12 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	3 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.T2ITCAST.KM.MITTM0.S4: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.0169							
Asian							
Relugolix	94	94 (100.0)	0	4.0 [4.0;5.0]	-25.0	16.473 [11.085;24.481]	<.0001
Leuprolide	51	50 (98.0)	1 (2.0)	29.0 [22.0;29.0]			
Black or African American							
Relugolix	21	21 (100.0)	0	5.0 [4.0;5.0]	-18.0	4.568 [2.217;9.412]	<.0001
Leuprolide	12	12 (100.0)	0	23.0 [17.0;29.0]			
White							
Relugolix	292	290 (99.3)	2 (0.7)	4.0 [NE;NE]	-23.0	12.037 [9.294;15.591]	<.0001
Leuprolide	139	138 (99.3)	1 (0.7)	27.0 [23.0;29.0]			
Others							
Relugolix	14	14 (100.0)	0	4.0 [3.0;6.0]	-25.0	17.528 [6.889;44.595]	<.0001
Leuprolide	7	7 (100.0)	0	29.0 [22.0;30.0]			
Not Reported							
Relugolix	6	6 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	4 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

Table MOR.T2ITCAST.KM.MITTM0.S6: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: 0.1099							
< 250 ng/dL							
Relugolix	37	37 (100.0)	0	4.0 [4.0;5.0]	-16.5	7.271 [4.102;12.888]	<.0001
Leuprolide	20	20 (100.0)	0	20.5 [15.0;22.0]			
>= 250 ng/dL							
Relugolix	383	381 (99.5)	2 (0.5)	4.0 [NE;NE]	-25.0	11.709 [9.303;14.739]	<.0001
Leuprolide	185	183 (98.9)	2 (1.1)	29.0 [27.0;29.0]			
Missing							
Relugolix	7	7 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	8 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.T2ITCAST.KM.MITTM0.S1: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.1181							
<= 75 years old							
Relugolix	304	302 (99.3)	2 (0.7)	4.0 [NE;NE]	-23.0	10.486 [8.242;13.340]	<.0001
Leuprolide	153	152 (99.3)	1 (0.7)	27.0 [22.0;29.0]			
> 75 years old							
Relugolix	123	123 (100.0)	0	4.0 [NE;NE]	-25.0	14.115 [9.866;20.194]	<.0001
Leuprolide	60	59 (98.3)	1 (1.7)	29.0 [23.0;29.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2ITCAST.KM.MITTM0.S2: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region I, Interaction p-value: 0.1570							
North and South America							
Relugolix	161	161 (100.0)	0	4.0 [4.0;5.0]	-23.0	10.510 [7.747;14.259]	<.0001
Leuprolide	80	80 (100.0)	0	27.0 [22.0;29.0]			
Europe							
Relugolix	155	153 (98.7)	2 (1.3)	4.0 [NE;NE]	-23.0	10.087 [7.420;13.714]	<.0001
Leuprolide	78	77 (98.7)	1 (1.3)	27.0 [22.0;29.0]			
Asia and Rest of World							
Relugolix	111	111 (100.0)	0	4.0 [4.0;5.0]	-25.0	15.013 [10.327;21.825]	<.0001
Leuprolide	55	54 (98.2)	1 (1.8)	29.0 [22.0;29.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.T2ITCAST.KM.MITTM0.S7: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.3642							
< 20 ng/mL							
Relugolix	320	318 (99.4)	2 (0.6)	4.0 [NE;NE]	-24.0	11.584 [9.153;14.661]	<.0001
Leuprolide	169	167 (98.8)	2 (1.2)	28.0 [27.0;29.0]			
>= 20 ng/mL							
Relugolix	107	107 (100.0)	0	4.0 [4.0;5.0]	-18.0	9.611 [6.514;14.179]	<.0001
Leuprolide	44	44 (100.0)	0	22.0 [21.0;29.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2ITCAST.KM.MITTM0.S3: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.6056							
Not Hispanic or Latino							
Relugolix	381	379 (99.5)	2 (0.5)	4.0 [NE;NE]	-24.0	11.182 [8.906;14.039]	<.0001
Leuprolide	188	186 (98.9)	2 (1.1)	28.0 [23.0;29.0]			
Hispanic or Latino							
Relugolix	37	37 (100.0)	0	5.0 [4.0;5.0]	-19.0	9.641 [5.518;16.843]	<.0001
Leuprolide	22	22 (100.0)	0	24.0 [22.0;29.0]			
Not Reported							
Relugolix	9	9 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	3 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.T2ITCAST.KM.MITTM0.S8: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.9633							
Asia (Excl. Korea)							
Relugolix	70	70 (100.0)	0	4.0 [3.0;5.0]	-23.5	11.296 [7.295;17.492]	<.0001
Leuprolide	36	36 (100.0)	0	27.5 [22.0;29.0]			
Rest of World							
Relugolix	357	355 (99.4)	2 (0.6)	4.0 [NE;NE]	-24.0	11.178 [8.866;14.094]	<.0001
Leuprolide	177	175 (98.9)	2 (1.1)	28.0 [23.0;29.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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4.1.4.1.2 Initiale profunde Kastration

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.T2IPCAST.KM.MITTM0.S3: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.0115							
Not Hispanic or Latino							
Relugolix	381	374 (98.2)	7 (1.8)	15.0 [NE;NE]	-14.0	4.200 [3.471;5.082]	<.0001
Leuprolide	188	185 (98.4)	3 (1.6)	29.0 [29.0;30.0]			
Hispanic or Latino							
Relugolix	37	37 (100.0)	0	15.0 [8.0;15.0]	-14.0	2.032 [1.195;3.457]	0.0089
Leuprolide	22	22 (100.0)	0	29.0 [29.0;33.0]			
Not Reported							
Relugolix	9	9 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	3 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.T2IPCAST.KM.MITTM0.S4: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.0321							
Asian							
Relugolix	94	93 (98.9)	1 (1.1)	15.0 [NE;NE]	-14.0	5.069 [3.543;7.254]	<.0001
Leuprolide	51	50 (98.0)	1 (2.0)	29.0 [29.0;32.0]			
Black or African American							
Relugolix	21	19 (90.5)	2 (9.5)	15.0 [8.0;17.0]	-16.0	1.908 [0.924;3.940]	0.0806
Leuprolide	12	12 (100.0)	0	31.0 [29.0;63.0]			
White							
Relugolix	292	288 (98.6)	4 (1.4)	15.0 [NE;NE]	-14.0	3.708 [2.998;4.587]	<.0001
Leuprolide	139	137 (98.6)	2 (1.4)	29.0 [29.0;30.0]			
Others							
Relugolix	14	14 (100.0)	0	12.0 [6.0;15.0]	-17.0	8.541 [3.374;21.623]	<.0001
Leuprolide	7	7 (100.0)	0	29.0 [29.0;52.0]			
Not Reported							
Relugolix	6	6 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	4 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

Table MOR.T2IPCAST.KM.MITTM0.S2: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region I, Interaction p-value: 0.1169							
North and South America							
Relugolix	161	159 (98.8)	2 (1.2)	15.0 [14.0;15.0]	-14.0	3.339 [2.537;4.394]	<.0001
Leuprolide	80	79 (98.8)	1 (1.3)	29.0 [29.0;30.0]			
Europe							
Relugolix	155	151 (97.4)	4 (2.6)	15.0 [NE;NE]	-14.0	3.519 [2.654;4.666]	<.0001
Leuprolide	78	77 (98.7)	1 (1.3)	29.0 [29.0;30.0]			
Asia and Rest of World							
Relugolix	111	110 (99.1)	1 (0.9)	15.0 [NE;NE]	-14.0	5.122 [3.642;7.202]	<.0001
Leuprolide	55	54 (98.2)	1 (1.8)	29.0 [29.0;30.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2IPCAST.KM.MITTM0.S8: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.1386							
Asia (Excl. Korea)							
Relugolix	70	70 (100.0)	0	15.0 [NE;NE]	-14.0	5.015 [3.302;7.616]	<.0001
Leuprolide	36	36 (100.0)	0	29.0 [NE;NE]			
Rest of World							
Relugolix	357	350 (98.0)	7 (2.0)	15.0 [NE;NE]	-14.0	3.574 [2.954;4.324]	<.0001
Leuprolide	177	174 (98.3)	3 (1.7)	29.0 [29.0;30.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2IPCAST.KM.MITTM0.S1: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.1686							
<= 75 years old							
Relugolix	304	297 (97.7)	7 (2.3)	15.0 [NE;NE]	-14.0	3.497 [2.851;4.289]	<.0001
Leuprolide	153	151 (98.7)	2 (1.3)	29.0 [29.0;30.0]			
> 75 years old							
Relugolix	123	123 (100.0)	0	15.0 [14.0;15.0]	-14.0	4.539 [3.289;6.264]	<.0001
Leuprolide	60	59 (98.3)	1 (1.7)	29.0 [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2IPCAST.KM.MITTM0.S7: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.2680							
< 20 ng/mL							
Relugolix	320	315 (98.4)	5 (1.6)	15.0 [NE;NE]	-14.0	3.880 [3.184;4.729]	<.0001
Leuprolide	169	166 (98.2)	3 (1.8)	29.0 [29.0;30.0]			
>= 20 ng/mL							
Relugolix	107	105 (98.1)	2 (1.9)	15.0 [NE;NE]	-14.0	3.092 [2.161;4.426]	<.0001
Leuprolide	44	44 (100.0)	0	29.0 [29.0;30.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2IPCAST.KM.MITTM0.S5: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.6068							
< 8							
Relugolix	252	247 (98.0)	5 (2.0)	15.0 [NE;NE]	-14.0	3.525 [2.833;4.388]	<.0001
Leuprolide	136	133 (97.8)	3 (2.2)	29.0 [29.0;30.0]			
>= 8							
Relugolix	163	161 (98.8)	2 (1.2)	15.0 [14.0;15.0]	-14.0	3.864 [2.908;5.133]	<.0001
Leuprolide	74	74 (100.0)	0	29.0 [29.0;30.0]			
Missing							
Relugolix	12	12 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	3 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.T2IPCAST.KM.MITTM0.S6: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: 0.8933							
< 250 ng/dL							
Relugolix	37	37 (100.0)	0	6.0 [5.0;13.0]	-22.0	3.830 [2.209;6.643]	<.0001
Leuprolide	20	20 (100.0)	0	28.0 [22.0;29.0]			
>= 250 ng/dL							
Relugolix	383	376 (98.2)	7 (1.8)	15.0 [NE;NE]	-14.0	3.682 [3.052;4.441]	<.0001
Leuprolide	185	182 (98.4)	3 (1.6)	29.0 [29.0;30.0]			
Missing							
Relugolix	7	7 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	8 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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4.1.4.1.3 Anhaltende Kastration

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.T2STCW5.KM.MITTM0.S1: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.0702							
<= 75 years old							
Relugolix	304	14 (4.6)	290 (95.4)	NE [NE;NE]	NE	0.492 [0.234;1.031]	0.0603
Leuprolide	153	14 (9.2)	139 (90.8)	NE [NE;NE]			
> 75 years old							
Relugolix	123	1 (0.8)	122 (99.2)	NE [NE;NE]	NE	0.063 [0.008;0.513]	0.0097
Leuprolide	60	7 (11.7)	53 (88.3)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2STCW5.KM.MITTM0.S3: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.1376							
Not Hispanic or Latino							
Relugolix	381	12 (3.1)	369 (96.9)	NE [NE;NE]	NE	0.297 [0.144;0.612]	0.0010
Leuprolide	188	19 (10.1)	169 (89.9)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	37	3 (8.1)	34 (91.9)	NE [NE;NE]	NE	1.796 [0.187;17.269]	0.6119
Leuprolide	22	1 (4.5)	21 (95.5)	NE [NE;NE]			
Not Reported							
Relugolix	9	0	9 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.T2STCW5.KM.MITTM0.S7: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.2963							
< 20 ng/mL							
Relugolix	320	10 (3.1)	310 (96.9)	NE [NE;NE]	NE	0.280 [0.129;0.606]	0.0012
Leuprolide	169	18 (10.7)	151 (89.3)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	107	5 (4.7)	102 (95.3)	NE [NE;NE]	NE	0.665 [0.159;2.784]	0.5768
Leuprolide	44	3 (6.8)	41 (93.2)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2STCW5.KM.MITTM0.S5: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.6501							
< 8							
Relugolix	252	8 (3.2)	244 (96.8)	NE [NE;NE]	NE	0.319 [0.132;0.770]	0.0111
Leuprolide	136	13 (9.6)	123 (90.4)	NE [NE;NE]			
>= 8							
Relugolix	163	7 (4.3)	156 (95.7)	NE [NE;NE]	NE	0.438 [0.154;1.250]	0.1229
Leuprolide	74	7 (9.5)	67 (90.5)	NE [NE;NE]			
Missing							
Relugolix	12	0	12 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.T2STCW5.KM.MITTM0.S4: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.6719							
Asian							
Relugolix	94	3 (3.2)	91 (96.8)	NE [NE;NE]	NE	0.220 [0.057;0.850]	0.0281
Leuprolide	51	7 (13.7)	44 (86.3)	NE [NE;NE]			
Black or African American							
Relugolix	21	2 (9.5)	19 (90.5)	NE [NE;NE]	NE	1.209 [0.110;13.339]	0.8768
Leuprolide	12	1 (8.3)	11 (91.7)	NE [NE;NE]			
White							
Relugolix	292	8 (2.7)	284 (97.3)	NE [NE;NE]	NE	0.303 [0.124;0.741]	0.0089
Leuprolide	139	12 (8.6)	127 (91.4)	NE [NE;NE]			
Others							
Relugolix	14	1 (7.1)	13 (92.9)	NE [NE;NE]	NE	0.448 [0.028;7.169]	0.5705
Leuprolide	7	1 (14.3)	6 (85.7)	NE [29.0;NE]			
Not Reported							
Relugolix	6	1 (16.7)	5 (83.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

Table MOR.T2STCW5.KM.MITTM0.S2: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region I, Interaction p-value: 0.9658							
North and South America							
Relugolix	161	7 (4.3)	154 (95.7)	NE [NE;NE]	NE	0.368 [0.137;0.988]	0.0473
Leuprolide	80	9 (11.3)	71 (88.8)	NE [NE;NE]			
Europe							
Relugolix	155	3 (1.9)	152 (98.1)	NE [NE;NE]	NE	0.291 [0.070;1.219]	0.0913
Leuprolide	78	5 (6.4)	73 (93.6)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	111	5 (4.5)	106 (95.5)	NE [NE;NE]	NE	0.336 [0.107;1.058]	0.0624
Leuprolide	55	7 (12.7)	48 (87.3)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2STCW5.KM.MITTM0.S8: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.9894							
Asia (Excl. Korea)							
Relugolix	70	2 (2.9)	68 (97.1)	NE [NE;NE]	NE	0.336 [0.056;2.012]	0.2324
Leuprolide	36	3 (8.3)	33 (91.7)	NE [NE;NE]			
Rest of World							
Relugolix	357	13 (3.6)	344 (96.4)	NE [NE;NE]	NE	0.341 [0.167;0.695]	0.0031
Leuprolide	177	18 (10.2)	159 (89.8)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2STCW5.KM.MITTM0.S6: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: NC							
< 250 ng/dL							
Relugolix	37	0	37 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	20	1 (5.0)	19 (95.0)	NC [NC;NC]			
>= 250 ng/dL							
Relugolix	383	15 (3.9)	368 (96.1)	NE [NE;NE]	NE	0.345 [0.176;0.673]	0.0018
Leuprolide	185	20 (10.8)	165 (89.2)	NE [NE;NE]			
Missing							
Relugolix	7	0	7 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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4.1.4.1.4 Anhaltende profunde Kastration

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Table MOR.T2SPCW5.KM.MITTM0.S6: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: 0.1516							
< 250 ng/dL							
Relugolix	37	6 (16.2)	31 (83.8)	NE [NE;NE]	NE	1.675 [0.338;8.297]	0.5276
Leuprolide	20	2 (10.0)	18 (90.0)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	383	78 (20.4)	305 (79.6)	NE [NE;NE]	NE	0.506 [0.363;0.707]	<.0001
Leuprolide	185	62 (33.5)	123 (66.5)	NE [NE;NE]			
Missing							
Relugolix	7	0	7 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	2 (25.0)	6 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.T2SPCW5.KM.MITTM0.S7: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.2086							
< 20 ng/mL							
Relugolix	320	62 (19.4)	258 (80.6)	NE [NE;NE]	NE	0.489 [0.341;0.702]	0.0001
Leuprolide	169	56 (33.1)	113 (66.9)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	107	22 (20.6)	85 (79.4)	NE [NE;NE]	NE	0.834 [0.395;1.761]	0.6332
Leuprolide	44	10 (22.7)	34 (77.3)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2SPCW5.KM.MITTM0.S1: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.2707							
<= 75 years old							
Relugolix	304	74 (24.3)	230 (75.7)	NE [NE;NE]	NE	0.586 [0.413;0.833]	0.0029
Leuprolide	153	54 (35.3)	99 (64.7)	NE [NE;NE]			
> 75 years old							
Relugolix	123	10 (8.1)	113 (91.9)	NE [NE;NE]	NE	0.351 [0.152;0.814]	0.0146
Leuprolide	60	12 (20.0)	48 (80.0)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2SPCW5.KM.MITTM0.S3: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.4608							
Not Hispanic or Latino							
Relugolix	381	72 (18.9)	309 (81.1)	NE [NE;NE]	NE	0.541 [0.381;0.767]	0.0006
Leuprolide	188	56 (29.8)	132 (70.2)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	37	11 (29.7)	26 (70.3)	NE [NE;NE]	NE	0.781 [0.314;1.942]	0.5943
Leuprolide	22	8 (36.4)	14 (63.6)	NE [57.0;NE]			
Not Reported							
Relugolix	9	1 (11.1)	8 (88.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.T2SPCW5.KM.MITTM0.S4: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.4835							
Asian							
Relugolix	94	17 (18.1)	77 (81.9)	NE [NE;NE]	NE	0.562 [0.277;1.140]	0.1105
Leuprolide	51	14 (27.5)	37 (72.5)	NE [NE;NE]			
Black or African American							
Relugolix	21	9 (42.9)	12 (57.1)	NE [57.0;NE]	NE	0.876 [0.293;2.622]	0.8129
Leuprolide	12	5 (41.7)	7 (58.3)	NE [29.0;NE]			
White							
Relugolix	292	55 (18.8)	237 (81.2)	NE [NE;NE]	NE	0.537 [0.359;0.803]	0.0025
Leuprolide	139	42 (30.2)	97 (69.8)	NE [NE;NE]			
Others							
Relugolix	14	2 (14.3)	12 (85.7)	NE [NE;NE]	NE	0.175 [0.032;0.956]	0.0442
Leuprolide	7	4 (57.1)	3 (42.9)	225.0 [29.0;NE]			
Not Reported							
Relugolix	6	1 (16.7)	5 (83.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	1 (25.0)	3 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

Table MOR.T2SPCW5.KM.MITTM0.S8: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.5076							
Asia (Excl. Korea)							
Relugolix	70	14 (20.0)	56 (80.0)	NE [NE;NE]	NE	0.703 [0.304;1.624]	0.4089
Leuprolide	36	9 (25.0)	27 (75.0)	NE [NE;NE]			
Rest of World							
Relugolix	357	70 (19.6)	287 (80.4)	NE [NE;NE]	NE	0.517 [0.364;0.734]	0.0002
Leuprolide	177	57 (32.2)	120 (67.8)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2SPCW5.KM.MITTM0.S5: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Gleason Score at Study Entry, Interaction p-value: 0.7295							
< 8							
Relugolix	252	53 (21.0)	199 (79.0)	NE [NE;NE]	NE	0.577 [0.386;0.863]	0.0074
Leuprolide	136	43 (31.6)	93 (68.4)	NE [NE;NE]			
>= 8							
Relugolix	163	29 (17.8)	134 (82.2)	NE [NE;NE]	NE	0.511 [0.294;0.890]	0.0177
Leuprolide	74	22 (29.7)	52 (70.3)	NE [NE;NE]			
Missing							
Relugolix	12	2 (16.7)	10 (83.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.T2SPCW5.KM.MITTM0.S2: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region I, Interaction p-value: 0.8855							
North and South America							
Relugolix	161	31 (19.3)	130 (80.7)	NE [NE;NE]	NE	0.513 [0.305;0.865]	0.0123
Leuprolide	80	26 (32.5)	54 (67.5)	NE [NE;NE]			
Europe							
Relugolix	155	31 (20.0)	124 (80.0)	NE [NE;NE]	NE	0.522 [0.308;0.885]	0.0158
Leuprolide	78	25 (32.1)	53 (67.9)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	111	22 (19.8)	89 (80.2)	NE [NE;NE]	NE	0.626 [0.324;1.206]	0.1614
Leuprolide	55	15 (27.3)	40 (72.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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4.1.4.1.5 Wiederanstieg der Testosteronkonzentration

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.TG50SFU.BIN.MITTM0.S8: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.0313						
Asia (Excl. Korea)						
Relugolix	70	22 (31.4)	7.792	5.657	0.259	0.0027
Leuprolide	36	2 (5.6)	[1.717;35.367]	[1.408;22.726]	[0.127;0.391]	
Rest of World						
Relugolix	357	182 (51.0)	91.000	45.118	0.499	<.0001
Leuprolide	177	2 (1.1)	[22.236;372.420]	[11.330;179.661]	[0.444;0.553]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat.

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Table MOR.TG50SFU.BIN.MITTM0.S4: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.0666						
Asian						
Relugolix	94	34 (36.2)	9.067	6.149	0.303	<.0001
Leuprolide	51	3 (5.9)	[2.624;31.330]	[1.986;19.038]	[0.186;0.420]	
Black or African American						
Relugolix	21	13 (61.9)	39.706	15.955	0.619	0.0005
Leuprolide	12	0	[2.070;761.738]	[1.032;246.626]	[0.411;0.827]	
White						
Relugolix	292	150 (51.4)	>99	71.404	0.507	<.0001
Leuprolide	139	1 (0.7)	[NE;NE]	[10.097;504.941]	[0.447;0.566]	
Others						
Relugolix	14	5 (35.7)	8.684	5.867	0.357	0.1235
Leuprolide	7	0	[0.412;183.233]	[0.369;93.155]	[0.106;0.608]	
Not Reported						
Relugolix	6	2 (33.3)	NC	NC	NC	NC
Leuprolide	4	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.TG50SFU.BIN.MITTM0.S2: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: 0.0710						
North and South America						
Relugolix	161	85 (52.8)	88.355	42.236	0.515	<.0001
Leuprolide	80	1 (1.3)	[12.000;650.550]	[5.990;297.799]	[0.435;0.596]	
Europe						
Relugolix	155	76 (49.0)	>99	77.481	0.490	<.0001
Leuprolide	78	0	[NE;NE]	[4.867;1233.584]	[0.412;0.569]	
Asia and Rest of World						
Relugolix	111	43 (38.7)	10.961	7.102	0.333	<.0001
Leuprolide	55	3 (5.5)	[3.220;37.306]	[2.306;21.874]	[0.224;0.442]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.TG50SFU.BIN.MITTM0.S1: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.7267						
<= 75 years old						
Relugolix	304	158 (52.0)	54.110	26.507	0.500	<.0001
Leuprolide	153	3 (2.0)	[16.882;173.434]	[8.600;81.698]	[0.440;0.560]	
> 75 years old						
Relugolix	123	46 (37.4)	35.247	22.439	0.357	<.0001
Leuprolide	60	1 (1.7)	[4.723;263.049]	[3.170;158.819]	[0.266;0.449]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat.

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Table MOR.TG50SFU.BIN.MITTM0.S6: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.7903						
< 250 ng/dL						
Relugolix	37	15 (40.5)	28.244	17.132	0.405	0.0005
Leuprolide	20	0	[1.587;502.672]	[1.079;272.107]	[0.247;0.564]	
>= 250 ng/dL						
Relugolix	383	188 (49.1)	43.626	22.702	0.469	<.0001
Leuprolide	185	4 (2.2)	[15.877;119.875]	[8.566;60.169]	[0.415;0.524]	
Missing						
Relugolix	7	1 (14.3)	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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Table MOR.TG50SFU.BIN.MITTM0.S7: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.8041						
< 20 ng/mL						
Relugolix	320	175 (54.7)	49.784	23.105	0.523	<.0001
Leuprolide	169	4 (2.4)	[18.025;137.500]	[8.729;61.161]	[0.464;0.582]	
>= 20 ng/mL						
Relugolix	107	29 (27.1)	33.446	24.583	0.271	<.0001
Leuprolide	44	0	[1.995;560.718]	[1.535;393.685]	[0.187;0.355]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat.

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Table MOR.TG50SFU.BIN.MITTM0.S3: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.9266						
Not Hispanic or Latino						
Relugolix	381	180 (47.2)	41.194	22.205	0.451	<.0001
Leuprolide	188	4 (2.1)	[14.992;113.192]	[8.373;58.886]	[0.397;0.505]	
Hispanic or Latino						
Relugolix	37	19 (51.4)	47.432	23.605	0.514	<.0001
Leuprolide	22	0	[2.679;839.688]	[1.496;372.568]	[0.352;0.675]	
Not Reported						
Relugolix	9	5 (55.6)	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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Table MOR.TG50SFU.BIN.MITTM0.S5: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.9704						
< 8						
Relugolix	252	132 (52.4)	48.767	23.746	0.502	<.0001
Leuprolide	136	3 (2.2)	[15.125;157.232]	[7.708;73.158]	[0.435;0.568]	
>= 8						
Relugolix	163	67 (41.1)	50.948	30.417	0.398	<.0001
Leuprolide	74	1 (1.4)	[6.910;375.651]	[4.305;214.935]	[0.318;0.478]	
Missing						
Relugolix	12	5 (41.7)	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_BIN.SAS

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4.1.4.2 Prostataspezifisches-Antigen-Ansprechrate

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.PSAR50W3.BIN.MITTM0.S2: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: 0.0875						
North and South America						
Relugolix	161	123 (76.4)	39.921	10.186	0.689	<.0001
Leuprolide	80	6 (7.5)	[16.101;98.979]	[4.696;22.096]	[0.602;0.776]	
Europe						
Relugolix	155	117 (75.5)	11.931	3.680	0.550	<.0001
Leuprolide	78	16 (20.5)	[6.165;23.090]	[2.356;5.748]	[0.437;0.662]	
Asia and Rest of World						
Relugolix	111	91 (82.0)	23.256	5.010	0.656	<.0001
Leuprolide	55	9 (16.4)	[9.812;55.117]	[2.739;9.164]	[0.535;0.777]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen.

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Table MOR.PSAR50W3.BIN.MITTM0.S1: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.1717						
<= 75 years old						
Relugolix	304	246 (80.9)	25.255	5.628	0.665	<.0001
Leuprolide	153	22 (14.4)	[14.797;43.105]	[3.808;8.316]	[0.594;0.736]	
> 75 years old						
Relugolix	123	85 (69.1)	12.675	4.607	0.541	<.0001
Leuprolide	60	9 (15.0)	[5.666;28.358]	[2.494;8.511]	[0.419;0.663]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_BIN.SAS

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Table MOR.PSAR50W3.BIN.MITTM0.S8: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.2284						
Asia (Excl. Korea)						
Relugolix	70	56 (80.0)	12.000	3.200	0.550	<.0001
Leuprolide	36	9 (25.0)	[4.618;31.185]	[1.796;5.703]	[0.380;0.720]	
Rest of World						
Relugolix	357	275 (77.0)	23.628	6.197	0.646	<.0001
Leuprolide	177	22 (12.4)	[14.187;39.352]	[4.175;9.201]	[0.581;0.711]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen.

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Table MOR.PSAR50W3.BIN.MITTM0.S5: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.2527						
< 8						
Relugolix	252	189 (75.0)	16.429	4.857	0.596	<.0001
Leuprolide	136	21 (15.4)	[9.521;28.349]	[3.257;7.244]	[0.515;0.676]	
>= 8						
Relugolix	163	133 (81.6)	28.373	6.038	0.681	<.0001
Leuprolide	74	10 (13.5)	[13.068;61.606]	[3.377;10.795]	[0.583;0.779]	
Missing						
Relugolix	12	9 (75.0)	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_BIN.SAS

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Table MOR.PSAR50W3.BIN.MITTM0.S4: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.2904						
Asian						
Relugolix	94	75 (79.8)	16.184	4.069	0.602	<.0001
Leuprolide	51	10 (19.6)	[6.882;38.060]	[2.313;7.159]	[0.466;0.738]	
Black or African American						
Relugolix	21	17 (81.0)	97.222	20.682	0.810	<.0001
Leuprolide	12	0	[4.790;1973.469]	[1.354;315.918]	[0.642;0.977]	
White						
Relugolix	292	221 (75.7)	17.490	5.010	0.606	<.0001
Leuprolide	139	21 (15.1)	[10.236;29.884]	[3.360;7.469]	[0.529;0.683]	
Others						
Relugolix	14	13 (92.9)	>99	14.400	0.929	<.0001
Leuprolide	7	0	[NE;NE]	[0.978;211.943]	[0.794;1.000]	
Not Reported						
Relugolix	6	5 (83.3)	NC	NC	NC	NC
Leuprolide	4	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_BIN.SAS

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Table MOR.PSAR50W3.BIN.MITTM0.S6: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.3918						
< 250 ng/dL						
Relugolix	37	28 (75.7)	12.444	3.784	0.557	<.0001
Leuprolide	20	4 (20.0)	[3.297;46.975]	[1.546;9.263]	[0.334;0.780]	
>= 250 ng/dL						
Relugolix	383	298 (77.8)	23.519	5.998	0.648	<.0001
Leuprolide	185	24 (13.0)	[14.380;38.464]	[4.114;8.744]	[0.584;0.712]	
Missing						
Relugolix	7	5 (71.4)	NC	NC	NC	NC
Leuprolide	8	3 (37.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen; NC: Not calculated.

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Table MOR.PSAR50W3.BIN.MITTM0.S7: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.5058						
< 20 ng/mL						
Relugolix	320	243 (75.9)	22.241	6.111	0.635	<.0001
Leuprolide	169	21 (12.4)	[13.170;37.560]	[4.076;9.162]	[0.567;0.703]	
>= 20 ng/mL						
Relugolix	107	88 (82.2)	15.747	3.619	0.595	<.0001
Leuprolide	44	10 (22.7)	[6.651;37.286]	[2.084;6.284]	[0.452;0.739]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen.

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Table MOR.PSAR50W3.BIN.MITTM0.S3: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.5986						
Not Hispanic or Latino						
Relugolix	381	299 (78.5)	19.992	5.088	0.631	<.0001
Leuprolide	188	29 (15.4)	[12.556;31.831]	[3.625;7.139]	[0.564;0.697]	
Hispanic or Latino						
Relugolix	37	28 (75.7)	31.111	8.324	0.666	<.0001
Leuprolide	22	2 (9.1)	[6.059;159.759]	[2.193;31.600]	[0.483;0.849]	
Not Reported						
Relugolix	9	4 (44.4)	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen; NC: Not calculated.

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4.1.5 Gesundheitsbezogene Lebensqualität

4.1.5.1 Gesundheitsbezogene Lebensqualität (European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire C30)

4.1.5.1.1 Skala: Globaler Gesundheitszustand

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2GLBH15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.1475							
Asian							
Relugolix	94	45 (47.9)	49 (52.1)	343.0 [251.0;NE]	8.0	0.885 [0.555;1.412]	0.6085
Leuprolide	51	29 (56.9)	22 (43.1)	335.0 [169.0;NE]			
Black or African American							
Relugolix	21	10 (47.6)	11 (52.4)	NE [169.0;NE]	NE	0.902 [0.308;2.639]	0.8502
Leuprolide	12	5 (41.7)	7 (58.3)	254.0 [30.0;NE]			
White							
Relugolix	292	151 (51.7)	141 (48.3)	336.0 [253.0;341.0]	NE	1.253 [0.927;1.694]	0.1424
Leuprolide	139	59 (42.4)	80 (57.6)	NE [329.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.1475							
Others							
Relugolix	14	6 (42.9)	8 (57.1)	339.0 [169.0;NE]	249.0	0.352 [0.112;1.112]	0.0752
Leuprolide	7	6 (85.7)	1 (14.3)	90.0 [29.0;NE]			
Not Reported							
Relugolix	6	3 (50.0)	3 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	2 (50.0)	2 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITTM0.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.3670							
< 20 ng/mL							
Relugolix	320	155 (48.4)	165 (51.6)	340.0 [258.0;344.0]	3.0	0.999 [0.764;1.306]	0.9948
Leuprolide	169	82 (48.5)	87 (51.5)	337.0 [253.0;NE]			
>= 20 ng/mL							
Relugolix	107	60 (56.1)	47 (43.9)	256.0 [174.0;NE]	-83.0	1.306 [0.779;2.188]	0.3111
Leuprolide	44	19 (43.2)	25 (56.8)	339.0 [253.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITTM0.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.5639							
Asia (Excl. Korea)							
Relugolix	70	38 (54.3)	32 (45.7)	330.0 [169.0;NE]	-9.0	1.234 [0.704;2.163]	0.4620
Leuprolide	36	18 (50.0)	18 (50.0)	339.0 [169.0;NE]			
Rest of World							
Relugolix	357	177 (49.6)	180 (50.4)	337.0 [254.0;342.0]	-14.0	1.029 [0.792;1.336]	0.8311
Leuprolide	177	83 (46.9)	94 (53.1)	351.0 [254.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITTM0.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.6337							
< 8							
Relugolix	252	123 (48.8)	129 (51.2)	337.0 [250.0;NE]	0.0	1.052 [0.779;1.421]	0.7400
Leuprolide	136	65 (47.8)	71 (52.2)	337.0 [253.0;NE]			
>= 8							
Relugolix	163	88 (54.0)	75 (46.0)	337.0 [254.0;342.0]	-7.0	1.188 [0.796;1.774]	0.3982
Leuprolide	74	33 (44.6)	41 (55.4)	344.0 [334.0;NE]			
Missing							
Relugolix	12	4 (33.3)	8 (66.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	3 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITTM0.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.8106							
< 250 ng/dL							
Relugolix	37	18 (48.6)	19 (51.4)	337.0 [99.0;NE]	NE	0.953 [0.427;2.123]	0.9055
Leuprolide	20	9 (45.0)	11 (55.0)	NE [29.0;NE]			
>= 250 ng/dL							
Relugolix	383	192 (50.1)	191 (49.9)	337.0 [254.0;342.0]	-2.0	1.056 [0.820;1.359]	0.6739
Leuprolide	185	88 (47.6)	97 (52.4)	339.0 [258.0;NE]			
Missing							
Relugolix	7	5 (71.4)	2 (28.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITTM0.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.8195							
North and South America							
Relugolix	161	81 (50.3)	80 (49.7)	336.0 [253.0;NE]	NE	1.141 [0.767;1.696]	0.5148
Leuprolide	80	35 (43.8)	45 (56.3)	NE [253.0;NE]			
Europe							
Relugolix	155	78 (50.3)	77 (49.7)	340.0 [176.0;NE]	-11.0	1.087 [0.729;1.620]	0.6836
Leuprolide	78	35 (44.9)	43 (55.1)	351.0 [169.0;NE]			
Asia and Rest of World							
Relugolix	111	56 (50.5)	55 (49.5)	337.0 [176.0;NE]	2.0	0.947 [0.611;1.469]	0.8093
Leuprolide	55	31 (56.4)	24 (43.6)	335.0 [169.0;344.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITTM0.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.8264							
Not Hispanic or Latino							
Relugolix	381	195 (51.2)	186 (48.8)	337.0 [253.0;342.0]	0.0	1.082 [0.842;1.389]	0.5384
Leuprolide	188	90 (47.9)	98 (52.1)	337.0 [258.0;NE]			
Hispanic or Latino							
Relugolix	37	17 (45.9)	20 (54.1)	339.0 [175.0;NE]	NE	0.984 [0.438;2.208]	0.9687
Leuprolide	22	9 (40.9)	13 (59.1)	NE [85.0;NE]			
Not Reported							
Relugolix	9	3 (33.3)	6 (66.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITTM0.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.8869							
<= 75 years old							
Relugolix	304	151 (49.7)	153 (50.3)	337.0 [254.0;344.0]	-2.0	1.051 [0.794;1.392]	0.7292
Leuprolide	153	72 (47.1)	81 (52.9)	339.0 [175.0;NE]			
> 75 years old							
Relugolix	123	64 (52.0)	59 (48.0)	337.0 [175.0;NE]	-7.0	1.091 [0.703;1.693]	0.6963
Leuprolide	60	29 (48.3)	31 (51.7)	344.0 [253.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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4.1.5.1.2 Skala: Körperliche Funktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2PHYS15.KM.MITTM0.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.0626							
< 20 ng/mL							
Relugolix	320	76 (23.8)	244 (76.3)	NE [NE;NE]	NE	1.360 [0.892;2.076]	0.1534
Leuprolide	169	30 (17.8)	139 (82.2)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	107	21 (19.6)	86 (80.4)	NE [NE;NE]	NE	0.621 [0.305;1.263]	0.1880
Leuprolide	44	12 (27.3)	32 (72.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PHYS15.KM.MITTM0.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.4274							
Not Hispanic or Latino							
Relugolix	381	83 (21.8)	298 (78.2)	NE [NE;NE]	NE	1.099 [0.743;1.626]	0.6354
Leuprolide	188	36 (19.1)	152 (80.9)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	37	13 (35.1)	24 (64.9)	NE [255.0;NE]	NE	1.719 [0.613;4.826]	0.3034
Leuprolide	22	5 (22.7)	17 (77.3)	NE [NE;NE]			
Not Reported							
Relugolix	9	1 (11.1)	8 (88.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2PHYS15.KM.MITTM0.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.6155							
< 250 ng/dL							
Relugolix	37	6 (16.2)	31 (83.8)	NE [NE;NE]	NE	0.835 [0.236;2.960]	0.7806
Leuprolide	20	4 (20.0)	16 (80.0)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	383	89 (23.2)	294 (76.8)	NE [NE;NE]	NE	1.173 [0.796;1.727]	0.4201
Leuprolide	185	36 (19.5)	149 (80.5)	NE [NE;NE]			
Missing							
Relugolix	7	2 (28.6)	5 (71.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	2 (25.0)	6 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2PHYS15.KM.MITTM0.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.7193							
< 8							
Relugolix	252	56 (22.2)	196 (77.8)	NE [NE;NE]	NE	1.216 [0.759;1.948]	0.4169
Leuprolide	136	25 (18.4)	111 (81.6)	NE [NE;NE]			
>= 8							
Relugolix	163	36 (22.1)	127 (77.9)	NE [344.0;NE]	NE	1.057 [0.578;1.930]	0.8578
Leuprolide	74	15 (20.3)	59 (79.7)	NE [NE;NE]			
Missing							
Relugolix	12	5 (41.7)	7 (58.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2PHYS15.KM.MITTM0.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.7429							
<= 75 years old							
Relugolix	304	70 (23.0)	234 (77.0)	NE [344.0;NE]	NE	1.176 [0.767;1.805]	0.4568
Leuprolide	153	30 (19.6)	123 (80.4)	NE [NE;NE]			
> 75 years old							
Relugolix	123	27 (22.0)	96 (78.0)	NE [NE;NE]	NE	1.028 [0.521;2.030]	0.9358
Leuprolide	60	12 (20.0)	48 (80.0)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PHYS15.KM.MITTM0.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.8092							
Asia (Excl. Korea)							
Relugolix	70	12 (17.1)	58 (82.9)	NE [344.0;NE]	NE	1.269 [0.447;3.603]	0.6541
Leuprolide	36	5 (13.9)	31 (86.1)	NE [NE;NE]			
Rest of World							
Relugolix	357	85 (23.8)	272 (76.2)	NE [NE;NE]	NE	1.107 [0.752;1.628]	0.6067
Leuprolide	177	37 (20.9)	140 (79.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PHYS15.KM.MITTM0.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region I, Interaction p-value: 0.9126							
North and South America							
Relugolix	161	45 (28.0)	116 (72.0)	NE [344.0;NE]	NE	1.224 [0.709;2.115]	0.4684
Leuprolide	80	18 (22.5)	62 (77.5)	NE [341.0;NE]			
Europe							
Relugolix	155	31 (20.0)	124 (80.0)	NE [NE;NE]	NE	1.023 [0.552;1.895]	0.9430
Leuprolide	78	15 (19.2)	63 (80.8)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	111	21 (18.9)	90 (81.1)	NE [344.0;NE]	NE	1.128 [0.516;2.463]	0.7630
Leuprolide	55	9 (16.4)	46 (83.6)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PHYS15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.9603							
Asian							
Relugolix	94	16 (17.0)	78 (83.0)	NE [344.0;NE]	NE	1.070 [0.458;2.502]	0.8752
Leuprolide	51	8 (15.7)	43 (84.3)	NE [NE;NE]			
Black or African American							
Relugolix	21	6 (28.6)	15 (71.4)	NE [253.0;NE]	NE	1.412 [0.285;7.001]	0.6729
Leuprolide	12	2 (16.7)	10 (83.3)	NE [94.0;NE]			
White							
Relugolix	292	69 (23.6)	223 (76.4)	NE [NE;NE]	NE	1.168 [0.753;1.812]	0.4888
Leuprolide	139	28 (20.1)	111 (79.9)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PHYS15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.9603							
Others							
Relugolix	14	5 (35.7)	9 (64.3)	NE [29.0;NE]	NE	0.823 [0.196;3.451]	0.7904
Leuprolide	7	3 (42.9)	4 (57.1)	NE [29.0;NE]			
Not Reported							
Relugolix	6	1 (16.7)	5 (83.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	1 (25.0)	3 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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4.1.5.1.3 Skala: Rollenfunktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2ROLE15.KM.MITTM0.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.0070							
Not Hispanic or Latino							
Relugolix	381	169 (44.4)	212 (55.6)	344.0 [337.0;NE]	2.0	1.024 [0.787;1.331]	0.8619
Leuprolide	188	83 (44.1)	105 (55.9)	342.0 [334.0;NE]			
Hispanic or Latino							
Relugolix	37	24 (64.9)	13 (35.1)	169.0 [85.0;255.0]	NE	4.056 [1.546;10.638]	0.0044
Leuprolide	22	5 (22.7)	17 (77.3)	NE [NE;NE]			
Not Reported							
Relugolix	9	7 (77.8)	2 (22.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITTM0.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.2849							
Asia (Excl. Korea)							
Relugolix	70	33 (47.1)	37 (52.9)	344.0 [253.0;NE]	NE	1.622 [0.837;3.141]	0.1519
Leuprolide	36	12 (33.3)	24 (66.7)	NE [334.0;NE]			
Rest of World							
Relugolix	357	167 (46.8)	190 (53.2)	340.0 [267.0;NE]	-2.0	1.098 [0.839;1.437]	0.4935
Leuprolide	177	78 (44.1)	99 (55.9)	342.0 [335.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITTM0.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.3208							
< 20 ng/mL							
Relugolix	320	144 (45.0)	176 (55.0)	342.0 [337.0;NE]	0.0	1.086 [0.819;1.440]	0.5657
Leuprolide	169	73 (43.2)	96 (56.8)	342.0 [335.0;NE]			
>= 20 ng/mL							
Relugolix	107	56 (52.3)	51 (47.7)	337.0 [170.0;NE]	NE	1.481 [0.860;2.551]	0.1566
Leuprolide	44	17 (38.6)	27 (61.4)	NE [252.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITTM0.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.4688							
< 250 ng/dL							
Relugolix	37	18 (48.6)	19 (51.4)	337.0 [169.0;NE]	NE	1.570 [0.655;3.758]	0.3116
Leuprolide	20	7 (35.0)	13 (65.0)	NE [169.0;NE]			
>= 250 ng/dL							
Relugolix	383	178 (46.5)	205 (53.5)	342.0 [333.0;NE]	0.0	1.120 [0.860;1.459]	0.3988
Leuprolide	185	80 (43.2)	105 (56.8)	342.0 [335.0;NE]			
Missing							
Relugolix	7	4 (57.1)	3 (42.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	3 (37.5)	5 (62.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITTM0.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.5619							
North and South America							
Relugolix	161	83 (51.6)	78 (48.4)	255.0 [169.0;NE]	-87.0	1.354 [0.912;2.010]	0.1331
Leuprolide	80	35 (43.8)	45 (56.3)	342.0 [260.0;NE]			
Europe							
Relugolix	155	68 (43.9)	87 (56.1)	342.0 [334.0;NE]	NE	0.991 [0.657;1.496]	0.9670
Leuprolide	78	34 (43.6)	44 (56.4)	NE [258.0;NE]			
Asia and Rest of World							
Relugolix	111	49 (44.1)	62 (55.9)	344.0 [333.0;NE]	4.0	1.198 [0.718;1.998]	0.4887
Leuprolide	55	21 (38.2)	34 (61.8)	340.0 [334.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITTM0.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.5877							
<= 75 years old							
Relugolix	304	135 (44.4)	169 (55.6)	344.0 [337.0;NE]	NE	1.116 [0.829;1.503]	0.4695
Leuprolide	153	64 (41.8)	89 (58.2)	NE [335.0;NE]			
> 75 years old							
Relugolix	123	65 (52.8)	58 (47.2)	337.0 [172.0;NE]	-5.0	1.297 [0.823;2.044]	0.2623
Leuprolide	60	26 (43.3)	34 (56.7)	342.0 [253.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.7998							
Asian							
Relugolix	94	42 (44.7)	52 (55.3)	344.0 [260.0;NE]	4.0	1.309 [0.761;2.252]	0.3301
Leuprolide	51	19 (37.3)	32 (62.7)	340.0 [335.0;NE]			
Black or African American							
Relugolix	21	10 (47.6)	11 (52.4)	NE [78.0;NE]	NE	1.028 [0.351;3.011]	0.9593
Leuprolide	12	5 (41.7)	7 (58.3)	274.0 [85.0;NE]			
White							
Relugolix	292	135 (46.2)	157 (53.8)	342.0 [267.0;NE]	0.0	1.084 [0.802;1.464]	0.5998
Leuprolide	139	62 (44.6)	77 (55.4)	342.0 [331.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.7998							
Others							
Relugolix	14	9 (64.3)	5 (35.7)	170.0 [32.0;NE]	NE	1.925 [0.521;7.114]	0.3264
Leuprolide	7	3 (42.9)	4 (57.1)	NE [29.0;NE]			
Not Reported							
Relugolix	6	4 (66.7)	2 (33.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	1 (25.0)	3 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITTM0.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.9076							
< 8							
Relugolix	252	118 (46.8)	134 (53.2)	340.0 [253.0;NE]	-2.0	1.185 [0.865;1.622]	0.2906
Leuprolide	136	58 (42.6)	78 (57.4)	342.0 [334.0;NE]			
>= 8							
Relugolix	163	76 (46.6)	87 (53.4)	344.0 [267.0;NE]	-13.0	1.222 [0.801;1.865]	0.3521
Leuprolide	74	30 (40.5)	44 (59.5)	357.0 [335.0;NE]			
Missing							
Relugolix	12	6 (50.0)	6 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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4.1.5.1.4 Skala: Kognitive Funktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2COGN15.KM.MITTM0.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.1587							
Not Hispanic or Latino							
Relugolix	381	170 (44.6)	211 (55.4)	343.0 [337.0;NE]	6.0	0.891 [0.691;1.150]	0.3761
Leuprolide	188	91 (48.4)	97 (51.6)	337.0 [253.0;NE]			
Hispanic or Latino							
Relugolix	37	21 (56.8)	16 (43.2)	175.0 [85.0;NE]	NE	1.610 [0.737;3.516]	0.2324
Leuprolide	22	9 (40.9)	13 (59.1)	NE [84.0;NE]			
Not Reported							
Relugolix	9	7 (77.8)	2 (22.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	3 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITTM0.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.2912							
< 8							
Relugolix	252	113 (44.8)	139 (55.2)	NE [257.0;NE]	NE	1.058 [0.773;1.450]	0.7237
Leuprolide	136	59 (43.4)	77 (56.6)	NE [253.0;NE]			
>= 8							
Relugolix	163	80 (49.1)	83 (50.9)	342.0 [253.0;NE]	13.0	0.814 [0.560;1.183]	0.2795
Leuprolide	74	42 (56.8)	32 (43.2)	329.0 [169.0;339.0]			
Missing							
Relugolix	12	5 (41.7)	7 (58.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITTM0.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.2949							
North and South America							
Relugolix	161	77 (47.8)	84 (52.2)	337.0 [176.0;NE]	0.0	1.020 [0.692;1.505]	0.9187
Leuprolide	80	38 (47.5)	42 (52.5)	337.0 [170.0;NE]			
Europe							
Relugolix	155	68 (43.9)	87 (56.1)	350.0 [333.0;NE]	13.0	0.744 [0.505;1.097]	0.1359
Leuprolide	78	41 (52.6)	37 (47.4)	337.0 [91.0;NE]			
Asia and Rest of World							
Relugolix	111	53 (47.7)	58 (52.3)	NE [169.0;NE]	NE	1.184 [0.731;1.918]	0.4927
Leuprolide	55	24 (43.6)	31 (56.4)	344.0 [253.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITTM0.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.3268							
< 20 ng/mL							
Relugolix	320	140 (43.8)	180 (56.3)	NE [337.0;NE]	NE	0.876 [0.667;1.151]	0.3434
Leuprolide	169	82 (48.5)	87 (51.5)	337.0 [253.0;NE]			
>= 20 ng/mL							
Relugolix	107	58 (54.2)	49 (45.8)	255.0 [169.0;NE]	-83.0	1.165 [0.707;1.920]	0.5489
Leuprolide	44	21 (47.7)	23 (52.3)	338.0 [169.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.3573							
Asian							
Relugolix	94	47 (50.0)	47 (50.0)	337.0 [168.0;NE]	-7.0	1.172 [0.717;1.918]	0.5265
Leuprolide	51	24 (47.1)	27 (52.9)	344.0 [169.0;NE]			
Black or African American							
Relugolix	21	9 (42.9)	12 (57.1)	NE [86.0;NE]	NE	0.513 [0.191;1.379]	0.1859
Leuprolide	12	7 (58.3)	5 (41.7)	166.0 [29.0;NE]			
White							
Relugolix	292	132 (45.2)	160 (54.8)	343.0 [336.0;NE]	6.0	0.936 [0.696;1.258]	0.6603
Leuprolide	139	66 (47.5)	73 (52.5)	337.0 [253.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.3573							
Others							
Relugolix	14	6 (42.9)	8 (57.1)	NE [30.0;NE]	NE	0.509 [0.155;1.668]	0.2648
Leuprolide	7	5 (71.4)	2 (28.6)	93.0 [29.0;NE]			
Not Reported							
Relugolix	6	4 (66.7)	2 (33.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	1 (25.0)	3 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITTM0.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.4732							
Asia (Excl. Korea)							
Relugolix	70	35 (50.0)	35 (50.0)	337.0 [85.0;NE]	-7.0	1.145 [0.641;2.045]	0.6465
Leuprolide	36	17 (47.2)	19 (52.8)	344.0 [92.0;NE]			
Rest of World							
Relugolix	357	163 (45.7)	194 (54.3)	343.0 [336.0;NE]	6.0	0.907 [0.699;1.179]	0.4669
Leuprolide	177	86 (48.6)	91 (51.4)	337.0 [253.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITTM0.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.6415							
<= 75 years old							
Relugolix	304	139 (45.7)	165 (54.3)	NE [260.0;NE]	NE	0.911 [0.689;1.205]	0.5144
Leuprolide	153	76 (49.7)	77 (50.3)	337.0 [246.0;NE]			
> 75 years old							
Relugolix	123	59 (48.0)	64 (52.0)	342.0 [252.0;NE]	-2.0	1.035 [0.656;1.633]	0.8838
Leuprolide	60	27 (45.0)	33 (55.0)	344.0 [253.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITTM0.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.7156							
< 250 ng/dL							
Relugolix	37	17 (45.9)	20 (54.1)	NE [89.0;NE]	NE	1.080 [0.481;2.424]	0.8524
Leuprolide	20	9 (45.0)	11 (55.0)	339.0 [84.0;NE]			
>= 250 ng/dL							
Relugolix	383	177 (46.2)	206 (53.8)	342.0 [336.0;NE]	5.0	0.922 [0.715;1.189]	0.5330
Leuprolide	185	90 (48.6)	95 (51.4)	337.0 [253.0;NE]			
Missing							
Relugolix	7	4 (57.1)	3 (42.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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4.1.5.1.5 Skala: Emotionale Funktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2EMOT15.KM.MITTM0.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.0364							
< 20 ng/mL							
Relugolix	320	90 (28.1)	230 (71.9)	NE [NE;NE]	NE	1.085 [0.758;1.554]	0.6540
Leuprolide	169	45 (26.6)	124 (73.4)	357.0 [NE;NE]			
>= 20 ng/mL							
Relugolix	107	23 (21.5)	84 (78.5)	NE [350.0;NE]	NE	0.493 [0.259;0.939]	0.0313
Leuprolide	44	16 (36.4)	28 (63.6)	342.0 [334.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITTM0.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.2153							
Not Hispanic or Latino							
Relugolix	381	97 (25.5)	284 (74.5)	350.0 [350.0;NE]	-7.0	0.858 [0.615;1.198]	0.3692
Leuprolide	188	54 (28.7)	134 (71.3)	357.0 [NE;NE]			
Hispanic or Latino							
Relugolix	37	13 (35.1)	24 (64.9)	NE [254.0;NE]	NE	1.704 [0.607;4.782]	0.3112
Leuprolide	22	5 (22.7)	17 (77.3)	NE [339.0;NE]			
Not Reported							
Relugolix	9	3 (33.3)	6 (66.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITTM0.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.5192							
< 8							
Relugolix	252	67 (26.6)	185 (73.4)	NE [NE;NE]	NE	1.020 [0.678;1.535]	0.9255
Leuprolide	136	35 (25.7)	101 (74.3)	NE [NE;NE]			
>= 8							
Relugolix	163	44 (27.0)	119 (73.0)	350.0 [344.0;NE]	-7.0	0.825 [0.502;1.357]	0.4489
Leuprolide	74	24 (32.4)	50 (67.6)	357.0 [342.0;NE]			
Missing							
Relugolix	12	2 (16.7)	10 (83.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITTM0.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.6148							
< 250 ng/dL							
Relugolix	37	10 (27.0)	27 (73.0)	NE [NE;NE]	NE	1.132 [0.387;3.313]	0.8208
Leuprolide	20	5 (25.0)	15 (75.0)	NE [336.0;NE]			
>= 250 ng/dL							
Relugolix	383	100 (26.1)	283 (73.9)	350.0 [350.0;NE]	-7.0	0.849 [0.611;1.179]	0.3281
Leuprolide	185	55 (29.7)	130 (70.3)	357.0 [NE;NE]			
Missing							
Relugolix	7	3 (42.9)	4 (57.1)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	1 (12.5)	7 (87.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.6463							
Asian							
Relugolix	94	17 (18.1)	77 (81.9)	NE [NE;NE]	NE	0.671 [0.325;1.382]	0.2786
Leuprolide	51	13 (25.5)	38 (74.5)	NE [NE;NE]			
Black or African American							
Relugolix	21	5 (23.8)	16 (76.2)	NE [254.0;NE]	NE	0.574 [0.154;2.137]	0.4076
Leuprolide	12	4 (33.3)	8 (66.7)	NE [166.0;NE]			
White							
Relugolix	292	86 (29.5)	206 (70.5)	350.0 [350.0;NE]	-7.0	1.040 [0.715;1.514]	0.8369
Leuprolide	139	40 (28.8)	99 (71.2)	357.0 [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.6463							
Others							
Relugolix	14	5 (35.7)	9 (64.3)	NE [85.0;NE]	NE	0.833 [0.199;3.488]	0.8030
Leuprolide	7	3 (42.9)	4 (57.1)	339.0 [29.0;NE]			
Not Reported							
Relugolix	6	0	6 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	1 (25.0)	3 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITTM0.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.9655							
<= 75 years old							
Relugolix	304	79 (26.0)	225 (74.0)	NE [NE;NE]	NE	0.899 [0.622;1.300]	0.5707
Leuprolide	153	44 (28.8)	109 (71.2)	NE [342.0;NE]			
> 75 years old							
Relugolix	123	34 (27.6)	89 (72.4)	350.0 [350.0;NE]	-7.0	0.913 [0.510;1.634]	0.7581
Leuprolide	60	17 (28.3)	43 (71.7)	357.0 [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITTM0.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.9904							
Asia (Excl. Korea)							
Relugolix	70	13 (18.6)	57 (81.4)	NE [344.0;NE]	NE	0.907 [0.362;2.276]	0.8354
Leuprolide	36	7 (19.4)	29 (80.6)	NE [NE;NE]			
Rest of World							
Relugolix	357	100 (28.0)	257 (72.0)	350.0 [350.0;NE]	-7.0	0.902 [0.647;1.256]	0.5403
Leuprolide	177	54 (30.5)	123 (69.5)	357.0 [342.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2EMOT15.KM.MITTM0.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.9930							
North and South America							
Relugolix	161	46 (28.6)	115 (71.4)	NE [343.0;NE]	NE	0.913 [0.561;1.487]	0.7147
Leuprolide	80	25 (31.3)	55 (68.8)	357.0 [340.0;NE]			
Europe							
Relugolix	155	45 (29.0)	110 (71.0)	350.0 [NE;NE]	NE	0.914 [0.557;1.500]	0.7207
Leuprolide	78	24 (30.8)	54 (69.2)	NE [342.0;NE]			
Asia and Rest of World							
Relugolix	111	22 (19.8)	89 (80.2)	NE [NE;NE]	NE	0.871 [0.431;1.761]	0.7006
Leuprolide	55	12 (21.8)	43 (78.2)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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4.1.5.1.6 Skala: Soziale Funktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2SOC15.KM.MITTM0.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.0072							
Not Hispanic or Latino							
Relugolix	381	160 (42.0)	221 (58.0)	344.0 [339.0;NE]	4.0	0.819 [0.631;1.063]	0.1337
Leuprolide	188	88 (46.8)	100 (53.2)	340.0 [260.0;NE]			
Hispanic or Latino							
Relugolix	37	23 (62.2)	14 (37.8)	175.5 [90.0;NE]	NE	2.960 [1.204;7.278]	0.0180
Leuprolide	22	6 (27.3)	16 (72.7)	NE [339.0;NE]			
Not Reported							
Relugolix	9	3 (33.3)	6 (66.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITTM0.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: 0.3349							
< 250 ng/dL							
Relugolix	37	19 (51.4)	18 (48.6)	339.0 [89.0;NE]	-3.0	1.327 [0.581;3.032]	0.5024
Leuprolide	20	8 (40.0)	12 (60.0)	342.0 [57.0;NE]			
>= 250 ng/dL							
Relugolix	383	163 (42.6)	220 (57.4)	344.0 [338.0;NE]	4.0	0.866 [0.666;1.126]	0.2830
Leuprolide	185	85 (45.9)	100 (54.1)	340.0 [262.0;NE]			
Missing							
Relugolix	7	4 (57.1)	3 (42.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	3 (37.5)	5 (62.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITTM0.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.3717							
< 8							
Relugolix	252	111 (44.0)	141 (56.0)	342.0 [337.0;NE]	2.0	0.981 [0.715;1.345]	0.9035
Leuprolide	136	59 (43.4)	77 (56.6)	340.0 [260.0;NE]			
>= 8							
Relugolix	163	67 (41.1)	96 (58.9)	344.0 [339.0;NE]	2.0	0.776 [0.517;1.164]	0.2198
Leuprolide	74	36 (48.6)	38 (51.4)	342.0 [253.0;NE]			
Missing							
Relugolix	12	8 (66.7)	4 (33.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	1 (33.3)	2 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4125							
Asian							
Relugolix	94	26 (27.7)	68 (72.3)	NE [344.0;NE]	NE	0.720 [0.395;1.313]	0.2842
Leuprolide	51	18 (35.3)	33 (64.7)	NE [337.0;NE]			
Black or African American							
Relugolix	21	14 (66.7)	7 (33.3)	92.0 [36.0;337.0]	7.0	0.538 [0.238;1.215]	0.1358
Leuprolide	12	10 (83.3)	2 (16.7)	85.0 [29.0;166.0]			
White							
Relugolix	292	137 (46.9)	155 (53.1)	341.0 [337.0;NE]	1.0	0.977 [0.727;1.312]	0.8763
Leuprolide	139	65 (46.8)	74 (53.2)	340.0 [255.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4125							
Others							
Relugolix	14	6 (42.9)	8 (57.1)	339.0 [169.0;NE]	NE	1.625 [0.328;8.052]	0.5521
Leuprolide	7	2 (28.6)	5 (71.4)	NE [92.0;NE]			
Not Reported							
Relugolix	6	3 (50.0)	3 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	1 (25.0)	3 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITTM0.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.4649							
North and South America							
Relugolix	161	89 (55.3)	72 (44.7)	253.0 [170.0;339.0]	-21.0	1.090 [0.753;1.579]	0.6466
Leuprolide	80	41 (51.3)	39 (48.8)	274.0 [169.0;NE]			
Europe							
Relugolix	155	67 (43.2)	88 (56.8)	344.0 [337.0;NE]	4.0	0.851 [0.570;1.272]	0.4324
Leuprolide	78	37 (47.4)	41 (52.6)	340.0 [246.0;NE]			
Asia and Rest of World							
Relugolix	111	30 (27.0)	81 (73.0)	NE [344.0;NE]	NE	0.733 [0.409;1.315]	0.2977
Leuprolide	55	18 (32.7)	37 (67.3)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITTM0.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.5766							
< 20 ng/mL							
Relugolix	320	142 (44.4)	178 (55.6)	342.0 [337.0;NE]	2.0	0.953 [0.721;1.259]	0.7345
Leuprolide	169	76 (45.0)	93 (55.0)	340.0 [267.0;NE]			
>= 20 ng/mL							
Relugolix	107	44 (41.1)	63 (58.9)	344.0 [337.0;NE]	NE	0.804 [0.474;1.364]	0.4180
Leuprolide	44	20 (45.5)	24 (54.5)	NE [166.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITTM0.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.8252							
Asia (Excl. Korea)							
Relugolix	70	19 (27.1)	51 (72.9)	NE [NE;NE]	NE	0.982 [0.457;2.113]	0.9637
Leuprolide	36	10 (27.8)	26 (72.2)	NE [NE;NE]			
Rest of World							
Relugolix	357	167 (46.8)	190 (53.2)	342.0 [337.0;344.0]	3.0	0.897 [0.691;1.163]	0.4123
Leuprolide	177	86 (48.6)	91 (51.4)	339.0 [255.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITTM0.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.9260							
<= 75 years old							
Relugolix	304	131 (43.1)	173 (56.9)	342.0 [337.0;NE]	0.0	0.908 [0.678;1.215]	0.5150
Leuprolide	153	69 (45.1)	84 (54.9)	342.0 [260.0;NE]			
> 75 years old							
Relugolix	123	55 (44.7)	68 (55.3)	344.0 [337.0;NE]	5.0	0.931 [0.588;1.476]	0.7624
Leuprolide	60	27 (45.0)	33 (55.0)	339.0 [258.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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4.1.5.2 Gesundheitsbezogene Lebensqualität (European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire PR25)

4.1.5.2.1 Skala: Sexuelle Aktivität

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2SEXA15.KM.MITTM0.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.1372							
<= 75 years old							
Relugolix	304	69 (22.7)	235 (77.3)	NE [NE;NE]	NE	0.645 [0.449;0.927]	0.0177
Leuprolide	153	51 (33.3)	102 (66.7)	NE [NE;NE]			
> 75 years old							
Relugolix	123	33 (26.8)	90 (73.2)	NE [NE;NE]	NE	1.116 [0.597;2.085]	0.7310
Leuprolide	60	14 (23.3)	46 (76.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITTM0.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.5555							
Not Hispanic or Latino							
Relugolix	381	82 (21.5)	299 (78.5)	NE [NE;NE]	NE	0.709 [0.503;1.000]	0.0503
Leuprolide	188	54 (28.7)	134 (71.3)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	37	14 (37.8)	23 (62.2)	NE [251.0;NE]	NE	0.932 [0.403;2.153]	0.8683
Leuprolide	22	9 (40.9)	13 (59.1)	NE [90.0;NE]			
Not Reported							
Relugolix	9	6 (66.7)	3 (33.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITTM0.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.5739							
< 8							
Relugolix	252	53 (21.0)	199 (79.0)	NE [NE;NE]	NE	0.768 [0.503;1.172]	0.2210
Leuprolide	136	36 (26.5)	100 (73.5)	NE [NE;NE]			
>= 8							
Relugolix	163	44 (27.0)	119 (73.0)	NE [NE;NE]	NE	0.640 [0.401;1.024]	0.0626
Leuprolide	74	29 (39.2)	45 (60.8)	NE [335.0;NE]			
Missing							
Relugolix	12	5 (41.7)	7 (58.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITTM0.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.5797							
Asia (Excl. Korea)							
Relugolix	70	8 (11.4)	62 (88.6)	NE [NE;NE]	NE	1.024 [0.308;3.399]	0.9694
Leuprolide	36	4 (11.1)	32 (88.9)	NE [NE;NE]			
Rest of World							
Relugolix	357	94 (26.3)	263 (73.7)	NE [NE;NE]	NE	0.721 [0.522;0.995]	0.0465
Leuprolide	177	61 (34.5)	116 (65.5)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITTM0.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.6502							
North and South America							
Relugolix	161	43 (26.7)	118 (73.3)	NE [NE;NE]	NE	0.795 [0.488;1.293]	0.3551
Leuprolide	80	26 (32.5)	54 (67.5)	NE [NE;NE]			
Europe							
Relugolix	155	42 (27.1)	113 (72.9)	NE [NE;NE]	NE	0.817 [0.498;1.340]	0.4226
Leuprolide	78	25 (32.1)	53 (67.9)	NE [338.0;NE]			
Asia and Rest of World							
Relugolix	111	17 (15.3)	94 (84.7)	NE [NE;NE]	NE	0.555 [0.274;1.127]	0.1032
Leuprolide	55	14 (25.5)	41 (74.5)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITTM0.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.6610							
< 20 ng/mL							
Relugolix	320	80 (25.0)	240 (75.0)	NE [NE;NE]	NE	0.732 [0.519;1.032]	0.0750
Leuprolide	169	55 (32.5)	114 (67.5)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	107	22 (20.6)	85 (79.4)	NE [NE;NE]	NE	0.880 [0.417;1.858]	0.7374
Leuprolide	44	10 (22.7)	34 (77.3)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITTM0.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.7978							
< 250 ng/dL							
Relugolix	37	5 (13.5)	32 (86.5)	NE [NE;NE]	NE	0.905 [0.216;3.787]	0.8915
Leuprolide	20	3 (15.0)	17 (85.0)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	383	96 (25.1)	287 (74.9)	NE [NE;NE]	NE	0.747 [0.540;1.034]	0.0783
Leuprolide	185	59 (31.9)	126 (68.1)	NE [NE;NE]			
Missing							
Relugolix	7	1 (14.3)	6 (85.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	3 (37.5)	5 (62.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.9478							
Asian							
Relugolix	94	15 (16.0)	79 (84.0)	NE [NE;NE]	NE	0.653 [0.306;1.395]	0.2710
Leuprolide	51	12 (23.5)	39 (76.5)	NE [NE;NE]			
Black or African American							
Relugolix	21	10 (47.6)	11 (52.4)	NE [85.0;NE]	NE	0.793 [0.302;2.084]	0.6376
Leuprolide	12	7 (58.3)	5 (41.7)	330.0 [36.0;NE]			
White							
Relugolix	292	71 (24.3)	221 (75.7)	NE [NE;NE]	NE	0.810 [0.550;1.194]	0.2873
Leuprolide	139	40 (28.8)	99 (71.2)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.9478							
Others							
Relugolix	14	5 (35.7)	9 (64.3)	NE [32.0;NE]	NE	0.615 [0.165;2.292]	0.4688
Leuprolide	7	4 (57.1)	3 (42.9)	176.0 [29.0;NE]			
Not Reported							
Relugolix	6	1 (16.7)	5 (83.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	2 (50.0)	2 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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4.1.5.2.2 Skala: Sexualfunktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2SEXF15.KM.MITTM0.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.0002							
Not Hispanic or Latino							
Relugolix	381	42 (11.0)	339 (89.0)	252.0 [169.0;335.0]	-85.0	1.495 [0.883;2.530]	0.1345
Leuprolide	188	21 (11.2)	167 (88.8)	337.0 [172.0;NE]			
Hispanic or Latino							
Relugolix	37	7 (18.9)	30 (81.1)	256.0 [85.0;NE]	227.0	0.132 [0.041;0.427]	0.0007
Leuprolide	22	5 (22.7)	17 (77.3)	29.0 [28.0;NE]			
Not Reported							
Relugolix	9	0	9 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	0	3 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SEXF15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.1140							
Asian							
Relugolix	94	6 (6.4)	88 (93.6)	247.0 [29.0;NE]	NE	3.081 [0.370;25.679]	0.2984
Leuprolide	51	1 (2.0)	50 (98.0)	NE [29.0;NE]			
Black or African American							
Relugolix	21	4 (19.0)	17 (81.0)	341.0 [36.0;NE]	11.0	0.514 [0.128;2.070]	0.3492
Leuprolide	12	4 (33.3)	8 (66.7)	330.0 [85.0;NE]			
White							
Relugolix	292	34 (11.6)	258 (88.4)	252.0 [86.0;NE]	-85.0	1.312 [0.751;2.290]	0.3398
Leuprolide	139	20 (14.4)	119 (85.6)	337.0 [165.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXF15.KM.MITTM0.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.1140							
Others							
Relugolix	14	4 (28.6)	10 (71.4)	130.5 [34.0;NE]	101.5	0.085 [0.006;1.224]	0.0701
Leuprolide	7	1 (14.3)	6 (85.7)	29.0 [NE;NE]			
Not Reported							
Relugolix	6	1 (16.7)	5 (83.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	4	0	4 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2SEXF15.KM.MITTM0.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.2888							
< 250 ng/dL							
Relugolix	37	3 (8.1)	34 (91.9)	NE [99.0;NE]	NE	0.495 [0.100;2.455]	0.3892
Leuprolide	20	3 (15.0)	17 (85.0)	253.0 [29.0;NE]			
>= 250 ng/dL							
Relugolix	383	43 (11.2)	340 (88.8)	252.0 [169.0;335.0]	-78.0	1.231 [0.735;2.062]	0.4299
Leuprolide	185	22 (11.9)	163 (88.1)	330.0 [169.0;NE]			
Missing							
Relugolix	7	3 (42.9)	4 (57.1)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	1 (12.5)	7 (87.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2SEXF15.KM.MITTM0.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.3355							
North and South America							
Relugolix	161	28 (17.4)	133 (82.6)	253.0 [170.0;NE]	0.0	0.938 [0.493;1.784]	0.8456
Leuprolide	80	14 (17.5)	66 (82.5)	253.0 [165.0;NE]			
Europe							
Relugolix	155	13 (8.4)	142 (91.6)	253.0 [32.0;NE]	-84.0	1.545 [0.689;3.464]	0.2905
Leuprolide	78	11 (14.1)	67 (85.9)	337.0 [85.0;NE]			
Asia and Rest of World							
Relugolix	111	8 (7.2)	103 (92.8)	247.0 [78.0;NE]	NE	3.918 [0.490;31.354]	0.1981
Leuprolide	55	1 (1.8)	54 (98.2)	NE [29.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXF15.KM.MITTM0.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.3874							
<= 75 years old							
Relugolix	304	44 (14.5)	260 (85.5)	173.0 [99.0;256.0]	-157.0	1.333 [0.796;2.232]	0.2741
Leuprolide	153	22 (14.4)	131 (85.6)	330.0 [169.0;338.0]			
> 75 years old							
Relugolix	123	5 (4.1)	118 (95.9)	NE [247.0;NE]	NE	0.714 [0.191;2.665]	0.6165
Leuprolide	60	4 (6.7)	56 (93.3)	NE [29.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXF15.KM.MITTM0.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.6622							
< 20 ng/mL							
Relugolix	320	36 (11.3)	284 (88.8)	252.0 [99.0;NE]	-85.0	1.148 [0.669;1.972]	0.6159
Leuprolide	169	21 (12.4)	148 (87.6)	337.0 [165.0;NE]			
>= 20 ng/mL							
Relugolix	107	13 (12.1)	94 (87.9)	253.0 [169.0;NE]	-4.0	1.489 [0.530;4.188]	0.4502
Leuprolide	44	5 (11.4)	39 (88.6)	257.0 [130.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2SEXF15.KM.MITTM0.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.8978							
< 8							
Relugolix	252	33 (13.1)	219 (86.9)	253.0 [169.0;NE]	-84.0	1.271 [0.689;2.343]	0.4431
Leuprolide	136	15 (11.0)	121 (89.0)	337.0 [165.0;NE]			
>= 8							
Relugolix	163	16 (9.8)	147 (90.2)	247.0 [90.0;NE]	-10.0	1.358 [0.598;3.086]	0.4643
Leuprolide	74	9 (12.2)	65 (87.8)	257.0 [169.0;NE]			
Missing							
Relugolix	12	0	12 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	3	2 (66.7)	1 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SEXF15.KM.MITTM0.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: NC							
Asia (Excl. Korea)							
Relugolix	70	3 (4.3)	67 (95.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	36	0	36 (100.0)	NC [NC;NC]			
Rest of World							
Relugolix	357	46 (12.9)	311 (87.1)	253.0 [169.0;341.0]	-77.0	1.093 [0.674;1.773]	0.7182
Leuprolide	177	26 (14.7)	151 (85.3)	330.0 [169.0;338.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Non-Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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4.1.6 Sicherheit

4.1.6.1 Gesamtrate jeglicher UE

Myovant Sciences, Inc.: HERO AMNOG

Table AE.TEAE.ANY.BIN.SAFM0.S3: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.0025						
Not Hispanic or Latino						
Relugolix	381	350 (91.9)	0.502	0.959	-0.039	0.1114
Leuprolide	188	180 (95.7)	[0.226;1.114]	[0.920;1.001]	[-0.079;0.001]	
Hispanic or Latino						
Relugolix	37	37 (100.0)	18.243	1.227	0.182	0.0161
Leuprolide	22	18 (81.8)	[0.932;357.140]	[1.000;1.506]	[0.021;0.343]	
Not Reported						
Relugolix	9	9 (100.0)	NC	NC	NC	NC
Leuprolide	3	3 (100.0)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAE.ANY.BIN.SAFM0.S5: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.0493						
< 8						
Relugolix	252	233 (92.5)	0.372	0.953	-0.046	0.0743
Leuprolide	136	132 (97.1)	[0.124;1.115]	[0.910;0.997]	[-0.089;-0.003]	
>= 8						
Relugolix	163	151 (92.6)	1.525	1.039	0.034	0.4500
Leuprolide	74	66 (89.2)	[0.596;3.905]	[0.949;1.137]	[-0.047;0.116]	
Missing						
Relugolix	12	12 (100.0)	NC	NC	NC	NC
Leuprolide	3	3 (100.0)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAE.ANY.BIN.SAFM0.S2: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: 0.1559						
North and South America						
Relugolix	161	156 (96.9)	2.080	1.034	0.031	0.3066
Leuprolide	80	75 (93.8)	[0.584;7.405]	[0.970;1.101]	[-0.028;0.091]	
Europe						
Relugolix	155	140 (90.3)	0.373	0.939	-0.058	0.1915
Leuprolide	78	75 (96.2)	[0.105;1.331]	[0.878;1.005]	[-0.121;0.005]	
Asia and Rest of World						
Relugolix	111	100 (90.1)	0.713	0.972	-0.026	0.7753
Leuprolide	55	51 (92.7)	[0.216;2.351]	[0.882;1.070]	[-0.115;0.062]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAE.ANY.BIN.SAFM0.S7: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.3981						
< 20 ng/mL						
Relugolix	320	297 (92.8)	0.642	0.974	-0.025	0.3342
Leuprolide	169	161 (95.3)	[0.281;1.467]	[0.931;1.019]	[-0.067;0.018]	
>= 20 ng/mL						
Relugolix	107	99 (92.5)	1.238	1.018	0.016	0.7465
Leuprolide	44	40 (90.9)	[0.353;4.342]	[0.914;1.134]	[-0.082;0.115]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAE.ANY.BIN.SAFM0.S4: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Race, Interaction p-value: 0.4444						
Asian						
Relugolix	94	82 (87.2)	0.582	0.947	-0.049	0.4204
Leuprolide	51	47 (92.2)	[0.177;1.906]	[0.847;1.058]	[-0.149;0.051]	
Black or African American						
Relugolix	21	20 (95.2)	4.000	1.143	0.119	0.5381
Leuprolide	12	10 (83.3)	[0.323;49.596]	[0.872;1.498]	[-0.111;0.349]	
White						
Relugolix	292	275 (94.2)	0.604	0.977	-0.022	0.4826
Leuprolide	139	134 (96.4)	[0.218;1.671]	[0.936;1.020]	[-0.063;0.019]	
Others						
Relugolix	14	13 (92.9)	2.167	1.083	0.071	1.0000
Leuprolide	7	6 (85.7)	[0.115;40.811]	[0.775;1.515]	[-0.221;0.364]	
Not Reported						
Relugolix	6	6 (100.0)	NC	NC	NC	NC
Leuprolide	4	4 (100.0)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

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Table AE.TEAE.ANY.BIN.SAFM0.S1: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.5322						
<= 75 years old						
Relugolix	304	281 (92.4)	0.854	0.989	-0.010	0.8484
Leuprolide	153	143 (93.5)	[0.396;1.844]	[0.938;1.043]	[-0.059;0.039]	
> 75 years old						
Relugolix	123	115 (93.5)	0.496	0.967	-0.032	0.5018
Leuprolide	60	58 (96.7)	[0.102;2.410]	[0.905;1.033]	[-0.095;0.031]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

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Table AE.TEAE.ANY.BIN.SAFM0.S6: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.8934						
< 250 ng/dL						
Relugolix	37	35 (94.6)	0.921	0.996	-0.004	1.0000
Leuprolide	20	19 (95.0)	[0.078;10.830]	[0.877;1.130]	[-0.124;0.116]	
>= 250 ng/dL						
Relugolix	383	354 (92.4)	0.772	0.983	-0.016	0.6001
Leuprolide	185	174 (94.1)	[0.377;1.581]	[0.938;1.029]	[-0.059;0.027]	
Missing						
Relugolix	7	7 (100.0)	NC	NC	NC	NC
Leuprolide	8	8 (100.0)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

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Table AE.TEAE.ANY.BIN.SAFM0.S8: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.9032						
Asia (Excl. Korea)						
Relugolix	70	62 (88.6)	0.705	0.966	-0.031	0.7460
Leuprolide	36	33 (91.7)	[0.175;2.836]	[0.849;1.100]	[-0.148;0.086]	
Rest of World						
Relugolix	357	334 (93.6)	0.778	0.986	-0.014	0.6989
Leuprolide	177	168 (94.9)	[0.352;1.719]	[0.944;1.030]	[-0.055;0.028]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

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4.1.6.2 Häufige jegliche UE nach SOC und PT

Myovant Sciences, Inc.: HERO AMNOG

Table AE.TEAE.SPT.BIN.SAFM0.S6: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Vomiting

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.4840						
< 250 ng/dL						
Relugolix	37	0	0.099	0.111	-0.100	0.1190
Leuprolide	20	2 (10.0)	[0.005;2.162]	[0.006;2.196]	[-0.231;0.031]	
>= 250 ng/dL						
Relugolix	383	5 (1.3)	0.293	0.302	-0.030	0.0342
Leuprolide	185	8 (4.3)	[0.094;0.907]	[0.100;0.910]	[-0.062;0.001]	
Missing						
Relugolix	7	1 (14.3)	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Non-Metastatic Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Non-Metastatic Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

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Table AE.TEAE.SPT.BIN.SAFM0.S8: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Vomiting

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.5382						
Asia (Excl. Korea)						
Relugolix	70	2 (2.9)	0.500	0.514	-0.027	0.6033
Leuprolide	36	2 (5.6)	[0.067;3.705]	[0.076;3.502]	[-0.111;0.057]	
Rest of World						
Relugolix	357	4 (1.1)	0.239	0.248	-0.034	0.0245
Leuprolide	177	8 (4.5)	[0.071;0.806]	[0.076;0.812]	[-0.066;-0.002]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Non-Metastatic Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Non-Metastatic Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

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Table AE.TEAE.SPT.BIN.SAFM0.S7: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Vomiting

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.5883						
< 20 ng/mL						
Relugolix	320	4 (1.3)	0.344	0.352	-0.023	0.1013
Leuprolide	169	6 (3.6)	[0.096;1.236]	[0.101;1.231]	[-0.053;0.007]	
>= 20 ng/mL						
Relugolix	107	2 (1.9)	0.190	0.206	-0.072	0.0600
Leuprolide	44	4 (9.1)	[0.034;1.081]	[0.039;1.082]	[-0.161;0.017]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Non-Metastatic Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Non-Metastatic Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

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Table AE.TEAE.SPT.BIN.SAFM0.S3: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Vomiting

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.6117						
Not Hispanic or Latino						
Relugolix	381	5 (1.3)	0.264	0.274	-0.035	0.0186
Leuprolide	188	9 (4.8)	[0.087;0.801]	[0.093;0.807]	[-0.067;-0.002]	
Hispanic or Latino						
Relugolix	37	1 (2.7)	0.583	0.595	-0.018	1.0000
Leuprolide	22	1 (4.5)	[0.035;9.822]	[0.039;9.036]	[-0.120;0.083]	
Not Reported						
Relugolix	9	0	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Non-Metastatic Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Non-Metastatic Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

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Myovant Sciences, Inc.: HERO AMNOG

Table AE.TEAE.SPT.BIN.SAFM0.S4: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Vomiting

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.6318						
Asian						
Relugolix	94	2 (2.1)	0.348	0.362	-0.038	0.3448
Leuprolide	51	3 (5.9)	[0.056;2.153]	[0.062;2.095]	[-0.108;0.033]	
Black or African American						
Relugolix	21	0	0.581	0.591	0.000	1.0000
Leuprolide	12	0	[0.011;31.159]	[0.012;28.034]		
White						
Relugolix	292	3 (1.0)	0.196	0.204	-0.040	0.0152
Leuprolide	139	7 (5.0)	[0.050;0.769]	[0.054;0.777]	[-0.078;-0.002]	
Others						
Relugolix	14	1 (7.1)	1.667	1.600	0.071	1.0000
Leuprolide	7	0	[0.060;46.227]	[0.073;34.933]	[-0.063;0.206]	
Not Reported						
Relugolix	6	0	NC	NC	NC	NC
Leuprolide	4	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Non-Metastatic Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Non-Metastatic Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

Table AE.TEAE.SPT.BIN.SAFM0.S1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Vomiting

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.7003						
<= 75 years old						
Relugolix	304	5 (1.6)	0.268	0.280	-0.042	0.0195
Leuprolide	153	9 (5.9)	[0.088;0.813]	[0.095;0.820]	[-0.082;-0.002]	
> 75 years old						
Relugolix	123	1 (0.8)	0.484	0.488	-0.009	0.5495
Leuprolide	60	1 (1.7)	[0.030;7.867]	[0.031;7.666]	[-0.045;0.028]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Non-Metastatic Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Non-Metastatic Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.TEAE.SPT.BIN.SAFM0.S2: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Vomiting

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: NC						
North and South America						
Relugolix	161	2 (1.2)	NC	NC	NC	NC
Leuprolide	80	6 (7.5)	[NC;NC]	[NC;NC]	[NC;NC]	
Europe						
Relugolix	155	2 (1.3)	NC	NC	NC	NC
Leuprolide	78	1 (1.3)	[NC;NC]	[NC;NC]	[NC;NC]	
Asia and Rest of World						
Relugolix	111	2 (1.8)	NC	NC	NC	NC
Leuprolide	55	3 (5.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Non-Metastatic Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Non-Metastatic Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.TEAE.SPT.BIN.SAFM0.S5: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Vomiting

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: NC						
< 8						
Relugolix	252	2 (0.8)	NC	NC	NC	NC
Leuprolide	136	5 (3.7)	[NC;NC]	[NC;NC]	[NC;NC]	
>= 8						
Relugolix	163	4 (2.5)	NC	NC	NC	NC
Leuprolide	74	5 (6.8)	[NC;NC]	[NC;NC]	[NC;NC]	
Missing						
Relugolix	12	0	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Non-Metastatic Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Non-Metastatic Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

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4.1.6.3 Gesamtrate der schweren UE (CTCAE-Grad ≥ 3)

Myovant Sciences, Inc.: HERO AMNOG

Table AE.G35TEAE.ANY.BIN.SAFM0.S3: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.0319						
Not Hispanic or Latino						
Relugolix	381	55 (14.4)	0.764	0.798	-0.036	0.2709
Leuprolide	188	34 (18.1)	[0.478;1.221]	[0.540;1.179]	[-0.102;0.029]	
Hispanic or Latino						
Relugolix	37	8 (21.6)	5.793	4.757	0.171	0.1337
Leuprolide	22	1 (4.5)	[0.673;49.901]	[0.637;35.529]	[0.012;0.329]	
Not Reported						
Relugolix	9	1 (11.1)	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

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Table AE.G35TEAE.ANY.BIN.SAFM0.S7: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.1187						
< 20 ng/mL						
Relugolix	320	51 (15.9)	1.092	1.077	0.011	0.7939
Leuprolide	169	25 (14.8)	[0.650;1.836]	[0.693;1.674]	[-0.055;0.078]	
>= 20 ng/mL						
Relugolix	107	13 (12.1)	0.470	0.535	-0.106	0.1337
Leuprolide	44	10 (22.7)	[0.189;1.172]	[0.254;1.127]	[-0.244;0.033]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

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Table AE.G35TEAE.ANY.BIN.SAFM0.S4: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.4707						
Asian						
Relugolix	94	11 (11.7)	0.833	0.853	-0.020	0.7939
Leuprolide	51	7 (13.7)	[0.302;2.300]	[0.352;2.064]	[-0.135;0.094]	
Black or African American						
Relugolix	21	5 (23.8)	0.938	0.952	-0.012	1.0000
Leuprolide	12	3 (25.0)	[0.180;4.871]	[0.275;3.302]	[-0.317;0.293]	
White						
Relugolix	292	43 (14.7)	0.787	0.819	-0.033	0.3985
Leuprolide	139	25 (18.0)	[0.459;1.352]	[0.522;1.284]	[-0.108;0.043]	
Others						
Relugolix	14	4 (28.6)	6.429	4.800	0.286	0.2550
Leuprolide	7	0	[0.299;138.252]	[0.294;78.376]	[0.049;0.522]	
Not Reported						
Relugolix	6	1 (16.7)	NC	NC	NC	NC
Leuprolide	4	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

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Table AE.G35TEAE.ANY.BIN.SAFM0.S8: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.5798						
Asia (Excl. Korea)						
Relugolix	70	5 (7.1)	0.615	0.643	-0.040	0.4849
Leuprolide	36	4 (11.1)	[0.155;2.449]	[0.184;2.248]	[-0.159;0.079]	
Rest of World						
Relugolix	357	59 (16.5)	0.932	0.944	-0.010	0.8064
Leuprolide	177	31 (17.5)	[0.578;1.504]	[0.635;1.402]	[-0.078;0.058]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

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Table AE.G35TEAE.ANY.BIN.SAFM0.S2: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: 0.6758						
North and South America						
Relugolix	161	31 (19.3)	1.124	1.100	0.018	0.8611
Leuprolide	80	14 (17.5)	[0.560;2.257]	[0.621;1.948]	[-0.086;0.121]	
Europe						
Relugolix	155	21 (13.5)	0.716	0.755	-0.044	0.4377
Leuprolide	78	14 (17.9)	[0.342;1.500]	[0.406;1.402]	[-0.145;0.057]	
Asia and Rest of World						
Relugolix	111	12 (10.8)	0.831	0.849	-0.019	0.7968
Leuprolide	55	7 (12.7)	[0.308;2.245]	[0.354;2.036]	[-0.124;0.086]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

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Table AE.G35TEAE.ANY.BIN.SAFM0.S5: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.7405						
< 8						
Relugolix	252	39 (15.5)	0.949	0.957	-0.007	0.8843
Leuprolide	136	22 (16.2)	[0.537;1.678]	[0.592;1.545]	[-0.083;0.069]	
>= 8						
Relugolix	163	24 (14.7)	0.810	0.838	-0.028	0.5681
Leuprolide	74	13 (17.6)	[0.387;1.696]	[0.452;1.553]	[-0.131;0.074]	
Missing						
Relugolix	12	1 (8.3)	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

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Table AE.G35TEAE.ANY.BIN.SAFM0.S6: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.8782						
< 250 ng/dL						
Relugolix	37	8 (21.6)	0.828	0.865	-0.034	0.7538
Leuprolide	20	5 (25.0)	[0.230;2.975]	[0.326;2.295]	[-0.265;0.198]	
>= 250 ng/dL						
Relugolix	383	56 (14.6)	0.921	0.933	-0.011	0.8019
Leuprolide	185	29 (15.7)	[0.566;1.500]	[0.617;1.409]	[-0.074;0.053]	
Missing						
Relugolix	7	0	NC	NC	NC	NC
Leuprolide	8	1 (12.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.G35TEAE.ANY.BIN.SAFM0.S1: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.9194						
<= 75 years old						
Relugolix	304	44 (14.5)	0.910	0.923	-0.012	0.7809
Leuprolide	153	24 (15.7)	[0.530;1.561]	[0.584;1.458]	[-0.082;0.058]	
> 75 years old						
Relugolix	123	20 (16.3)	0.865	0.887	-0.021	0.8340
Leuprolide	60	11 (18.3)	[0.385;1.945]	[0.455;1.730]	[-0.138;0.097]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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4.1.6.4 Häufige schwere UE (CTCAE-Grad ≥ 3) nach SOC und PT

Myovant Sciences, Inc.: HERO AMNOG

Table AE.G35TEAE.SPT.BIN.SAFM0.S: Frequent Grade 3 or Above Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

System Organ Class: NA, Preferred Term: NA

Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
No SOCs or PTs meet the IQWiG frequent event rules in the overall Safety Non-Metastatic Population AND have a significant treatment effect (p-value <0.05) in the overall Safety Non-Metastatic Population for this endpoint.						

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Non-Metastatic Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Non-Metastatic Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03. MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NA: Not applicable.

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4.1.6.5 Gesamtrate der SUE

Myovant Sciences, Inc.: HERO AMNOG

Table AE.STEAE.ANY.BIN.SAFM0.S7: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.0742						
< 20 ng/mL						
Relugolix	320	32 (10.0)	0.932	0.939	-0.007	0.8756
Leuprolide	169	18 (10.7)	[0.506;1.716]	[0.544;1.622]	[-0.063;0.050]	
>= 20 ng/mL						
Relugolix	107	8 (7.5)	0.314	0.366	-0.130	0.0432
Leuprolide	44	9 (20.5)	[0.112;0.878]	[0.151;0.886]	[-0.259;-0.001]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

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Date/time of run: 02AUG2022 16:21 Data Cut Date: 23SEP2020

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Table AE.STEAE.ANY.BIN.SAFM0.S5: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.1165						
< 8						
Relugolix	252	25 (9.9)	0.960	0.964	-0.004	1.0000
Leuprolide	136	14 (10.3)	[0.481;1.914]	[0.518;1.792]	[-0.067;0.059]	
>= 8						
Relugolix	163	13 (8.0)	0.407	0.454	-0.096	0.0418
Leuprolide	74	13 (17.6)	[0.178;0.927]	[0.221;0.931]	[-0.192;0.000]	
Missing						
Relugolix	12	2 (16.7)	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAE.ANY.BIN.SAFM0.S1: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.1991						
<= 75 years old						
Relugolix	304	29 (9.5)	0.903	0.912	-0.009	0.7422
Leuprolide	153	16 (10.5)	[0.474;1.719]	[0.511;1.627]	[-0.068;0.049]	
> 75 years old						
Relugolix	123	11 (8.9)	0.437	0.488	-0.094	0.0891
Leuprolide	60	11 (18.3)	[0.178;1.077]	[0.224;1.061]	[-0.204;0.016]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAE.ANY.BIN.SAFM0.S3: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.2538						
Not Hispanic or Latino						
Relugolix	381	37 (9.7)	0.641	0.676	-0.047	0.1202
Leuprolide	188	27 (14.4)	[0.377;1.090]	[0.425;1.076]	[-0.105;0.012]	
Hispanic or Latino						
Relugolix	37	2 (5.4)	3.169	3.026	0.054	0.5243
Leuprolide	22	0	[0.145;69.088]	[0.152;60.294]	[-0.019;0.127]	
Not Reported						
Relugolix	9	1 (11.1)	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

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Table AE.STEAE.ANY.BIN.SAFM0.S8: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.8047						
Asia (Excl. Korea)						
Relugolix	70	5 (7.1)	0.846	0.857	-0.012	1.0000
Leuprolide	36	3 (8.3)	[0.190;3.760]	[0.217;3.386]	[-0.120;0.097]	
Rest of World						
Relugolix	357	35 (9.8)	0.693	0.723	-0.038	0.1911
Leuprolide	177	24 (13.6)	[0.398;1.206]	[0.444;1.177]	[-0.097;0.022]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAE.ANY.BIN.SAFM0.S6: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.8753						
< 250 ng/dL						
Relugolix	37	6 (16.2)	0.774	0.811	-0.038	0.7282
Leuprolide	20	4 (20.0)	[0.191;3.145]	[0.259;2.541]	[-0.250;0.174]	
>= 250 ng/dL						
Relugolix	383	34 (8.9)	0.686	0.714	-0.036	0.2327
Leuprolide	185	23 (12.4)	[0.392;1.202]	[0.433;1.176]	[-0.091;0.020]	
Missing						
Relugolix	7	0	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAE.ANY.BIN.SAFM0.S2: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: 0.8802						
North and South America						
Relugolix	161	14 (8.7)	0.667	0.696	-0.038	0.3672
Leuprolide	80	10 (12.5)	[0.282;1.575]	[0.323;1.496]	[-0.123;0.046]	
Europe						
Relugolix	155	15 (9.7)	0.653	0.686	-0.044	0.3782
Leuprolide	78	11 (14.1)	[0.284;1.498]	[0.331;1.422]	[-0.134;0.046]	
Asia and Rest of World						
Relugolix	111	11 (9.9)	0.898	0.908	-0.010	1.0000
Leuprolide	55	6 (10.9)	[0.314;2.572]	[0.355;2.327]	[-0.109;0.089]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAE.ANY.BIN.SAFM0.S4: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.9861						
Asian						
Relugolix	94	9 (9.6)	0.794	0.814	-0.022	0.7768
Leuprolide	51	6 (11.8)	[0.266;2.372]	[0.307;2.158]	[-0.128;0.085]	
Black or African American						
Relugolix	21	2 (9.5)	0.526	0.571	-0.071	0.6100
Leuprolide	12	2 (16.7)	[0.064;4.316]	[0.092;3.552]	[-0.317;0.174]	
White						
Relugolix	292	29 (9.9)	0.696	0.727	-0.037	0.2551
Leuprolide	139	19 (13.7)	[0.376;1.291]	[0.423;1.249]	[-0.104;0.029]	
Others						
Relugolix	14	0	0.517	0.533	0.000	1.0000
Leuprolide	7	0	[0.009;28.748]	[0.012;24.441]		
Not Reported						
Relugolix	6	0	NC	NC	NC	NC
Leuprolide	4	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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4.1.6.6 Gesamtrate der SUE ohne MACE-Events

Myovant Sciences, Inc.: HERO AMNOG

Table AE.STEAES1.ANY.BIN.SAFM0.S1: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.1795						
<= 75 years old						
Relugolix	304	27 (8.9)	1.258	1.235	0.017	0.5943
Leuprolide	153	11 (7.2)	[0.607;2.610]	[0.630;2.423]	[-0.035;0.069]	
> 75 years old						
Relugolix	123	11 (8.9)	0.557	0.596	-0.061	0.2192
Leuprolide	60	9 (15.0)	[0.217;1.426]	[0.261;1.361]	[-0.164;0.043]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAES1.ANY.BIN.SAFM0.S5: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.2226						
< 8						
Relugolix	252	24 (9.5)	1.196	1.177	0.014	0.7130
Leuprolide	136	11 (8.1)	[0.567;2.523]	[0.595;2.330]	[-0.044;0.073]	
>= 8						
Relugolix	163	12 (7.4)	0.574	0.605	-0.048	0.2283
Leuprolide	74	9 (12.2)	[0.231;1.429]	[0.267;1.374]	[-0.133;0.037]	
Missing						
Relugolix	12	2 (16.7)	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAES1.ANY.BIN.SAFM0.S7: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.2305						
< 20 ng/mL						
Relugolix	320	30 (9.4)	1.145	1.132	0.011	0.7423
Leuprolide	169	14 (8.3)	[0.590;2.224]	[0.617;2.075]	[-0.042;0.063]	
>= 20 ng/mL						
Relugolix	107	8 (7.5)	0.512	0.548	-0.062	0.2345
Leuprolide	44	6 (13.6)	[0.167;1.573]	[0.202;1.488]	[-0.175;0.051]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events.

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Table AE.STEAES1.ANY.BIN.SAFM0.S3: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.3578						
Not Hispanic or Latino						
Relugolix	381	35 (9.2)	0.850	0.864	-0.015	0.6511
Leuprolide	188	20 (10.6)	[0.476;1.517]	[0.513;1.454]	[-0.067;0.038]	
Hispanic or Latino						
Relugolix	37	2 (5.4)	3.169	3.026	0.054	0.5243
Leuprolide	22	0	[0.145;69.088]	[0.152;60.294]	[-0.019;0.127]	
Not Reported						
Relugolix	9	1 (11.1)	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAES1.ANY.BIN.SAFM0.S6: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.5638						
< 250 ng/dL						
Relugolix	37	5 (13.5)	0.625	0.676	-0.065	0.7054
Leuprolide	20	4 (20.0)	[0.147;2.652]	[0.204;2.237]	[-0.272;0.142]	
>= 250 ng/dL						
Relugolix	383	33 (8.6)	0.996	0.996	-0.000	1.0000
Leuprolide	185	16 (8.6)	[0.533;1.860]	[0.563;1.763]	[-0.050;0.049]	
Missing						
Relugolix	7	0	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAES1.ANY.BIN.SAFM0.S8: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.6782						
Asia (Excl. Korea)						
Relugolix	70	5 (7.1)	1.308	1.286	0.016	1.0000
Leuprolide	36	2 (5.6)	[0.241;7.098]	[0.262;6.304]	[-0.080;0.112]	
Rest of World						
Relugolix	357	33 (9.2)	0.900	0.909	-0.009	0.7555
Leuprolide	177	18 (10.2)	[0.491;1.647]	[0.527;1.568]	[-0.063;0.044]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAES1.ANY.BIN.SAFM0.S2: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: 0.9669						
North and South America						
Relugolix	161	14 (8.7)	0.857	0.870	-0.013	0.8132
Leuprolide	80	8 (10.0)	[0.344;2.136]	[0.381;1.987]	[-0.092;0.066]	
Europe						
Relugolix	155	14 (9.0)	1.007	1.006	0.001	1.0000
Leuprolide	78	7 (9.0)	[0.389;2.607]	[0.424;2.392]	[-0.077;0.078]	
Asia and Rest of World						
Relugolix	111	10 (9.0)	0.990	0.991	-0.001	1.0000
Leuprolide	55	5 (9.1)	[0.321;3.052]	[0.356;2.758]	[-0.094;0.092]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAES1.ANY.BIN.SAFM0.S4: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.9877						
Asian						
Relugolix	94	8 (8.5)	0.856	0.868	-0.013	0.7700
Leuprolide	51	5 (9.8)	[0.265;2.767]	[0.300;2.516]	[-0.112;0.086]	
Black or African American						
Relugolix	21	2 (9.5)	1.158	1.143	0.012	1.0000
Leuprolide	12	1 (8.3)	[0.094;14.286]	[0.115;11.323]	[-0.189;0.212]	
White						
Relugolix	292	28 (9.6)	0.947	0.952	-0.005	0.8635
Leuprolide	139	14 (10.1)	[0.482;1.862]	[0.518;1.750]	[-0.065;0.056]	
Others						
Relugolix	14	0	0.517	0.533	0.000	1.0000
Leuprolide	7	0	[0.009;28.748]	[0.012;24.441]		
Not Reported						
Relugolix	6	0	NC	NC	NC	NC
Leuprolide	4	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events; NC: Not calculated.

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4.1.6.7 Häufige SUE nach SOC und PT

Myovant Sciences, Inc.: HERO AMNOG

Table AE.STEAE.SPT.BIN.SAFM0.S: Frequent Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

System Organ Class: NA, Preferred Term: NA

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
No SOCs or PTs meet the IQWiG frequent event rules in the overall Safety Non-Metastatic Population for this endpoint.						
Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Non-Metastatic Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Non-Metastatic Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0. [1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates. [2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution. [3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution. [4] P-value based on a Fisher's exact test. The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI. A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD. The reference group for the OR, RR and RD is Leuprolide. Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NA: Not applicable.						

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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4.1.6.8 Absetzen der Studienmedikation aufgrund von UE

Myovant Sciences, Inc.: HERO AMNOG

Table AE.TEAED.ANY.BIN.SAFM0.S7: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.1540						
< 20 ng/mL						
Relugolix	320	10 (3.1)	11.464	11.121	0.031	0.0178
Leuprolide	169	0	[0.668;196.841]	[0.656;188.636]	[0.012;0.050]	
>= 20 ng/mL						
Relugolix	107	2 (1.9)	0.819	0.822	-0.004	1.0000
Leuprolide	44	1 (2.3)	[0.072;9.271]	[0.077;8.839]	[-0.055;0.047]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAED.ANY.BIN.SAFM0.S5: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Gleason Score at Study Entry, Interaction p-value: 0.1643						
< 8						
Relugolix	252	10 (4.0)	11.821	11.372	0.040	0.0169
Leuprolide	136	0	[0.687;203.288]	[0.671;192.582]	[0.016;0.064]	
>= 8						
Relugolix	163	2 (1.2)	0.907	0.908	-0.001	1.0000
Leuprolide	74	1 (1.4)	[0.081;10.161]	[0.084;9.857]	[-0.033;0.030]	
Missing						
Relugolix	12	0	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAED.ANY.BIN.SAFM0.S6: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Baseline Testosterone Level, Interaction p-value: 0.5687						
< 250 ng/dL						
Relugolix	37	1 (2.7)	1.685	1.658	0.027	1.0000
Leuprolide	20	0	[0.066;43.282]	[0.071;38.919]	[-0.025;0.079]	
>= 250 ng/dL						
Relugolix	383	11 (2.9)	5.441	5.313	0.023	0.1153
Leuprolide	185	1 (0.5)	[0.697;42.464]	[0.691;40.845]	[0.004;0.043]	
Missing						
Relugolix	7	0	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAED.ANY.BIN.SAFM0.S1: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.7071						
<= 75 years old						
Relugolix	304	10 (3.3)	5.170	5.033	0.026	0.1090
Leuprolide	153	1 (0.7)	[0.656;40.765]	[0.650;38.956]	[0.003;0.050]	
> 75 years old						
Relugolix	123	2 (1.6)	2.490	2.460	0.016	1.0000
Leuprolide	60	0	[0.118;52.676]	[0.120;50.445]	[-0.006;0.039]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAED.ANY.BIN.SAFM0.S3: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Ethnicity, Interaction p-value: 0.8100						
Not Hispanic or Latino						
Relugolix	381	10 (2.6)	5.040	4.934	0.021	0.1114
Leuprolide	188	1 (0.5)	[0.640;39.671]	[0.636;38.261]	[0.002;0.040]	
Hispanic or Latino						
Relugolix	37	2 (5.4)	3.169	3.026	0.054	0.5243
Leuprolide	22	0	[0.145;69.088]	[0.152;60.294]	[-0.019;0.127]	
Not Reported						
Relugolix	9	0	NC	NC	NC	NC
Leuprolide	3	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

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Table AE.TEAED.ANY.BIN.SAFM0.S2: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: NC						
North and South America						
Relugolix	161	4 (2.5)	NC	NC	NC	NC
Leuprolide	80	0	[NC;NC]	[NC;NC]	[NC;NC]	
Europe						
Relugolix	155	4 (2.6)	NC	NC	NC	NC
Leuprolide	78	0	[NC;NC]	[NC;NC]	[NC;NC]	
Asia and Rest of World						
Relugolix	111	4 (3.6)	NC	NC	NC	NC
Leuprolide	55	1 (1.8)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

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Table AE.TEAED.ANY.BIN.SAFM0.S4: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Race, Interaction p-value: NC						
Asian						
Relugolix	94	4 (4.3)	NC	NC	NC	NC
Leuprolide	51	1 (2.0)	[NC;NC]	[NC;NC]	[NC;NC]	
Black or African American						
Relugolix	21	0	NC	NC	NC	NC
Leuprolide	12	0	[NC;NC]	[NC;NC]	[NC;NC]	
White						
Relugolix	292	8 (2.7)	NC	NC	NC	NC
Leuprolide	139	0	[NC;NC]	[NC;NC]	[NC;NC]	
Others						
Relugolix	14	0	NC	NC	NC	NC
Leuprolide	7	0	[NC;NC]	[NC;NC]	[NC;NC]	
Not Reported						
Relugolix	6	0	NC	NC	NC	NC
Leuprolide	4	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAED.ANY.BIN.SAFM0.S8: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Non-Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: NC						
Asia (Excl. Korea)						
Relugolix	70	3 (4.3)	NC	NC	NC	NC
Leuprolide	36	1 (2.8)	[NC;NC]	[NC;NC]	[NC;NC]	
Rest of World						
Relugolix	357	9 (2.5)	NC	NC	NC	NC
Leuprolide	177	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Non-Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

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5 Weitere Ergebnisse der supportiv dargestellten Gesamtpopulation der Studie HERO

5.1 Subgruppenergebnisse

5.1.1 Mortalität

5.1.1.1 Gesamtüberleben

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Table MOR.OS.KM.MITT.S1: Time to Overall Survival, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.0563							
<= 75 years old							
Relugolix	509	13 (2.6)	496 (97.4)	NE [NE;NE]	NE	1.313 [0.468;3.682]	0.6052
Leuprolide	254	5 (2.0)	249 (98.0)	NE [NE;NE]			
> 75 years old							
Relugolix	208	4 (1.9)	204 (98.1)	NE [NE;NE]	NE	0.275 [0.081;0.940]	0.0396
Leuprolide	103	7 (6.8)	96 (93.2)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.OS.KM.MITT.S2: Time to Overall Survival, by Subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.2872							
North and South America							
Relugolix	253	10 (4.0)	243 (96.0)	NE [NE;NE]	NE	1.264 [0.396;4.030]	0.6922
Leuprolide	126	4 (3.2)	122 (96.8)	NE [NE;NE]			
Europe							
Relugolix	271	5 (1.8)	266 (98.2)	NE [NE;NE]	NE	0.349 [0.111;1.100]	0.0723
Leuprolide	135	7 (5.2)	128 (94.8)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	193	2 (1.0)	191 (99.0)	NE [NE;NE]	NE	1.005 [0.091;11.080]	0.9969
Leuprolide	96	1 (1.0)	95 (99.0)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.OS.KM.MITT.S7: Time to Overall Survival, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.4544							
< 20 ng/mL							
Relugolix	428	8 (1.9)	420 (98.1)	NE [NE;NE]	NE	1.000 [0.301;3.321]	0.9999
Leuprolide	213	4 (1.9)	209 (98.1)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	289	9 (3.1)	280 (96.9)	NE [NE;NE]	NE	0.557 [0.215;1.444]	0.2287
Leuprolide	144	8 (5.6)	136 (94.4)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.OS.KM.MITT.S5: Time to Overall Survival, by Subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.6964							
< 8							
Relugolix	356	5 (1.4)	351 (98.6)	NE [NE;NE]	NE	0.888 [0.212;3.716]	0.8709
Leuprolide	185	3 (1.6)	182 (98.4)	NE [NE;NE]			
>= 8							
Relugolix	341	12 (3.5)	329 (96.5)	NE [NE;NE]	NE	0.637 [0.268;1.511]	0.3058
Leuprolide	166	9 (5.4)	157 (94.6)	NE [NE;NE]			
Missing							
Relugolix	20	0	20 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	0	6 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.OS.KM.MITT.S8: Time to Overall Survival, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.8117							
Asia (Excl. Korea)							
Relugolix	104	1 (1.0)	103 (99.0)	NE [NE;NE]	NE	0.509 [0.032;8.136]	0.6329
Leuprolide	53	1 (1.9)	52 (98.1)	NE [NE;NE]			
Rest of World							
Relugolix	613	16 (2.6)	597 (97.4)	NE [NE;NE]	NE	0.722 [0.335;1.555]	0.4054
Leuprolide	304	11 (3.6)	293 (96.4)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.OS.KM.MITT.S6: Time to Overall Survival, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: 0.8726							
< 250 ng/dL							
Relugolix	72	1 (1.4)	71 (98.6)	NE [NE;NE]	NE	0.553 [0.035;8.846]	0.6756
Leuprolide	39	1 (2.6)	38 (97.4)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	635	16 (2.5)	619 (97.5)	NE [NE;NE]	NE	0.700 [0.325;1.509]	0.3628
Leuprolide	307	11 (3.6)	296 (96.4)	NE [NE;NE]			
Missing							
Relugolix	10	0	10 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.OS.KM.MITT.S4: Time to Overall Survival, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.9644							
Asian							
Relugolix	157	2 (1.3)	155 (98.7)	NE [NE;NE]	NE	0.567 [0.080;4.027]	0.5708
Leuprolide	88	2 (2.3)	86 (97.7)	NE [NE;NE]			
Black or African American							
Relugolix	34	1 (2.9)	33 (97.1)	NE [NE;NE]	NE	0.488 [0.031;7.813]	0.6125
Leuprolide	16	1 (6.3)	15 (93.8)	NE [NE;NE]			
White							
Relugolix	492	13 (2.6)	479 (97.4)	NE [NE;NE]	NE	0.683 [0.292;1.598]	0.3797
Leuprolide	234	9 (3.8)	225 (96.2)	NE [NE;NE]			
Others							
Relugolix	21	0	21 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	13	1 (7.7)	12 (92.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

Table MOR.OS.KM.MITT.S3: Time to Overall Survival, by Subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: NC							
Not Hispanic or Latino							
Relugolix	640	14 (2.2)	626 (97.8)	NE [NE;NE]	NE	0.567 [0.262;1.225]	0.1490
Leuprolide	312	12 (3.8)	300 (96.2)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	3 (4.7)	61 (95.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	37	0	37 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	13	0	13 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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5.1.2 Mortalität/ Morbidität

5.1.2.1 Major Adverse Cardiovascular Events

5.1.2.1.1 Hauptanalyse des kombinierten Endpunkts

Table MC.T2MACE1.KM.SAF.S3: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.1446							
Not Hispanic or Latino							
Relugolix	640	19 (3.0)	621 (97.0)	NE [NE;NE]	NE	0.453 [0.242;0.848]	0.0134
Leuprolide	312	20 (6.4)	292 (93.6)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	4 (6.3)	60 (93.8)	NE [NE;NE]	NE	2.471 [0.276;22.115]	0.4186
Leuprolide	37	1 (2.7)	36 (97.3)	NE [NE;NE]			
Not Reported							
Relugolix	13	0	13 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAF.S7: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.2478							
< 20 ng/mL							
Relugolix	428	8 (1.9)	420 (98.1)	NE [NE;NE]	NE	0.359 [0.144;0.893]	0.0275
Leuprolide	213	11 (5.2)	202 (94.8)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	289	15 (5.2)	274 (94.8)	NE [NE;NE]	NE	0.734 [0.330;1.634]	0.4488
Leuprolide	144	10 (6.9)	134 (93.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAF.S2: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.4316							
North and South America							
Relugolix	253	12 (4.7)	241 (95.3)	NE [NE;NE]	NE	0.858 [0.338;2.179]	0.7471
Leuprolide	126	7 (5.6)	119 (94.4)	NE [NE;NE]			
Europe							
Relugolix	271	7 (2.6)	264 (97.4)	NE [NE;NE]	NE	0.376 [0.140;1.010]	0.0524
Leuprolide	135	9 (6.7)	126 (93.3)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	193	4 (2.1)	189 (97.9)	NE [NE;NE]	NE	0.394 [0.106;1.469]	0.1654
Leuprolide	96	5 (5.2)	91 (94.8)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAF.S4: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4930							
Asian							
Relugolix	157	4 (2.5)	153 (97.5)	NE [NE;NE]	NE	0.368 [0.104;1.306]	0.1219
Leuprolide	88	6 (6.8)	82 (93.2)	NE [NE;NE]			
Black or African American							
Relugolix	34	0	34 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	16	2 (12.5)	14 (87.5)	NC [NC;NC]			
White							
Relugolix	492	17 (3.5)	475 (96.5)	NE [NE;NE]	NE	0.613 [0.298;1.263]	0.1844
Leuprolide	234	13 (5.6)	221 (94.4)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAF.S4: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4930							
Others							
Relugolix	21	1 (4.8)	20 (95.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	13	1 (7.7)	12 (92.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAF.S5: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.4991							
< 8							
Relugolix	356	9 (2.5)	347 (97.5)	NE [NE;NE]	NE	0.676 [0.252;1.816]	0.4378
Leuprolide	185	7 (3.8)	178 (96.2)	NE [NE;NE]			
>= 8							
Relugolix	341	13 (3.8)	328 (96.2)	NE [NE;NE]	NE	0.441 [0.207;0.937]	0.0333
Leuprolide	166	14 (8.4)	152 (91.6)	NE [NE;NE]			
Missing							
Relugolix	20	1 (5.0)	19 (95.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	0	6 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAF.S6: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.5427							
< 250 ng/dL							
Relugolix	72	2 (2.8)	70 (97.2)	NE [NE;NE]	NE	1.080 [0.098;11.923]	0.9498
Leuprolide	39	1 (2.6)	38 (97.4)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	635	21 (3.3)	614 (96.7)	NE [NE;NE]	NE	0.500 [0.271;0.923]	0.0266
Leuprolide	307	20 (6.5)	287 (93.5)	NE [NE;NE]			
Missing							
Relugolix	10	0	10 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAF.S1: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.5482							
<= 75 years old							
Relugolix	509	16 (3.1)	493 (96.9)	NE [NE;NE]	NE	0.613 [0.295;1.274]	0.1898
Leuprolide	254	13 (5.1)	241 (94.9)	NE [NE;NE]			
> 75 years old							
Relugolix	208	7 (3.4)	201 (96.6)	NE [NE;NE]	NE	0.418 [0.152;1.152]	0.0917
Leuprolide	103	8 (7.8)	95 (92.2)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE1.KM.SAF.S8: Time to Pre-defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.6103							
Asia (Excl. Korea)							
Relugolix	104	3 (2.9)	101 (97.1)	NE [NE;NE]	NE	0.377 [0.084;1.686]	0.2020
Leuprolide	53	4 (7.5)	49 (92.5)	NE [NE;NE]			
Rest of World							
Relugolix	613	20 (3.3)	593 (96.7)	NE [NE;NE]	NE	0.577 [0.302;1.101]	0.0952
Leuprolide	304	17 (5.6)	287 (94.4)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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5.1.2.1.2 Sensitivitätsanalyse des kombinierten Endpunkts

Table MC.T2MACE2.KM.SAF.S3: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.1763							
Not Hispanic or Latino							
Relugolix	640	12 (1.9)	628 (98.1)	NE [NE;NE]	NE	0.357 [0.169;0.755]	0.0070
Leuprolide	312	16 (5.1)	296 (94.9)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	3 (4.7)	61 (95.3)	NE [NE;NE]	NE	1.849 [0.192;17.777]	0.5946
Leuprolide	37	1 (2.7)	36 (97.3)	NE [NE;NE]			
Not Reported							
Relugolix	13	0	13 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE2.KM.SAF.S2: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.3346							
North and South America							
Relugolix	253	7 (2.8)	246 (97.2)	NE [NE;NE]	NE	0.875 [0.256;2.988]	0.8310
Leuprolide	126	4 (3.2)	122 (96.8)	NE [NE;NE]			
Europe							
Relugolix	271	4 (1.5)	267 (98.5)	NE [NE;NE]	NE	0.241 [0.073;0.801]	0.0203
Leuprolide	135	8 (5.9)	127 (94.1)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	193	4 (2.1)	189 (97.9)	NE [NE;NE]	NE	0.394 [0.106;1.468]	0.1654
Leuprolide	96	5 (5.2)	91 (94.8)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

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Table MC.T2MACE2.KM.SAF.S1: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.3627							
<= 75 years old							
Relugolix	509	11 (2.2)	498 (97.8)	NE [NE;NE]	NE	0.547 [0.232;1.288]	0.1672
Leuprolide	254	10 (3.9)	244 (96.1)	NE [NE;NE]			
> 75 years old							
Relugolix	208	4 (1.9)	204 (98.1)	NE [NE;NE]	NE	0.273 [0.080;0.932]	0.0382
Leuprolide	103	7 (6.8)	96 (93.2)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE2.KM.SAF.S7: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.4746							
< 20 ng/mL							
Relugolix	428	6 (1.4)	422 (98.6)	NE [NE;NE]	NE	0.329 [0.117;0.924]	0.0349
Leuprolide	213	9 (4.2)	204 (95.8)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	289	9 (3.1)	280 (96.9)	NE [NE;NE]	NE	0.549 [0.212;1.424]	0.2176
Leuprolide	144	8 (5.6)	136 (94.4)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE2.KM.SAF.S4: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.7592							
Asian							
Relugolix	157	4 (2.5)	153 (97.5)	NE [NE;NE]	NE	0.368 [0.104;1.305]	0.1216
Leuprolide	88	6 (6.8)	82 (93.2)	NE [NE;NE]			
Black or African American							
Relugolix	34	0	34 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	16	1 (6.3)	15 (93.8)	NC [NC;NC]			
White							
Relugolix	492	10 (2.0)	482 (98.0)	NE [NE;NE]	NE	0.468 [0.195;1.125]	0.0899
Leuprolide	234	10 (4.3)	224 (95.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2MACE2.KM.SAF.S4: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.7592							
Others							
Relugolix	21	1 (4.8)	20 (95.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	13	0	13 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2MACE2.KM.SAF.S5: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Gleason Score at Study Entry, Interaction p-value: 0.8142							
< 8							
Relugolix	356	6 (1.7)	350 (98.3)	NE [NE;NE]	NE	0.450 [0.151;1.340]	0.1516
Leuprolide	185	7 (3.8)	178 (96.2)	NE [NE;NE]			
>= 8							
Relugolix	341	8 (2.3)	333 (97.7)	NE [NE;NE]	NE	0.379 [0.150;0.961]	0.0410
Leuprolide	166	10 (6.0)	156 (94.0)	NE [NE;NE]			
Missing							
Relugolix	20	1 (5.0)	19 (95.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	0	6 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

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Table MC.T2MACE2.KM.SAF.S8: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.8344							
Asia (Excl. Korea)							
Relugolix	104	3 (2.9)	101 (97.1)	NE [NE;NE]	NE	0.377 [0.084;1.686]	0.2019
Leuprolide	53	4 (7.5)	49 (92.5)	NE [NE;NE]			
Rest of World							
Relugolix	613	12 (2.0)	601 (98.0)	NE [NE;NE]	NE	0.452 [0.206;0.990]	0.0472
Leuprolide	304	13 (4.3)	291 (95.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

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Table MC.T2MACE2.KM.SAF.S6: Time to Post-hoc Defined Major Adverse Cardiovascular Events, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: NC							
< 250 ng/dL							
Relugolix	72	1 (1.4)	71 (98.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	39	0	39 (100.0)	NC [NC;NC]			
>= 250 ng/dL							
Relugolix	635	14 (2.2)	621 (97.8)	NE [NE;NE]	NE	0.392 [0.193;0.796]	0.0095
Leuprolide	307	17 (5.5)	290 (94.5)	NE [NE;NE]			
Missing							
Relugolix	10	0	10 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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5.1.2.1.3 Einzelkomponenten

Myovant Sciences, Inc.: HERO AMNOG

Table MC.T2DTHALL.KM.SAF.S1: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.1854							
<= 75 years old							
Relugolix	509	8 (1.6)	501 (98.4)	NE [NE;NE]	NE	0.807 [0.264;2.466]	0.7062
Leuprolide	254	5 (2.0)	249 (98.0)	NE [NE;NE]			
> 75 years old							
Relugolix	208	3 (1.4)	205 (98.6)	NE [NE;NE]	NE	0.242 [0.061;0.969]	0.0450
Leuprolide	103	6 (5.8)	97 (94.2)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2DTHALL.KM.SAF.S2: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.2643							
North and South America							
Relugolix	253	7 (2.8)	246 (97.2)	NE [NE;NE]	NE	0.886 [0.259;3.025]	0.8462
Leuprolide	126	4 (3.2)	122 (96.8)	NE [NE;NE]			
Europe							
Relugolix	271	4 (1.5)	267 (98.5)	NE [NE;NE]	NE	0.324 [0.092;1.149]	0.0811
Leuprolide	135	6 (4.4)	129 (95.6)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	193	0	193 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	96	1 (1.0)	95 (99.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2DTHALL.KM.SAF.S5: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.5472							
< 8							
Relugolix	356	3 (0.8)	353 (99.2)	NE [NE;NE]	NE	0.798 [0.133;4.773]	0.8044
Leuprolide	185	2 (1.1)	183 (98.9)	NE [NE;NE]			
>= 8							
Relugolix	341	8 (2.3)	333 (97.7)	NE [NE;NE]	NE	0.428 [0.165;1.109]	0.0807
Leuprolide	166	9 (5.4)	157 (94.6)	NE [NE;NE]			
Missing							
Relugolix	20	0	20 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	0	6 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2DTHALL.KM.SAF.S7: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.6605							
< 20 ng/mL							
Relugolix	428	3 (0.7)	425 (99.3)	NE [NE;NE]	NE	0.376 [0.084;1.681]	0.2005
Leuprolide	213	4 (1.9)	209 (98.1)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	289	8 (2.8)	281 (97.2)	NE [NE;NE]	NE	0.564 [0.205;1.556]	0.2687
Leuprolide	144	7 (4.9)	137 (95.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2DTHALL.KM.SAF.S6: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.9462							
< 250 ng/dL							
Relugolix	72	1 (1.4)	71 (98.6)	NE [NE;NE]	NE	0.535 [0.033;8.557]	0.6585
Leuprolide	39	1 (2.6)	38 (97.4)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	635	10 (1.6)	625 (98.4)	NE [NE;NE]	NE	0.484 [0.202;1.163]	0.1048
Leuprolide	307	10 (3.3)	297 (96.7)	NE [NE;NE]			
Missing							
Relugolix	10	0	10 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

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Table MC.T2DTHALL.KM.SAF.S3: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: NC							
Not Hispanic or Latino							
Relugolix	640	9 (1.4)	631 (98.6)	NE [NE;NE]	NE	0.394 [0.163;0.951]	0.0384
Leuprolide	312	11 (3.5)	301 (96.5)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	2 (3.1)	62 (96.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	37	0	37 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	13	0	13 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2DTHALL.KM.SAF.S4: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: NC							
Asian							
Relugolix	157	0	157 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	88	2 (2.3)	86 (97.7)	NC [NC;NC]			
Black or African American							
Relugolix	34	0	34 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	16	1 (6.3)	15 (93.8)	NC [NC;NC]			
White							
Relugolix	492	10 (2.0)	482 (98.0)	NE [NE;NE]	NE	0.588 [0.232;1.491]	0.2634
Leuprolide	234	8 (3.4)	226 (96.6)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

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Table MC.T2DTHALL.KM.SAF.S4: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: NC							
Others							
Relugolix	21	0	21 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	13	1 (7.7)	12 (92.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHALL.KM.SAF.S8: Time to Adverse Events leading to Death (All Causes), by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: NC							
Asia (Excl. Korea)							
Relugolix	104	0	104 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	53	1 (1.9)	52 (98.1)	NC [NC;NC]			
Rest of World							
Relugolix	613	11 (1.8)	602 (98.2)	NE [NE;NE]	NE	0.544 [0.231;1.281]	0.1634
Leuprolide	304	10 (3.3)	294 (96.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

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Table MC.T2DTHCV.KM.SAF.S1: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: NC							
<= 75 years old							
Relugolix	509	3 (0.6)	506 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	254	1 (0.4)	253 (99.6)	NC [NC;NC]			
> 75 years old							
Relugolix	208	0	208 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	103	5 (4.9)	98 (95.1)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHCV.KM.SAF.S2: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region I, Interaction p-value: NC							
North and South America							
Relugolix	253	2 (0.8)	251 (99.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	126	0	126 (100.0)	NC [NC;NC]			
Europe							
Relugolix	271	1 (0.4)	270 (99.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	135	5 (3.7)	130 (96.3)	NC [NC;NC]			
Asia and Rest of World							
Relugolix	193	0	193 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	96	1 (1.0)	95 (99.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHCV.KM.SAF.S3: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: NC							
Not Hispanic or Latino							
Relugolix	640	2 (0.3)	638 (99.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	312	6 (1.9)	306 (98.1)	NC [NC;NC]			
Hispanic or Latino							
Relugolix	64	1 (1.6)	63 (98.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	37	0	37 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	13	0	13 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHCV.KM.SAF.S4: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: NC							
Asian							
Relugolix	157	0	157 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	88	1 (1.1)	87 (98.9)	NC [NC;NC]			
Black or African American							
Relugolix	34	0	34 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	16	0	16 (100.0)	NC [NC;NC]			
White							
Relugolix	492	3 (0.6)	489 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	234	5 (2.1)	229 (97.9)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHCV.KM.SAF.S4: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: NC							
Others							
Relugolix	21	0	21 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	13	0	13 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2DTHCV.KM.SAF.S5: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: NC							
< 8							
Relugolix	356	0	356 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	185	2 (1.1)	183 (98.9)	NC [NC;NC]			
>= 8							
Relugolix	341	3 (0.9)	338 (99.1)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	166	4 (2.4)	162 (97.6)	NC [NC;NC]			
Missing							
Relugolix	20	0	20 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	0	6 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2DTHCV.KM.SAF.S6: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: NC							
< 250 ng/dL							
Relugolix	72	0	72 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	39	0	39 (100.0)	NC [NC;NC]			
>= 250 ng/dL							
Relugolix	635	3 (0.5)	632 (99.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	307	6 (2.0)	301 (98.0)	NC [NC;NC]			
Missing							
Relugolix	10	0	10 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2DTHCV.KM.SAF.S7: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: NC							
< 20 ng/mL							
Relugolix	428	1 (0.2)	427 (99.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	213	2 (0.9)	211 (99.1)	NC [NC;NC]			
>= 20 ng/mL							
Relugolix	289	2 (0.7)	287 (99.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	144	4 (2.8)	140 (97.2)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2DTHCV.KM.SAF.S8: Time to Cardiovascular Events (including MI and Stroke) leading to Death, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: NC							
Asia (Excl. Korea)							
Relugolix	104	0	104 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	53	1 (1.9)	52 (98.1)	NC [NC;NC]			
Rest of World							
Relugolix	613	3 (0.5)	610 (99.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	304	5 (1.6)	299 (98.4)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDMI.KM.SAF.S1: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: NC							
<= 75 years old							
Relugolix	509	6 (1.2)	503 (98.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	254	2 (0.8)	252 (99.2)	NC [NC;NC]			
> 75 years old							
Relugolix	208	2 (1.0)	206 (99.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	103	1 (1.0)	102 (99.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDMI.KM.SAF.S2: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: NC							
North and South America							
Relugolix	253	4 (1.6)	249 (98.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	126	2 (1.6)	124 (98.4)	NC [NC;NC]			
Europe							
Relugolix	271	1 (0.4)	270 (99.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	135	0	135 (100.0)	NC [NC;NC]			
Asia and Rest of World							
Relugolix	193	3 (1.6)	190 (98.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	96	1 (1.0)	95 (99.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2NDMI.KM.SAF.S3: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: NC							
Not Hispanic or Latino							
Relugolix	640	7 (1.1)	633 (98.9)	NE [NE;NE]	NE	1.126 [0.291;4.353]	0.8639
Leuprolide	312	3 (1.0)	309 (99.0)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	1 (1.6)	63 (98.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	37	0	37 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	13	0	13 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

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Table MC.T2NDMI.KM.SAF.S4: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: NC							
Asian							
Relugolix	157	3 (1.9)	154 (98.1)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	88	2 (2.3)	86 (97.7)	NC [NC;NC]			
Black or African American							
Relugolix	34	0	34 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	16	1 (6.3)	15 (93.8)	NC [NC;NC]			
White							
Relugolix	492	4 (0.8)	488 (99.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	234	0	234 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDMI.KM.SAF.S4: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: NC							
Others							
Relugolix	21	1 (4.8)	20 (95.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	13	0	13 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDMI.KM.SAF.S5: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Gleason Score at Study Entry, Interaction p-value: NC							
< 8							
Relugolix	356	5 (1.4)	351 (98.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	185	0	185 (100.0)	NC [NC;NC]			
>= 8							
Relugolix	341	3 (0.9)	338 (99.1)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	166	3 (1.8)	163 (98.2)	NC [NC;NC]			
Missing							
Relugolix	20	0	20 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	0	6 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDMI.KM.SAF.S6: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: NC							
< 250 ng/dL							
Relugolix	72	1 (1.4)	71 (98.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	39	0	39 (100.0)	NC [NC;NC]			
>= 250 ng/dL							
Relugolix	635	7 (1.1)	628 (98.9)	NE [NE;NE]	NE	1.126 [0.291;4.355]	0.8633
Leuprolide	307	3 (1.0)	304 (99.0)	NE [NE;NE]			
Missing							
Relugolix	10	0	10 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

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Table MC.T2NDMI.KM.SAF.S7: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: NC							
< 20 ng/mL							
Relugolix	428	4 (0.9)	424 (99.1)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	213	1 (0.5)	212 (99.5)	NC [NC;NC]			
>= 20 ng/mL							
Relugolix	289	4 (1.4)	285 (98.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	144	2 (1.4)	142 (98.6)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDMI.KM.SAF.S8: Time to Non-deadly Myocardial Infarction, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: NC							
Asia (Excl. Korea)							
Relugolix	104	2 (1.9)	102 (98.1)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	53	0	53 (100.0)	NC [NC;NC]			
Rest of World							
Relugolix	613	6 (1.0)	607 (99.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	304	3 (1.0)	301 (99.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDSTRK.KM.SAF.S3: Time to Non-deadly Stroke, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.4369							
Not Hispanic or Latino							
Relugolix	640	3 (0.5)	637 (99.5)	NE [NE;NE]	NE	0.178 [0.047;0.671]	0.0108
Leuprolide	312	8 (2.6)	304 (97.4)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	1 (1.6)	63 (98.4)	NE [NE;NE]	NE	0.602 [0.038;9.622]	0.7196
Leuprolide	37	1 (2.7)	36 (97.3)	NE [NE;NE]			
Not Reported							
Relugolix	13	0	13 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2NDSTRK.KM.SAF.S1: Time to Non-deadly Stroke, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: NC							
<= 75 years old							
Relugolix	509	2 (0.4)	507 (99.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	254	7 (2.8)	247 (97.2)	NC [NC;NC]			
> 75 years old							
Relugolix	208	2 (1.0)	206 (99.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	103	2 (1.9)	101 (98.1)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDSTRK.KM.SAF.S2: Time to Non-deadly Stroke, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: NC							
North and South America							
Relugolix	253	1 (0.4)	252 (99.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	126	3 (2.4)	123 (97.6)	NC [NC;NC]			
Europe							
Relugolix	271	2 (0.7)	269 (99.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	135	3 (2.2)	132 (97.8)	NC [NC;NC]			
Asia and Rest of World							
Relugolix	193	1 (0.5)	192 (99.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	96	3 (3.1)	93 (96.9)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDSTRK.KM.SAF.S4: Time to Non-deadly Stroke, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: NC							
Asian							
Relugolix	157	1 (0.6)	156 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	88	3 (3.4)	85 (96.6)	NC [NC;NC]			
Black or African American							
Relugolix	34	0	34 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	16	1 (6.3)	15 (93.8)	NC [NC;NC]			
White							
Relugolix	492	3 (0.6)	489 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	234	5 (2.1)	229 (97.9)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDSTRK.KM.SAF.S4: Time to Non-deadly Stroke, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: NC							
Others							
Relugolix	21	0	21 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	13	0	13 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDSTRK.KM.SAF.S5: Time to Non-deadly Stroke, by subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: NC							
< 8							
Relugolix	356	1 (0.3)	355 (99.7)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	185	5 (2.7)	180 (97.3)	NC [NC;NC]			
>= 8							
Relugolix	341	2 (0.6)	339 (99.4)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	166	4 (2.4)	162 (97.6)	NC [NC;NC]			
Missing							
Relugolix	20	1 (5.0)	19 (95.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	0	6 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDSTRK.KM.SAF.S6: Time to Non-deadly Stroke, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: NC							
< 250 ng/dL							
Relugolix	72	0	72 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	39	0	39 (100.0)	NC [NC;NC]			
>= 250 ng/dL							
Relugolix	635	4 (0.6)	631 (99.4)	NE [NE;NE]	NE	0.210 [0.065;0.683]	0.0094
Leuprolide	307	9 (2.9)	298 (97.1)	NE [NE;NE]			
Missing							
Relugolix	10	0	10 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated; NE: Non-estimable.

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Table MC.T2NDSTRK.KM.SAF.S7: Time to Non-deadly Stroke, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: NC							
< 20 ng/mL							
Relugolix	428	1 (0.2)	427 (99.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	213	7 (3.3)	206 (96.7)	NC [NC;NC]			
>= 20 ng/mL							
Relugolix	289	3 (1.0)	286 (99.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	144	2 (1.4)	142 (98.6)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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Table MC.T2NDSTRK.KM.SAF.S8: Time to Non-deadly Stroke, by subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: NC							
Asia (Excl. Korea)							
Relugolix	104	1 (1.0)	103 (99.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	53	3 (5.7)	50 (94.3)	NC [NC;NC]			
Rest of World							
Relugolix	613	3 (0.5)	610 (99.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	304	6 (2.0)	298 (98.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NC: Not calculated.

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5.1.3 Morbidität

5.1.3.1 Gesundheitszustand (EuroQol-5-Dimension Visual Analog Scale)

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2EQ5D15.KM.MITT.S7: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.1121							
< 20 ng/mL							
Relugolix	428	117 (27.3)	311 (72.7)	NE [NE;NE]	NE	1.039 [0.756;1.429]	0.8135
Leuprolide	213	56 (26.3)	157 (73.7)	351.0 [344.0;NE]			
>= 20 ng/mL							
Relugolix	289	83 (28.7)	206 (71.3)	NE [344.0;NE]	NE	0.711 [0.505;1.002]	0.0512
Leuprolide	144	54 (37.5)	90 (62.5)	343.0 [340.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EQ5D15.KM.MITT.S5: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.4132							
< 8							
Relugolix	356	97 (27.2)	259 (72.8)	NE [NE;NE]	NE	0.946 [0.678;1.319]	0.7425
Leuprolide	185	54 (29.2)	131 (70.8)	351.0 [344.0;NE]			
>= 8							
Relugolix	341	93 (27.3)	248 (72.7)	NE [NE;NE]	NE	0.776 [0.555;1.086]	0.1393
Leuprolide	166	54 (32.5)	112 (67.5)	344.0 [343.0;NE]			
Missing							
Relugolix	20	10 (50.0)	10 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	2 (33.3)	4 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2EQ5D15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4243							
Asian							
Relugolix	157	44 (28.0)	113 (72.0)	NE [NE;NE]	NE	0.843 [0.527;1.347]	0.4744
Leuprolide	88	29 (33.0)	59 (67.0)	NE [342.0;NE]			
Black or African American							
Relugolix	34	11 (32.4)	23 (67.6)	NE [253.0;NE]	NE	1.137 [0.362;3.573]	0.8256
Leuprolide	16	4 (25.0)	12 (75.0)	NE [100.0;NE]			
White							
Relugolix	492	138 (28.0)	354 (72.0)	NE [NE;NE]	NE	0.954 [0.712;1.277]	0.7510
Leuprolide	234	67 (28.6)	167 (71.4)	NE [343.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EQ5D15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4243							
Others							
Relugolix	21	4 (19.0)	17 (81.0)	NE [339.0;NE]	NE	0.329 [0.092;1.172]	0.0863
Leuprolide	11	6 (54.5)	5 (45.5)	351.0 [115.0;NE]			
Not Reported							
Relugolix	13	3 (23.1)	10 (76.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2EQ5D15.KM.MITT.S3: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.6324							
Not Hispanic or Latino							
Relugolix	640	174 (27.2)	466 (72.8)	NE [NE;NE]	NE	0.905 [0.702;1.166]	0.4405
Leuprolide	312	91 (29.2)	221 (70.8)	NE [344.0;NE]			
Hispanic or Latino							
Relugolix	64	23 (35.9)	41 (64.1)	NE [337.0;NE]	NE	1.080 [0.547;2.133]	0.8236
Leuprolide	37	13 (35.1)	24 (64.9)	NE [338.0;NE]			
Not Reported							
Relugolix	13	3 (23.1)	10 (76.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	6 (75.0)	2 (25.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2EQ5D15.KM.MITT.S2: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.7663							
North and South America							
Relugolix	253	70 (27.7)	183 (72.3)	NE [NE;NE]	NE	0.957 [0.638;1.437]	0.8332
Leuprolide	126	35 (27.8)	91 (72.2)	343.0 [343.0;NE]			
Europe							
Relugolix	271	75 (27.7)	196 (72.3)	NE [NE;NE]	NE	0.903 [0.615;1.326]	0.6032
Leuprolide	135	40 (29.6)	95 (70.4)	351.0 [NE;NE]			
Asia and Rest of World							
Relugolix	193	55 (28.5)	138 (71.5)	NE [344.0;NE]	NE	0.774 [0.507;1.183]	0.2371
Leuprolide	96	35 (36.5)	61 (63.5)	344.0 [342.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2EQ5D15.KM.MITT.S6: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.8910							
< 250 ng/dL							
Relugolix	72	20 (27.8)	52 (72.2)	344.0 [344.0;NE]	NE	0.855 [0.418;1.750]	0.6681
Leuprolide	39	12 (30.8)	27 (69.2)	NE [340.0;NE]			
>= 250 ng/dL							
Relugolix	635	175 (27.6)	460 (72.4)	NE [NE;NE]	NE	0.902 [0.700;1.161]	0.4214
Leuprolide	307	92 (30.0)	215 (70.0)	351.0 [344.0;NE]			
Missing							
Relugolix	10	5 (50.0)	5 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	6 (54.5)	5 (45.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2EQ5D15.KM.MITT.S8: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.9090							
Asia (Excl. Korea)							
Relugolix	104	28 (26.9)	76 (73.1)	NE [NE;NE]	NE	0.908 [0.491;1.679]	0.7582
Leuprolide	53	16 (30.2)	37 (69.8)	NE [344.0;NE]			
Rest of World							
Relugolix	613	172 (28.1)	441 (71.9)	NE [NE;NE]	NE	0.874 [0.679;1.123]	0.2920
Leuprolide	304	94 (30.9)	210 (69.1)	351.0 [343.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EQ5D15.KM.MITT.S1: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.9853							
<= 75 years old							
Relugolix	509	136 (26.7)	373 (73.3)	NE [NE;NE]	NE	0.879 [0.662;1.167]	0.3740
Leuprolide	254	74 (29.1)	180 (70.9)	NE [344.0;NE]			
> 75 years old							
Relugolix	208	64 (30.8)	144 (69.2)	NE [344.0;NE]	NE	0.884 [0.587;1.329]	0.5525
Leuprolide	103	36 (35.0)	67 (65.0)	344.0 [340.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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5.1.3.2 Symptomatik (European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire C30)

5.1.3.2.1 Skala: Fatigue

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2FAT15.KM.MITT.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Gleason Score at Study Entry, Interaction p-value: 0.0533							
< 8							
Relugolix	356	158 (44.4)	198 (55.6)	355.0 [260.0;NE]	NE	1.269 [0.959;1.679]	0.0958
Leuprolide	185	71 (38.4)	114 (61.6)	NE [338.0;NE]			
>= 8							
Relugolix	341	138 (40.5)	203 (59.5)	344.0 [340.0;NE]	1.0	0.856 [0.645;1.137]	0.2837
Leuprolide	166	73 (44.0)	93 (56.0)	343.0 [337.0;NE]			
Missing							
Relugolix	20	10 (50.0)	10 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	3 (50.0)	3 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITT.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.2535							
Not Hispanic or Latino							
Relugolix	640	268 (41.9)	372 (58.1)	355.0 [341.0;NE]	12.0	1.028 [0.832;1.269]	0.7998
Leuprolide	312	128 (41.0)	184 (59.0)	343.0 [338.0;NE]			
Hispanic or Latino							
Relugolix	64	30 (46.9)	34 (53.1)	339.0 [251.0;NE]	NE	1.547 [0.792;3.021]	0.2016
Leuprolide	37	12 (32.4)	25 (67.6)	NE [337.0;NE]			
Not Reported							
Relugolix	13	8 (61.5)	5 (38.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	7 (87.5)	1 (12.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITT.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.2951							
< 20 ng/mL							
Relugolix	428	190 (44.4)	238 (55.6)	343.0 [337.0;NE]	-1.0	1.139 [0.884;1.466]	0.3145
Leuprolide	213	88 (41.3)	125 (58.7)	344.0 [338.0;NE]			
>= 20 ng/mL							
Relugolix	289	116 (40.1)	173 (59.9)	NE [340.0;NE]	NE	0.918 [0.671;1.256]	0.5926
Leuprolide	144	59 (41.0)	85 (59.0)	343.0 [337.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.2994							
Asian							
Relugolix	157	59 (37.6)	98 (62.4)	NE [340.0;NE]	NE	0.872 [0.574;1.325]	0.5201
Leuprolide	88	35 (39.8)	53 (60.2)	344.0 [337.0;NE]			
Black or African American							
Relugolix	34	23 (67.6)	11 (32.4)	173.0 [84.0;257.0]	-157.0	1.809 [0.776;4.217]	0.1699
Leuprolide	16	7 (43.8)	9 (56.3)	330.0 [85.0;NE]			
White							
Relugolix	492	203 (41.3)	289 (58.7)	355.0 [341.0;NE]	-2.0	1.087 [0.850;1.389]	0.5054
Leuprolide	234	93 (39.7)	141 (60.3)	357.0 [338.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.2994							
Others							
Relugolix	21	12 (57.1)	9 (42.9)	339.0 [172.0;NE]	168.0	0.628 [0.256;1.537]	0.3080
Leuprolide	11	8 (72.7)	3 (27.3)	171.0 [73.0;NE]			
Not Reported							
Relugolix	13	9 (69.2)	4 (30.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITT.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: 0.3924							
< 250 ng/dL							
Relugolix	72	37 (51.4)	35 (48.6)	257.0 [173.0;NE]	-82.0	1.344 [0.757;2.387]	0.3133
Leuprolide	39	17 (43.6)	22 (56.4)	339.0 [330.0;NE]			
>= 250 ng/dL							
Relugolix	635	264 (41.6)	371 (58.4)	355.0 [340.0;NE]	11.0	1.029 [0.831;1.273]	0.7961
Leuprolide	307	124 (40.4)	183 (59.6)	344.0 [338.0;NE]			
Missing							
Relugolix	10	5 (50.0)	5 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	6 (54.5)	5 (45.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITT.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.5025							
<= 75 years old							
Relugolix	509	214 (42.0)	295 (58.0)	NE [339.0;NE]	NE	1.092 [0.861;1.384]	0.4698
Leuprolide	254	100 (39.4)	154 (60.6)	NE [338.0;NE]			
> 75 years old							
Relugolix	208	92 (44.2)	116 (55.8)	341.0 [330.0;NE]	3.0	0.944 [0.664;1.342]	0.7483
Leuprolide	103	47 (45.6)	56 (54.4)	338.0 [337.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITT.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.5030							
North and South America							
Relugolix	253	125 (49.4)	128 (50.6)	337.0 [251.0;343.0]	-1.0	1.113 [0.819;1.512]	0.4937
Leuprolide	126	61 (48.4)	65 (51.6)	338.0 [253.0;NE]			
Europe							
Relugolix	271	108 (39.9)	163 (60.1)	355.0 [342.0;NE]	NE	1.146 [0.813;1.614]	0.4369
Leuprolide	135	47 (34.8)	88 (65.2)	NE [338.0;NE]			
Asia and Rest of World							
Relugolix	193	73 (37.8)	120 (62.2)	NE [340.0;NE]	NE	0.862 [0.584;1.272]	0.4544
Leuprolide	96	39 (40.6)	57 (59.4)	343.0 [337.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2FAT15.KM.MITT.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.6521							
Asia (Excl. Korea)							
Relugolix	104	42 (40.4)	62 (59.6)	NE [337.0;NE]	NE	0.936 [0.559;1.569]	0.8026
Leuprolide	53	22 (41.5)	31 (58.5)	344.0 [337.0;NE]			
Rest of World							
Relugolix	613	264 (43.1)	349 (56.9)	343.0 [339.0;NE]	0.0	1.065 [0.861;1.317]	0.5641
Leuprolide	304	125 (41.1)	179 (58.9)	343.0 [338.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITT.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.1346							
<= 75 years old							
Relugolix	509	254 (49.9)	255 (50.1)	337.0 [258.0;341.0]	-3.0	1.226 [0.981;1.531]	0.0729
Leuprolide	254	112 (44.1)	142 (55.9)	340.0 [337.0;NE]			
> 75 years old							
Relugolix	208	105 (50.5)	103 (49.5)	337.0 [175.0;NE]	83.0	0.908 [0.656;1.256]	0.5587
Leuprolide	103	56 (54.4)	47 (45.6)	254.0 [169.0;342.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITT.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.1574							
< 8							
Relugolix	356	185 (52.0)	171 (48.0)	255.0 [173.0;338.0]	-85.0	1.289 [0.997;1.667]	0.0525
Leuprolide	185	85 (45.9)	100 (54.1)	340.0 [330.0;NE]			
>= 8							
Relugolix	341	164 (48.1)	177 (51.9)	339.0 [336.0;344.0]	1.0	0.986 [0.754;1.290]	0.9192
Leuprolide	166	79 (47.6)	87 (52.4)	338.0 [254.0;NE]			
Missing							
Relugolix	20	10 (50.0)	10 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	4 (66.7)	2 (33.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITT.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.2577							
< 250 ng/dL							
Relugolix	72	38 (52.8)	34 (47.2)	337.0 [91.0;NE]	NE	1.561 [0.859;2.838]	0.1440
Leuprolide	39	15 (38.5)	24 (61.5)	NE [169.0;NE]			
>= 250 ng/dL							
Relugolix	635	315 (49.6)	320 (50.4)	337.0 [258.0;340.0]	-2.0	1.086 [0.892;1.321]	0.4112
Leuprolide	307	146 (47.6)	161 (52.4)	339.0 [330.0;NE]			
Missing							
Relugolix	10	6 (60.0)	4 (40.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	7 (63.6)	4 (36.4)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITT.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.3789							
Asia (Excl. Korea)							
Relugolix	104	49 (47.1)	55 (52.9)	340.0 [171.0;NE]	NE	1.388 [0.825;2.335]	0.2164
Leuprolide	53	20 (37.7)	33 (62.3)	NE [253.0;NE]			
Rest of World							
Relugolix	613	310 (50.6)	303 (49.4)	337.0 [255.0;339.0]	0.0	1.082 [0.889;1.316]	0.4321
Leuprolide	304	148 (48.7)	156 (51.3)	337.0 [329.0;342.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITT.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.4245							
< 20 ng/mL							
Relugolix	428	221 (51.6)	207 (48.4)	260.0 [252.0;340.0]	-78.0	1.192 [0.942;1.508]	0.1444
Leuprolide	213	101 (47.4)	112 (52.6)	338.0 [257.0;NE]			
>= 20 ng/mL							
Relugolix	289	138 (47.8)	151 (52.2)	339.0 [333.0;341.0]	0.0	1.023 [0.764;1.370]	0.8794
Leuprolide	144	67 (46.5)	77 (53.5)	339.0 [260.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4964							
Asian							
Relugolix	157	75 (47.8)	82 (52.2)	339.0 [252.0;NE]	NE	1.305 [0.877;1.943]	0.1889
Leuprolide	88	36 (40.9)	52 (59.1)	NE [330.0;NE]			
Black or African American							
Relugolix	34	25 (73.5)	9 (26.5)	166.0 [30.0;253.0]	-6.0	1.212 [0.565;2.598]	0.6218
Leuprolide	16	9 (56.3)	7 (43.8)	172.0 [29.0;NE]			
White							
Relugolix	492	238 (48.4)	254 (51.6)	339.0 [260.0;344.0]	1.0	1.079 [0.861;1.353]	0.5074
Leuprolide	234	110 (47.0)	124 (53.0)	338.0 [330.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2PAIN15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4964							
Others							
Relugolix	21	13 (61.9)	8 (38.1)	253.0 [85.0;NE]	163.0	0.624 [0.259;1.507]	0.2947
Leuprolide	11	8 (72.7)	3 (27.3)	90.0 [27.0;NE]			
Not Reported							
Relugolix	13	8 (61.5)	5 (38.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	5 (62.5)	3 (37.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITT.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.5870							
North and South America							
Relugolix	253	146 (57.7)	107 (42.3)	253.0 [171.0;336.0]	-76.0	1.177 [0.883;1.570]	0.2667
Leuprolide	126	68 (54.0)	58 (46.0)	329.0 [172.0;340.0]			
Europe							
Relugolix	271	127 (46.9)	144 (53.1)	340.0 [330.0;NE]	2.0	0.992 [0.732;1.344]	0.9584
Leuprolide	135	62 (45.9)	73 (54.1)	338.0 [260.0;NE]			
Asia and Rest of World							
Relugolix	193	86 (44.6)	107 (55.4)	340.0 [260.0;NE]	-3.0	1.255 [0.856;1.838]	0.2445
Leuprolide	96	38 (39.6)	58 (60.4)	343.0 [339.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PAIN15.KM.MITT.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.6678							
Not Hispanic or Latino							
Relugolix	640	313 (48.9)	327 (51.1)	337.0 [260.0;341.0]	-2.0	1.121 [0.920;1.366]	0.2553
Leuprolide	312	144 (46.2)	168 (53.8)	339.0 [336.0;NE]			
Hispanic or Latino							
Relugolix	64	38 (59.4)	26 (40.6)	253.0 [169.0;338.0]	NE	1.280 [0.723;2.269]	0.3973
Leuprolide	37	17 (45.9)	20 (54.1)	NE [90.0;NE]			
Not Reported							
Relugolix	13	8 (61.5)	5 (38.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	7 (87.5)	1 (12.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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5.1.3.2.3 Skala: Übelkeit und Erbrechen

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2NAUS15.KM.MITT.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.1120							
Not Hispanic or Latino							
Relugolix	640	139 (21.7)	501 (78.3)	NE [NE;NE]	NE	0.881 [0.664;1.170]	0.3815
Leuprolide	312	73 (23.4)	239 (76.6)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	20 (31.3)	44 (68.8)	NE [NE;NE]	NE	1.837 [0.777;4.346]	0.1660
Leuprolide	37	7 (18.9)	30 (81.1)	NE [NE;NE]			
Not Reported							
Relugolix	13	4 (30.8)	9 (69.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	2 (25.0)	6 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITT.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.1536							
Asia (Excl. Korea)							
Relugolix	104	16 (15.4)	88 (84.6)	NE [NE;NE]	NE	0.583 [0.281;1.213]	0.1488
Leuprolide	53	13 (24.5)	40 (75.5)	NE [339.0;NE]			
Rest of World							
Relugolix	613	147 (24.0)	466 (76.0)	NE [NE;NE]	NE	1.034 [0.776;1.376]	0.8213
Leuprolide	304	69 (22.7)	235 (77.3)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITT.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.1716							
< 8							
Relugolix	356	80 (22.5)	276 (77.5)	NE [NE;NE]	NE	1.151 [0.780;1.700]	0.4790
Leuprolide	185	37 (20.0)	148 (80.0)	NE [NE;NE]			
>= 8							
Relugolix	341	78 (22.9)	263 (77.1)	NE [NE;NE]	NE	0.791 [0.547;1.145]	0.2150
Leuprolide	166	44 (26.5)	122 (73.5)	NE [344.0;NE]			
Missing							
Relugolix	20	5 (25.0)	15 (75.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	1 (16.7)	5 (83.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITT.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.2325							
North and South America							
Relugolix	253	72 (28.5)	181 (71.5)	NE [NE;NE]	NE	1.220 [0.797;1.868]	0.3596
Leuprolide	126	30 (23.8)	96 (76.2)	NE [NE;NE]			
Europe							
Relugolix	271	52 (19.2)	219 (80.8)	NE [NE;NE]	NE	0.957 [0.597;1.532]	0.8543
Leuprolide	135	26 (19.3)	109 (80.7)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	193	39 (20.2)	154 (79.8)	NE [NE;NE]	NE	0.690 [0.420;1.134]	0.1430
Leuprolide	96	26 (27.1)	70 (72.9)	NE [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITT.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.2953							
< 250 ng/dL							
Relugolix	72	16 (22.2)	56 (77.8)	NE [NE;NE]	NE	1.496 [0.585;3.824]	0.3999
Leuprolide	39	6 (15.4)	33 (84.6)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	635	144 (22.7)	491 (77.3)	NE [NE;NE]	NE	0.887 [0.671;1.173]	0.4007
Leuprolide	307	75 (24.4)	232 (75.6)	NE [NE;NE]			
Missing							
Relugolix	10	3 (30.0)	7 (70.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	1 (9.1)	10 (90.9)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2NAUS15.KM.MITT.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.3452							
< 20 ng/mL							
Relugolix	428	93 (21.7)	335 (78.3)	NE [NE;NE]	NE	1.075 [0.748;1.543]	0.6968
Leuprolide	213	43 (20.2)	170 (79.8)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	289	70 (24.2)	219 (75.8)	NE [NE;NE]	NE	0.831 [0.562;1.230]	0.3550
Leuprolide	144	39 (27.1)	105 (72.9)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.6561							
Asian							
Relugolix	157	28 (17.8)	129 (82.2)	NE [NE;NE]	NE	0.671 [0.384;1.172]	0.1608
Leuprolide	88	22 (25.0)	66 (75.0)	NE [344.0;NE]			
Black or African American							
Relugolix	34	16 (47.1)	18 (52.9)	337.0 [171.0;NE]	23.0	1.021 [0.420;2.484]	0.9628
Leuprolide	16	7 (43.8)	9 (56.3)	314.0 [94.0;NE]			
White							
Relugolix	492	107 (21.7)	385 (78.3)	NE [NE;NE]	NE	1.013 [0.722;1.420]	0.9424
Leuprolide	234	49 (20.9)	185 (79.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.6561							
Others							
Relugolix	21	6 (28.6)	15 (71.4)	NE [253.0;NE]	NE	1.019 [0.255;4.076]	0.9784
Leuprolide	11	3 (27.3)	8 (72.7)	NE [29.0;NE]			
Not Reported							
Relugolix	13	6 (46.2)	7 (53.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	1 (12.5)	7 (87.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2NAUS15.KM.MITT.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.6812							
<= 75 years old							
Relugolix	509	124 (24.4)	385 (75.6)	NE [NE;NE]	NE	0.936 [0.693;1.263]	0.6636
Leuprolide	254	65 (25.6)	189 (74.4)	NE [NE;NE]			
> 75 years old							
Relugolix	208	39 (18.8)	169 (81.3)	NE [NE;NE]	NE	1.071 [0.606;1.892]	0.8141
Leuprolide	103	17 (16.5)	86 (83.5)	NE [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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5.1.3.2.4 Skala: Atemnot

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2DYSP15.KM.MITT.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.1869							
< 20 ng/mL							
Relugolix	428	148 (34.6)	280 (65.4)	NE [344.0;NE]	NE	0.839 [0.641;1.096]	0.1978
Leuprolide	213	84 (39.4)	129 (60.6)	344.0 [340.0;NE]			
>= 20 ng/mL							
Relugolix	289	91 (31.5)	198 (68.5)	NE [350.0;NE]	NE	0.632 [0.457;0.873]	0.0054
Leuprolide	144	62 (43.1)	82 (56.9)	340.0 [337.0;343.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITT.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.2271							
<= 75 years old							
Relugolix	509	176 (34.6)	333 (65.4)	NE [344.0;NE]	NE	0.811 [0.636;1.035]	0.0917
Leuprolide	254	103 (40.6)	151 (59.4)	343.0 [339.0;NE]			
> 75 years old							
Relugolix	208	63 (30.3)	145 (69.7)	350.0 [343.0;NE]	8.0	0.612 [0.415;0.902]	0.0130
Leuprolide	103	43 (41.7)	60 (58.3)	342.0 [337.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITT.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.3312							
Not Hispanic or Latino							
Relugolix	640	219 (34.2)	421 (65.8)	350.0 [350.0;NE]	7.0	0.757 [0.609;0.942]	0.0127
Leuprolide	312	128 (41.0)	184 (59.0)	343.0 [339.0;NE]			
Hispanic or Latino							
Relugolix	64	12 (18.8)	52 (81.3)	NE [NE;NE]	NE	0.506 [0.231;1.109]	0.0887
Leuprolide	37	13 (35.1)	24 (64.9)	NE [337.0;NE]			
Not Reported							
Relugolix	13	8 (61.5)	5 (38.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	5 (62.5)	3 (37.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITT.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.3835							
< 250 ng/dL							
Relugolix	72	24 (33.3)	48 (66.7)	NE [342.0;NE]	NE	0.577 [0.319;1.045]	0.0698
Leuprolide	39	20 (51.3)	19 (48.7)	337.0 [169.0;NE]			
>= 250 ng/dL							
Relugolix	635	210 (33.1)	425 (66.9)	350.0 [350.0;NE]	7.0	0.766 [0.612;0.957]	0.0190
Leuprolide	307	122 (39.7)	185 (60.3)	343.0 [340.0;NE]			
Missing							
Relugolix	10	5 (50.0)	5 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	4 (36.4)	7 (63.6)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITT.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.4297							
Asia (Excl. Korea)							
Relugolix	104	35 (33.7)	69 (66.3)	NE [340.0;NE]	NE	0.619 [0.370;1.035]	0.0673
Leuprolide	53	25 (47.2)	28 (52.8)	339.0 [253.0;NE]			
Rest of World							
Relugolix	613	204 (33.3)	409 (66.7)	350.0 [344.0;NE]	7.0	0.776 [0.620;0.972]	0.0272
Leuprolide	304	121 (39.8)	183 (60.2)	343.0 [340.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITT.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.5023							
North and South America							
Relugolix	253	75 (29.6)	178 (70.4)	NE [342.0;NE]	NE	0.669 [0.470;0.954]	0.0262
Leuprolide	126	52 (41.3)	74 (58.7)	340.0 [337.0;NE]			
Europe							
Relugolix	271	99 (36.5)	172 (63.5)	350.0 [344.0;NE]	6.0	0.874 [0.626;1.220]	0.4283
Leuprolide	135	53 (39.3)	82 (60.7)	344.0 [338.0;NE]			
Asia and Rest of World							
Relugolix	193	65 (33.7)	128 (66.3)	NE [343.0;NE]	NE	0.690 [0.467;1.020]	0.0629
Leuprolide	96	41 (42.7)	55 (57.3)	343.0 [336.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITT.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.8399							
< 8							
Relugolix	356	109 (30.6)	247 (69.4)	NE [344.0;NE]	NE	0.731 [0.543;0.983]	0.0383
Leuprolide	185	73 (39.5)	112 (60.5)	344.0 [339.0;NE]			
>= 8							
Relugolix	341	122 (35.8)	219 (64.2)	350.0 [344.0;NE]	10.0	0.763 [0.569;1.024]	0.0718
Leuprolide	166	70 (42.2)	96 (57.8)	340.0 [337.0;NE]			
Missing							
Relugolix	20	8 (40.0)	12 (60.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	3 (50.0)	3 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.8855							
Asian							
Relugolix	157	54 (34.4)	103 (65.6)	NE [NE;NE]	NE	0.667 [0.442;1.008]	0.0544
Leuprolide	88	39 (44.3)	49 (55.7)	339.0 [260.0;NE]			
Black or African American							
Relugolix	34	11 (32.4)	23 (67.6)	NE [336.0;NE]	NE	0.995 [0.317;3.125]	0.9928
Leuprolide	16	4 (25.0)	12 (75.0)	NE [85.0;NE]			
White							
Relugolix	492	163 (33.1)	329 (66.9)	350.0 [344.0;NE]	7.0	0.749 [0.582;0.963]	0.0242
Leuprolide	234	97 (41.5)	137 (58.5)	343.0 [339.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DYSP15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.8855							
Others							
Relugolix	21	5 (23.8)	16 (76.2)	344.0 [NE;NE]	-7.0	0.975 [0.232;4.093]	0.9720
Leuprolide	11	3 (27.3)	8 (72.7)	351.0 [250.0;NE]			
Not Reported							
Relugolix	13	6 (46.2)	7 (53.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	3 (37.5)	5 (62.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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5.1.3.2.6 Skala: Appetitlosigkeit

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Table QS.T2APPT15.KM.MITT.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Gleason Score at Study Entry, Interaction p-value: 0.1312							
< 8							
Relugolix	356	83 (23.3)	273 (76.7)	NE [345.0;NE]	NE	1.372 [0.917;2.054]	0.1242
Leuprolide	185	33 (17.8)	152 (82.2)	NE [NE;NE]			
>= 8							
Relugolix	341	81 (23.8)	260 (76.2)	NE [NE;NE]	NE	0.897 [0.616;1.307]	0.5728
Leuprolide	166	41 (24.7)	125 (75.3)	NE [343.0;NE]			
Missing							
Relugolix	20	6 (30.0)	14 (70.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	3 (50.0)	3 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2APPT15.KM.MITT.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.3726							
<= 75 years old							
Relugolix	509	116 (22.8)	393 (77.2)	NE [345.0;NE]	NE	1.181 [0.845;1.649]	0.3302
Leuprolide	254	49 (19.3)	205 (80.7)	NE [NE;NE]			
> 75 years old							
Relugolix	208	54 (26.0)	154 (74.0)	NE [NE;NE]	NE	0.913 [0.578;1.441]	0.6949
Leuprolide	103	28 (27.2)	75 (72.8)	NE [342.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2APPT15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.3950							
Asian							
Relugolix	157	35 (22.3)	122 (77.7)	NE [NE;NE]	NE	1.071 [0.606;1.890]	0.8142
Leuprolide	88	18 (20.5)	70 (79.5)	NE [344.0;NE]			
Black or African American							
Relugolix	34	9 (26.5)	25 (73.5)	NE [NE;NE]	NE	0.541 [0.192;1.520]	0.2437
Leuprolide	16	6 (37.5)	10 (62.5)	341.0 [166.0;NE]			
White							
Relugolix	492	118 (24.0)	374 (76.0)	NE [NE;NE]	NE	1.144 [0.820;1.596]	0.4293
Leuprolide	234	49 (20.9)	185 (79.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2APPT15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.3950							
Others							
Relugolix	21	4 (19.0)	17 (81.0)	344.0 [NE;NE]	6.0	0.492 [0.123;1.969]	0.3162
Leuprolide	11	4 (36.4)	7 (63.6)	338.0 [169.0;NE]			
Not Reported							
Relugolix	13	4 (30.8)	9 (69.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2APPT15.KM.MITT.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.4124							
Asia (Excl. Korea)							
Relugolix	104	25 (24.0)	79 (76.0)	NE [344.0;NE]	NE	1.455 [0.679;3.117]	0.3350
Leuprolide	53	9 (17.0)	44 (83.0)	NE [344.0;NE]			
Rest of World							
Relugolix	613	145 (23.7)	468 (76.3)	NE [NE;NE]	NE	1.035 [0.776;1.380]	0.8164
Leuprolide	304	68 (22.4)	236 (77.6)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2APPT15.KM.MITT.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.4213							
< 250 ng/dL							
Relugolix	72	22 (30.6)	50 (69.4)	NE [NE;NE]	NE	1.539 [0.685;3.457]	0.2966
Leuprolide	39	8 (20.5)	31 (79.5)	NE [339.0;NE]			
>= 250 ng/dL							
Relugolix	635	145 (22.8)	490 (77.2)	NE [NE;NE]	NE	1.081 [0.805;1.450]	0.6051
Leuprolide	307	64 (20.8)	243 (79.2)	NE [NE;NE]			
Missing							
Relugolix	10	3 (30.0)	7 (70.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	5 (45.5)	6 (54.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2APPT15.KM.MITT.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.6109							
< 20 ng/mL							
Relugolix	428	99 (23.1)	329 (76.9)	NE [345.0;NE]	NE	1.150 [0.804;1.646]	0.4431
Leuprolide	213	43 (20.2)	170 (79.8)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	289	71 (24.6)	218 (75.4)	NE [NE;NE]	NE	0.999 [0.664;1.504]	0.9963
Leuprolide	144	34 (23.6)	110 (76.4)	NE [343.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2APPT15.KM.MITT.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.6121							
Not Hispanic or Latino							
Relugolix	640	147 (23.0)	493 (77.0)	NE [NE;NE]	NE	1.042 [0.781;1.392]	0.7781
Leuprolide	312	67 (21.5)	245 (78.5)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	19 (29.7)	45 (70.3)	NE [NE;NE]	NE	1.297 [0.587;2.867]	0.5206
Leuprolide	37	9 (24.3)	28 (75.7)	NE [NE;NE]			
Not Reported							
Relugolix	13	4 (30.8)	9 (69.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	1 (12.5)	7 (87.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2APPT15.KM.MITT.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.9831							
North and South America							
Relugolix	253	67 (26.5)	186 (73.5)	NE [345.0;NE]	NE	1.069 [0.702;1.630]	0.7552
Leuprolide	126	32 (25.4)	94 (74.6)	NE [341.0;NE]			
Europe							
Relugolix	271	59 (21.8)	212 (78.2)	NE [NE;NE]	NE	1.077 [0.679;1.708]	0.7540
Leuprolide	135	26 (19.3)	109 (80.7)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	193	44 (22.8)	149 (77.2)	NE [NE;NE]	NE	1.137 [0.664;1.947]	0.6402
Leuprolide	96	19 (19.8)	77 (80.2)	NE [343.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITT.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.2184							
North and South America							
Relugolix	253	130 (51.4)	123 (48.6)	253.0 [171.0;339.0]	1.0	0.933 [0.698;1.246]	0.6382
Leuprolide	126	71 (56.3)	55 (43.7)	252.0 [169.0;338.0]			
Europe							
Relugolix	271	142 (52.4)	129 (47.6)	260.0 [252.0;NE]	-81.0	1.281 [0.946;1.736]	0.1098
Leuprolide	135	59 (43.7)	76 (56.3)	341.0 [254.0;NE]			
Asia and Rest of World							
Relugolix	193	82 (42.5)	111 (57.5)	344.0 [337.0;NE]	5.0	0.892 [0.622;1.280]	0.5351
Leuprolide	96	46 (47.9)	50 (52.1)	339.0 [253.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITT.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.2354							
<= 75 years old							
Relugolix	509	254 (49.9)	255 (50.1)	337.0 [253.0;341.0]	-1.0	1.112 [0.896;1.381]	0.3358
Leuprolide	254	121 (47.6)	133 (52.4)	338.0 [256.0;NE]			
> 75 years old							
Relugolix	208	100 (48.1)	108 (51.9)	337.0 [253.0;NE]	83.0	0.876 [0.630;1.218]	0.4312
Leuprolide	103	55 (53.4)	48 (46.6)	254.0 [173.0;343.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITT.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.2608							
< 250 ng/dL							
Relugolix	72	43 (59.7)	29 (40.3)	171.0 [89.0;337.0]	-167.0	1.375 [0.802;2.360]	0.2473
Leuprolide	39	19 (48.7)	20 (51.3)	338.0 [169.0;NE]			
>= 250 ng/dL							
Relugolix	635	303 (47.7)	332 (52.3)	338.0 [257.0;NE]	1.0	0.989 [0.814;1.202]	0.9149
Leuprolide	307	152 (49.5)	155 (50.5)	337.0 [253.0;343.0]			
Missing							
Relugolix	10	8 (80.0)	2 (20.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	5 (45.5)	6 (54.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITT.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.4258							
Asia (Excl. Korea)							
Relugolix	104	47 (45.2)	57 (54.8)	344.0 [176.0;NE]	NE	1.256 [0.751;2.102]	0.3851
Leuprolide	53	21 (39.6)	32 (60.4)	NE [337.0;NE]			
Rest of World							
Relugolix	613	307 (50.1)	306 (49.9)	330.0 [253.0;340.0]	63.0	1.005 [0.828;1.219]	0.9628
Leuprolide	304	155 (51.0)	149 (49.0)	267.0 [252.0;341.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITT.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.5157							
< 8							
Relugolix	356	178 (50.0)	178 (50.0)	330.0 [176.0;344.0]	-9.0	1.093 [0.848;1.408]	0.4929
Leuprolide	185	90 (48.6)	95 (51.4)	339.0 [252.0;344.0]			
>= 8							
Relugolix	341	164 (48.1)	177 (51.9)	341.0 [254.0;NE]	4.0	0.968 [0.743;1.260]	0.8082
Leuprolide	166	83 (50.0)	83 (50.0)	337.0 [251.0;NE]			
Missing							
Relugolix	20	12 (60.0)	8 (40.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	3 (50.0)	3 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.6870							
Asian							
Relugolix	157	64 (40.8)	93 (59.2)	NE [341.0;NE]	NE	0.880 [0.594;1.302]	0.5213
Leuprolide	88	41 (46.6)	47 (53.4)	339.0 [256.0;NE]			
Black or African American							
Relugolix	34	21 (61.8)	13 (38.2)	176.0 [90.0;NE]	-77.0	1.170 [0.518;2.641]	0.7060
Leuprolide	16	8 (50.0)	8 (50.0)	253.0 [34.0;NE]			
White							
Relugolix	492	254 (51.6)	238 (48.4)	256.0 [176.0;338.0]	-81.0	1.091 [0.876;1.358]	0.4366
Leuprolide	234	117 (50.0)	117 (50.0)	337.0 [252.0;343.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.6870							
Others							
Relugolix	21	9 (42.9)	12 (57.1)	NE [171.0;NE]	NE	0.709 [0.252;1.993]	0.5147
Leuprolide	11	6 (54.5)	5 (45.5)	338.0 [85.0;NE]			
Not Reported							
Relugolix	13	6 (46.2)	7 (53.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITT.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.7819							
< 20 ng/mL							
Relugolix	428	222 (51.9)	206 (48.1)	256.0 [176.0;338.0]	-11.0	1.059 [0.842;1.332]	0.6266
Leuprolide	213	109 (51.2)	104 (48.8)	267.0 [176.0;NE]			
>= 20 ng/mL							
Relugolix	289	132 (45.7)	157 (54.3)	341.0 [256.0;NE]	2.0	1.004 [0.748;1.348]	0.9775
Leuprolide	144	67 (46.5)	77 (53.5)	339.0 [255.0;344.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INSO15.KM.MITT.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.8623							
Not Hispanic or Latino							
Relugolix	640	321 (50.2)	319 (49.8)	336.0 [253.0;341.0]	-2.0	1.057 [0.872;1.282]	0.5727
Leuprolide	312	153 (49.0)	159 (51.0)	338.0 [254.0;341.0]			
Hispanic or Latino							
Relugolix	64	28 (43.8)	36 (56.3)	339.0 [176.0;NE]	NE	0.999 [0.547;1.826]	0.9985
Leuprolide	37	17 (45.9)	20 (54.1)	NE [173.0;NE]			
Not Reported							
Relugolix	13	5 (38.5)	8 (61.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	6 (75.0)	2 (25.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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5.1.3.2.8 Skala: Diarrhoe

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Table QS.T2DIAR15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.3478							
Asian							
Relugolix	157	43 (27.4)	114 (72.6)	NE [NE;NE]	NE	1.167 [0.692;1.966]	0.5627
Leuprolide	88	21 (23.9)	67 (76.1)	NE [344.0;NE]			
Black or African American							
Relugolix	34	11 (32.4)	23 (67.6)	NE [252.0;NE]	NE	0.479 [0.192;1.191]	0.1132
Leuprolide	16	8 (50.0)	8 (50.0)	274.0 [36.0;NE]			
White							
Relugolix	492	140 (28.5)	352 (71.5)	NE [NE;NE]	NE	1.115 [0.825;1.506]	0.4781
Leuprolide	234	61 (26.1)	173 (73.9)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.3478							
Others							
Relugolix	21	9 (42.9)	12 (57.1)	NE [85.0;NE]	NE	1.330 [0.409;4.319]	0.6353
Leuprolide	11	4 (36.4)	7 (63.6)	339.0 [167.0;NE]			
Not Reported							
Relugolix	13	4 (30.8)	9 (69.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	1 (12.5)	7 (87.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITT.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.3496							
< 8							
Relugolix	356	90 (25.3)	266 (74.7)	NE [NE;NE]	NE	1.254 [0.864;1.819]	0.2344
Leuprolide	185	40 (21.6)	145 (78.4)	NE [NE;NE]			
>= 8							
Relugolix	341	112 (32.8)	229 (67.2)	NE [NE;NE]	NE	0.990 [0.714;1.372]	0.9496
Leuprolide	166	53 (31.9)	113 (68.1)	NE [344.0;NE]			
Missing							
Relugolix	20	5 (25.0)	15 (75.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	2 (33.3)	4 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITT.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.3512							
<= 75 years old							
Relugolix	509	156 (30.6)	353 (69.4)	NE [NE;NE]	NE	1.179 [0.887;1.568]	0.2570
Leuprolide	254	68 (26.8)	186 (73.2)	NE [NE;NE]			
> 75 years old							
Relugolix	208	51 (24.5)	157 (75.5)	NE [NE;NE]	NE	0.909 [0.570;1.450]	0.6890
Leuprolide	103	27 (26.2)	76 (73.8)	NE [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITT.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.3836							
< 20 ng/mL							
Relugolix	428	120 (28.0)	308 (72.0)	NE [NE;NE]	NE	1.207 [0.869;1.674]	0.2613
Leuprolide	213	51 (23.9)	162 (76.1)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	289	87 (30.1)	202 (69.9)	NE [NE;NE]	NE	0.971 [0.676;1.395]	0.8734
Leuprolide	144	44 (30.6)	100 (69.4)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITT.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.4373							
North and South America							
Relugolix	253	88 (34.8)	165 (65.2)	NE [NE;NE]	NE	0.946 [0.664;1.348]	0.7571
Leuprolide	126	47 (37.3)	79 (62.7)	NE [339.0;NE]			
Europe							
Relugolix	271	68 (25.1)	203 (74.9)	NE [NE;NE]	NE	1.383 [0.874;2.187]	0.1658
Leuprolide	135	25 (18.5)	110 (81.5)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	193	51 (26.4)	142 (73.6)	NE [NE;NE]	NE	1.101 [0.673;1.802]	0.7012
Leuprolide	96	23 (24.0)	73 (76.0)	NE [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITT.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.5704							
Not Hispanic or Latino							
Relugolix	640	182 (28.4)	458 (71.6)	NE [NE;NE]	NE	1.051 [0.811;1.361]	0.7072
Leuprolide	312	84 (26.9)	228 (73.1)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	20 (31.3)	44 (68.8)	NE [338.0;NE]	NE	1.325 [0.620;2.832]	0.4669
Leuprolide	37	10 (27.0)	27 (73.0)	NE [339.0;NE]			
Not Reported							
Relugolix	13	5 (38.5)	8 (61.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	1 (12.5)	7 (87.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITT.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.6264							
< 250 ng/dL							
Relugolix	72	21 (29.2)	51 (70.8)	NE [NE;NE]	NE	1.323 [0.606;2.888]	0.4826
Leuprolide	39	9 (23.1)	30 (76.9)	NE [341.0;NE]			
>= 250 ng/dL							
Relugolix	635	184 (29.0)	451 (71.0)	NE [NE;NE]	NE	1.078 [0.832;1.397]	0.5687
Leuprolide	307	83 (27.0)	224 (73.0)	NE [NE;NE]			
Missing							
Relugolix	10	2 (20.0)	8 (80.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	3 (27.3)	8 (72.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2DIAR15.KM.MITT.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.8735							
Asia (Excl. Korea)							
Relugolix	104	27 (26.0)	77 (74.0)	NE [344.0;NE]	NE	1.156 [0.586;2.282]	0.6761
Leuprolide	53	12 (22.6)	41 (77.4)	NE [344.0;NE]			
Rest of World							
Relugolix	613	180 (29.4)	433 (70.6)	NE [NE;NE]	NE	1.090 [0.840;1.413]	0.5180
Leuprolide	304	83 (27.3)	221 (72.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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5.1.3.2.9 Skala: Obstipation

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2CONS15.KM.MITT.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.0216							
< 20 ng/mL							
Relugolix	428	156 (36.4)	272 (63.6)	NE [NE;NE]	NE	1.284 [0.960;1.718]	0.0924
Leuprolide	213	64 (30.0)	149 (70.0)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	289	88 (30.4)	201 (69.6)	360.0 [350.0;NE]	NE	0.757 [0.537;1.068]	0.1129
Leuprolide	144	52 (36.1)	92 (63.9)	NE [339.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITT.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.0220							
<= 75 years old							
Relugolix	509	171 (33.6)	338 (66.4)	NE [NE;NE]	NE	1.230 [0.935;1.618]	0.1388
Leuprolide	254	73 (28.7)	181 (71.3)	NE [NE;NE]			
> 75 years old							
Relugolix	208	73 (35.1)	135 (64.9)	350.0 [350.0;NE]	NE	0.713 [0.488;1.041]	0.0794
Leuprolide	103	43 (41.7)	60 (58.3)	NE [246.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITT.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.1418							
North and South America							
Relugolix	253	94 (37.2)	159 (62.8)	360.0 [342.0;NE]	NE	1.096 [0.766;1.569]	0.6158
Leuprolide	126	44 (34.9)	82 (65.1)	NE [339.0;NE]			
Europe							
Relugolix	271	74 (27.3)	197 (72.7)	NE [350.0;NE]	NE	0.786 [0.540;1.145]	0.2104
Leuprolide	135	43 (31.9)	92 (68.1)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	193	76 (39.4)	117 (60.6)	NE [337.0;NE]	NE	1.382 [0.901;2.121]	0.1380
Leuprolide	96	29 (30.2)	67 (69.8)	NE [339.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITT.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.3739							
Asia (Excl. Korea)							
Relugolix	104	40 (38.5)	64 (61.5)	NE [337.0;NE]	NE	1.323 [0.741;2.363]	0.3441
Leuprolide	53	16 (30.2)	37 (69.8)	NE [339.0;NE]			
Rest of World							
Relugolix	613	204 (33.3)	409 (66.7)	360.0 [350.0;NE]	NE	0.995 [0.783;1.265]	0.9693
Leuprolide	304	100 (32.9)	204 (67.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITT.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.4160							
< 250 ng/dL							
Relugolix	72	21 (29.2)	51 (70.8)	NE [342.0;NE]	NE	0.793 [0.397;1.584]	0.5110
Leuprolide	39	13 (33.3)	26 (66.7)	NE [339.0;NE]			
>= 250 ng/dL							
Relugolix	635	219 (34.5)	416 (65.5)	360.0 [350.0;NE]	NE	1.074 [0.847;1.362]	0.5555
Leuprolide	307	99 (32.2)	208 (67.8)	NE [NE;NE]			
Missing							
Relugolix	10	4 (40.0)	6 (60.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	4 (36.4)	7 (63.6)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITT.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.4982							
Not Hispanic or Latino							
Relugolix	640	221 (34.5)	419 (65.5)	360.0 [350.0;NE]	NE	1.075 [0.847;1.363]	0.5525
Leuprolide	312	99 (31.7)	213 (68.3)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	17 (26.6)	47 (73.4)	NE [338.0;NE]	NE	0.822 [0.392;1.721]	0.6026
Leuprolide	37	12 (32.4)	25 (67.6)	340.0 [340.0;NE]			
Not Reported							
Relugolix	13	6 (46.2)	7 (53.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	5 (62.5)	3 (37.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.5877							
Asian							
Relugolix	157	64 (40.8)	93 (59.2)	NE [337.0;NE]	NE	1.359 [0.872;2.119]	0.1756
Leuprolide	88	28 (31.8)	60 (68.2)	NE [339.0;NE]			
Black or African American							
Relugolix	34	14 (41.2)	20 (58.8)	NE [169.0;NE]	NE	1.272 [0.458;3.533]	0.6440
Leuprolide	16	5 (31.3)	11 (68.8)	NE [162.0;NE]			
White							
Relugolix	492	159 (32.3)	333 (67.7)	360.0 [350.0;NE]	NE	0.956 [0.728;1.256]	0.7480
Leuprolide	234	77 (32.9)	157 (67.1)	NE [340.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.5877							
Others							
Relugolix	21	5 (23.8)	16 (76.2)	NE [NE;NE]	NE	1.288 [0.250;6.639]	0.7622
Leuprolide	11	2 (18.2)	9 (81.8)	NE [179.0;NE]			
Not Reported							
Relugolix	13	2 (15.4)	11 (84.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2CONS15.KM.MITT.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.7443							
< 8							
Relugolix	356	113 (31.7)	243 (68.3)	NE [NE;NE]	NE	1.066 [0.776;1.467]	0.6921
Leuprolide	185	57 (30.8)	128 (69.2)	NE [340.0;NE]			
>= 8							
Relugolix	341	122 (35.8)	219 (64.2)	350.0 [350.0;NE]	NE	0.990 [0.722;1.357]	0.9495
Leuprolide	166	57 (34.3)	109 (65.7)	NE [NE;NE]			
Missing							
Relugolix	20	9 (45.0)	11 (55.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	2 (33.3)	4 (66.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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5.1.3.3 Symptomatik (European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire PR25)

5.1.3.3.1 Skala: Miktionsbeschwerden

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2URIN15.KM.MITT.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.1094							
Asia (Excl. Korea)							
Relugolix	104	34 (32.7)	70 (67.3)	NE [344.0;NE]	NE	2.323 [1.075;5.018]	0.0320
Leuprolide	53	8 (15.1)	45 (84.9)	NE [NE;NE]			
Rest of World							
Relugolix	613	195 (31.8)	418 (68.2)	NE [NE;NE]	NE	1.196 [0.924;1.549]	0.1731
Leuprolide	304	82 (27.0)	222 (73.0)	345.0 [345.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITT.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.1900							
North and South America							
Relugolix	253	93 (36.8)	160 (63.2)	NE [339.0;NE]	NE	1.546 [1.035;2.311]	0.0335
Leuprolide	126	32 (25.4)	94 (74.6)	NE [NE;NE]			
Europe							
Relugolix	271	81 (29.9)	190 (70.1)	NE [NE;NE]	NE	0.983 [0.673;1.436]	0.9302
Leuprolide	135	40 (29.6)	95 (70.4)	345.0 [344.0;NE]			
Asia and Rest of World							
Relugolix	193	55 (28.5)	138 (71.5)	NE [NE;NE]	NE	1.582 [0.929;2.694]	0.0910
Leuprolide	96	18 (18.8)	78 (81.3)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITT.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Gleason Score at Study Entry, Interaction p-value: 0.2183							
< 8							
Relugolix	356	127 (35.7)	229 (64.3)	NE [344.0;NE]	NE	1.533 [1.097;2.142]	0.0124
Leuprolide	185	47 (25.4)	138 (74.6)	345.0 [345.0;NE]			
>= 8							
Relugolix	341	95 (27.9)	246 (72.1)	NE [NE;NE]	NE	1.120 [0.774;1.622]	0.5466
Leuprolide	166	40 (24.1)	126 (75.9)	NE [NE;NE]			
Missing							
Relugolix	20	7 (35.0)	13 (65.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	3 (50.0)	3 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITT.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.2284							
Not Hispanic or Latino							
Relugolix	640	202 (31.6)	438 (68.4)	NE [NE;NE]	NE	1.286 [0.990;1.670]	0.0594
Leuprolide	312	78 (25.0)	234 (75.0)	345.0 [345.0;NE]			
Hispanic or Latino							
Relugolix	64	24 (37.5)	40 (62.5)	NE [330.0;NE]	NE	2.210 [0.952;5.131]	0.0649
Leuprolide	37	7 (18.9)	30 (81.1)	NE [NE;NE]			
Not Reported							
Relugolix	13	3 (23.1)	10 (76.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	5 (62.5)	3 (37.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITT.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.2326							
< 20 ng/mL							
Relugolix	428	144 (33.6)	284 (66.4)	NE [NE;NE]	NE	1.463 [1.065;2.009]	0.0187
Leuprolide	213	52 (24.4)	161 (75.6)	345.0 [345.0;NE]			
>= 20 ng/mL							
Relugolix	289	85 (29.4)	204 (70.6)	NE [NE;NE]	NE	1.081 [0.737;1.585]	0.6897
Leuprolide	144	38 (26.4)	106 (73.6)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITT.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.3291							
<= 75 years old							
Relugolix	509	157 (30.8)	352 (69.2)	NE [NE;NE]	NE	1.200 [0.902;1.598]	0.2114
Leuprolide	254	67 (26.4)	187 (73.6)	345.0 [NE;NE]			
> 75 years old							
Relugolix	208	72 (34.6)	136 (65.4)	NE [NE;NE]	NE	1.578 [0.987;2.524]	0.0569
Leuprolide	103	23 (22.3)	80 (77.7)	NE [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.6849							
Asian							
Relugolix	157	51 (32.5)	106 (67.5)	NE [344.0;NE]	NE	1.677 [0.980;2.871]	0.0592
Leuprolide	88	18 (20.5)	70 (79.5)	NE [NE;NE]			
Black or African American							
Relugolix	34	16 (47.1)	18 (52.9)	NE [85.0;NE]	NE	0.973 [0.400;2.365]	0.9519
Leuprolide	16	7 (43.8)	9 (56.3)	NE [32.0;NE]			
White							
Relugolix	492	150 (30.5)	342 (69.5)	NE [NE;NE]	NE	1.208 [0.896;1.630]	0.2157
Leuprolide	234	60 (25.6)	174 (74.4)	345.0 [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.6849							
Others							
Relugolix	21	7 (33.3)	14 (66.7)	NE [176.0;NE]	NE	1.196 [0.309;4.626]	0.7954
Leuprolide	11	3 (27.3)	8 (72.7)	NE [87.0;NE]			
Not Reported							
Relugolix	13	5 (38.5)	8 (61.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	2 (25.0)	6 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2URIN15.KM.MITT.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.8988							
< 250 ng/dL							
Relugolix	72	21 (29.2)	51 (70.8)	NE [NE;NE]	NE	1.228 [0.562;2.681]	0.6060
Leuprolide	39	9 (23.1)	30 (76.9)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	635	203 (32.0)	432 (68.0)	NE [NE;NE]	NE	1.296 [0.998;1.682]	0.0520
Leuprolide	307	78 (25.4)	229 (74.6)	345.0 [345.0;NE]			
Missing							
Relugolix	10	5 (50.0)	5 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	3 (27.3)	8 (72.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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5.1.3.3.2 Skala: Darmfunktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2BOWE15.KM.MITT.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.0758							
< 20 ng/mL							
Relugolix	428	91 (21.3)	337 (78.7)	NE [NE;NE]	NE	1.385 [0.934;2.053]	0.1054
Leuprolide	213	34 (16.0)	179 (84.0)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	289	54 (18.7)	235 (81.3)	NE [NE;NE]	NE	0.812 [0.525;1.258]	0.3517
Leuprolide	144	32 (22.2)	112 (77.8)	NE [342.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2BOWE15.KM.MITT.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.1544							
Not Hispanic or Latino							
Relugolix	640	126 (19.7)	514 (80.3)	NE [NE;NE]	NE	1.059 [0.776;1.445]	0.7182
Leuprolide	312	58 (18.6)	254 (81.4)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	15 (23.4)	49 (76.6)	NE [339.0;NE]	NE	2.435 [0.808;7.337]	0.1138
Leuprolide	37	4 (10.8)	33 (89.2)	NE [NE;NE]			
Not Reported							
Relugolix	13	4 (30.8)	9 (69.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2BOWE15.KM.MITT.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.2101							
< 250 ng/dL							
Relugolix	72	9 (12.5)	63 (87.5)	NE [NE;NE]	NE	0.623 [0.232;1.673]	0.3480
Leuprolide	39	7 (17.9)	32 (82.1)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	635	134 (21.1)	501 (78.9)	NE [NE;NE]	NE	1.209 [0.883;1.655]	0.2358
Leuprolide	307	55 (17.9)	252 (82.1)	NE [NE;NE]			
Missing							
Relugolix	10	2 (20.0)	8 (80.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	4 (36.4)	7 (63.6)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2BOWE15.KM.MITT.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.3817							
<= 75 years old							
Relugolix	509	102 (20.0)	407 (80.0)	NE [NE;NE]	NE	1.206 [0.844;1.722]	0.3031
Leuprolide	254	43 (16.9)	211 (83.1)	NE [NE;NE]			
> 75 years old							
Relugolix	208	43 (20.7)	165 (79.3)	NE [NE;NE]	NE	0.915 [0.551;1.518]	0.7301
Leuprolide	103	23 (22.3)	80 (77.7)	NE [342.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2BOWE15.KM.MITT.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.7029							
North and South America							
Relugolix	253	68 (26.9)	185 (73.1)	NE [343.0;NE]	NE	1.272 [0.814;1.986]	0.2909
Leuprolide	126	27 (21.4)	99 (78.6)	NE [NE;NE]			
Europe							
Relugolix	271	44 (16.2)	227 (83.8)	NE [NE;NE]	NE	1.009 [0.605;1.683]	0.9737
Leuprolide	135	22 (16.3)	113 (83.7)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	193	33 (17.1)	160 (82.9)	NE [NE;NE]	NE	0.966 [0.538;1.735]	0.9082
Leuprolide	96	17 (17.7)	79 (82.3)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2BOWE15.KM.MITT.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.8311							
< 8							
Relugolix	356	69 (19.4)	287 (80.6)	NE [NE;NE]	NE	1.071 [0.713;1.609]	0.7408
Leuprolide	185	35 (18.9)	150 (81.1)	NE [NE;NE]			
>= 8							
Relugolix	341	72 (21.1)	269 (78.9)	NE [NE;NE]	NE	1.142 [0.746;1.749]	0.5414
Leuprolide	166	30 (18.1)	136 (81.9)	NE [NE;NE]			
Missing							
Relugolix	20	4 (20.0)	16 (80.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	1 (16.7)	5 (83.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2BOWE15.KM.MITT.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.8548							
Asia (Excl. Korea)							
Relugolix	104	18 (17.3)	86 (82.7)	NE [NE;NE]	NE	1.030 [0.463;2.292]	0.9431
Leuprolide	53	9 (17.0)	44 (83.0)	NE [NE;NE]			
Rest of World							
Relugolix	613	127 (20.7)	486 (79.3)	NE [NE;NE]	NE	1.116 [0.816;1.525]	0.4929
Leuprolide	304	57 (18.8)	247 (81.3)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2BOWE15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.9158							
Asian							
Relugolix	157	31 (19.7)	126 (80.3)	NE [NE;NE]	NE	1.184 [0.639;2.194]	0.5906
Leuprolide	88	15 (17.0)	73 (83.0)	NE [NE;NE]			
Black or African American							
Relugolix	34	14 (41.2)	20 (58.8)	NE [171.0;NE]	NE	0.865 [0.332;2.253]	0.7665
Leuprolide	16	6 (37.5)	10 (62.5)	258.0 [100.0;NE]			
White							
Relugolix	492	94 (19.1)	398 (80.9)	NE [NE;NE]	NE	1.143 [0.789;1.655]	0.4792
Leuprolide	234	40 (17.1)	194 (82.9)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2BOWE15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.9158							
Others							
Relugolix	21	3 (14.3)	18 (85.7)	NE [339.0;NE]	NE	0.748 [0.125;4.477]	0.7505
Leuprolide	11	2 (18.2)	9 (81.8)	NE [337.0;NE]			
Not Reported							
Relugolix	13	3 (23.1)	10 (76.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	3 (37.5)	5 (62.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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5.1.3.3.3 Skala: Nebenwirkungen der Hormontherapie

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2HRMN15.KM.MITT.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: 0.2524							
< 250 ng/dL							
Relugolix	72	39 (54.2)	33 (45.8)	287.0 [171.0;NE]	-55.0	1.379 [0.771;2.469]	0.2787
Leuprolide	39	16 (41.0)	23 (59.0)	342.0 [171.0;NE]			
>= 250 ng/dL							
Relugolix	635	319 (50.2)	316 (49.8)	336.0 [253.0;337.0]	6.0	0.965 [0.799;1.165]	0.7109
Leuprolide	307	163 (53.1)	144 (46.9)	330.0 [253.0;339.0]			
Missing							
Relugolix	10	8 (80.0)	2 (20.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	6 (54.5)	5 (45.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2HRMN15.KM.MITT.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.2654							
Asia (Excl. Korea)							
Relugolix	104	35 (33.7)	69 (66.3)	NE [NE;NE]	NE	0.761 [0.449;1.287]	0.3081
Leuprolide	53	23 (43.4)	30 (56.6)	NE [253.0;NE]			
Rest of World							
Relugolix	613	331 (54.0)	282 (46.0)	255.0 [250.0;336.0]	-68.0	1.045 [0.866;1.261]	0.6472
Leuprolide	304	162 (53.3)	142 (46.7)	323.0 [252.0;339.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2HRMN15.KM.MITT.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.4995							
North and South America							
Relugolix	253	134 (53.0)	119 (47.0)	251.0 [171.0;337.0]	-2.0	0.933 [0.702;1.241]	0.6346
Leuprolide	126	73 (57.9)	53 (42.1)	253.0 [168.0;339.0]			
Europe							
Relugolix	271	157 (57.9)	114 (42.1)	253.0 [176.0;312.0]	-84.0	1.147 [0.865;1.520]	0.3402
Leuprolide	135	70 (51.9)	65 (48.1)	337.0 [179.0;343.0]			
Asia and Rest of World							
Relugolix	193	75 (38.9)	118 (61.1)	344.0 [339.0;NE]	5.0	0.907 [0.622;1.323]	0.6118
Leuprolide	96	42 (43.8)	54 (56.3)	339.0 [335.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2HRMN15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.5514							
Asian							
Relugolix	157	57 (36.3)	100 (63.7)	NE [341.0;NE]	NE	0.790 [0.527;1.184]	0.2535
Leuprolide	88	40 (45.5)	48 (54.5)	339.0 [258.0;NE]			
Black or African American							
Relugolix	34	25 (73.5)	9 (26.5)	92.0 [85.0;176.0]	-166.0	1.346 [0.628;2.886]	0.4443
Leuprolide	16	9 (56.3)	7 (43.8)	258.0 [82.0;NE]			
White							
Relugolix	492	265 (53.9)	227 (46.1)	256.0 [251.0;337.0]	-67.0	1.030 [0.833;1.274]	0.7833
Leuprolide	234	126 (53.8)	108 (46.2)	323.0 [248.0;341.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2HRMN15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.5514							
Others							
Relugolix	21	12 (57.1)	9 (42.9)	172.0 [85.0;NE]	57.0	0.823 [0.324;2.092]	0.6827
Leuprolide	11	7 (63.6)	4 (36.4)	115.0 [83.0;NE]			
Not Reported							
Relugolix	13	7 (53.8)	6 (46.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	3 (37.5)	5 (62.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2HRMN15.KM.MITT.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.5711							
< 8							
Relugolix	356	184 (51.7)	172 (48.3)	260.0 [252.0;337.0]	-70.0	0.983 [0.771;1.253]	0.8879
Leuprolide	185	101 (54.6)	84 (45.4)	330.0 [176.0;339.0]			
>= 8							
Relugolix	341	173 (50.7)	168 (49.3)	337.0 [253.0;342.0]	-2.0	1.091 [0.836;1.423]	0.5234
Leuprolide	166	79 (47.6)	87 (52.4)	339.0 [253.0;NE]			
Missing							
Relugolix	20	9 (45.0)	11 (55.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	5 (83.3)	1 (16.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2HRMN15.KM.MITT.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.6421							
Not Hispanic or Latino							
Relugolix	640	326 (50.9)	314 (49.1)	335.0 [253.0;337.0]	0.0	0.982 [0.815;1.185]	0.8530
Leuprolide	312	165 (52.9)	147 (47.1)	335.0 [253.0;339.0]			
Hispanic or Latino							
Relugolix	64	31 (48.4)	33 (51.6)	337.0 [169.0;NE]	NE	1.141 [0.624;2.087]	0.6678
Leuprolide	37	16 (43.2)	21 (56.8)	NE [87.0;NE]			
Not Reported							
Relugolix	13	9 (69.2)	4 (30.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2HRMN15.KM.MITT.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.6508							
< 20 ng/mL							
Relugolix	428	231 (54.0)	197 (46.0)	255.0 [176.0;336.0]	-75.0	1.043 [0.834;1.303]	0.7126
Leuprolide	213	116 (54.5)	97 (45.5)	330.0 [176.0;341.0]			
>= 20 ng/mL							
Relugolix	289	135 (46.7)	154 (53.3)	337.0 [260.0;NE]	0.0	0.958 [0.717;1.281]	0.7736
Leuprolide	144	69 (47.9)	75 (52.1)	337.0 [253.0;344.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2HRMN15.KM.MITT.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.8144							
<= 75 years old							
Relugolix	509	266 (52.3)	243 (47.7)	258.0 [250.0;337.0]	-77.0	1.023 [0.832;1.258]	0.8262
Leuprolide	254	136 (53.5)	118 (46.5)	335.0 [252.0;339.0]			
> 75 years old							
Relugolix	208	100 (48.1)	108 (51.9)	337.0 [256.0;NE]	0.0	0.976 [0.693;1.373]	0.8874
Leuprolide	103	49 (47.6)	54 (52.4)	337.0 [179.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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5.1.3.3.4 Skala: Inkontinenzhilfe

Table QS.T2INCT15.KM.MITT.S2: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.0647							
North and South America							
Relugolix	253	15 (5.9)	238 (94.1)	NE [NE;NE]	NE	0.425 [0.205;0.882]	0.0216
Leuprolide	126	14 (11.1)	112 (88.9)	338.0 [170.0;NE]			
Europe							
Relugolix	271	29 (10.7)	242 (89.3)	NE [NE;NE]	NE	1.355 [0.704;2.608]	0.3630
Leuprolide	135	13 (9.6)	122 (90.4)	344.0 [344.0;NE]			
Asia and Rest of World							
Relugolix	193	12 (6.2)	181 (93.8)	357.0 [NE;NE]	NE	0.676 [0.262;1.744]	0.4177
Leuprolide	96	7 (7.3)	89 (92.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INCT15.KM.MITT.S7: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.1560							
< 20 ng/mL							
Relugolix	428	39 (9.1)	389 (90.9)	NE [NE;NE]	NE	0.997 [0.576;1.726]	0.9919
Leuprolide	213	19 (8.9)	194 (91.1)	344.0 [344.0;NE]			
>= 20 ng/mL							
Relugolix	289	17 (5.9)	272 (94.1)	357.0 [344.0;NE]	NE	0.523 [0.258;1.057]	0.0710
Leuprolide	144	15 (10.4)	129 (89.6)	NE [337.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INCT15.KM.MITT.S3: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.1835							
Not Hispanic or Latino							
Relugolix	640	50 (7.8)	590 (92.2)	357.0 [NE;NE]	NE	0.723 [0.463;1.129]	0.1537
Leuprolide	312	32 (10.3)	280 (89.7)	NE [344.0;NE]			
Hispanic or Latino							
Relugolix	64	5 (7.8)	59 (92.2)	NE [NE;NE]	NE	3.202 [0.374;27.411]	0.2881
Leuprolide	37	1 (2.7)	36 (97.3)	NE [NE;NE]			
Not Reported							
Relugolix	13	1 (7.7)	12 (92.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	1 (12.5)	7 (87.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2INCT15.KM.MITT.S1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.2477							
<= 75 years old							
Relugolix	509	41 (8.1)	468 (91.9)	NE [NE;NE]	NE	0.954 [0.559;1.628]	0.8623
Leuprolide	254	20 (7.9)	234 (92.1)	NE [NE;NE]			
> 75 years old							
Relugolix	208	15 (7.2)	193 (92.8)	357.0 [344.0;NE]	13.0	0.556 [0.265;1.168]	0.1212
Leuprolide	103	14 (13.6)	89 (86.4)	344.0 [259.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INCT15.KM.MITT.S6: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.4364							
< 250 ng/dL							
Relugolix	72	6 (8.3)	66 (91.7)	NE [260.0;NE]	NE	0.560 [0.188;1.666]	0.2971
Leuprolide	39	7 (17.9)	32 (82.1)	NE [169.0;NE]			
>= 250 ng/dL							
Relugolix	635	49 (7.7)	586 (92.3)	357.0 [NE;NE]	NE	0.900 [0.551;1.470]	0.6737
Leuprolide	307	24 (7.8)	283 (92.2)	NE [344.0;NE]			
Missing							
Relugolix	10	1 (10.0)	9 (90.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	3 (27.3)	8 (72.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2INCT15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.5897							
Asian							
Relugolix	157	9 (5.7)	148 (94.3)	357.0 [NE;NE]	NE	0.502 [0.182;1.386]	0.1835
Leuprolide	88	7 (8.0)	81 (92.0)	NE [NE;NE]			
Black or African American							
Relugolix	34	4 (11.8)	30 (88.2)	NE [252.0;NE]	NE	0.606 [0.111;3.312]	0.5633
Leuprolide	16	2 (12.5)	14 (87.5)	NE [85.0;NE]			
White							
Relugolix	492	40 (8.1)	452 (91.9)	NE [NE;NE]	NE	0.887 [0.535;1.473]	0.6438
Leuprolide	234	24 (10.3)	210 (89.7)	344.0 [338.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2INCT15.KM.MITT.S4: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.5897							
Others							
Relugolix	21	2 (9.5)	19 (90.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			
Not Reported							
Relugolix	13	1 (7.7)	12 (92.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	1 (12.5)	7 (87.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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Table QS.T2INCT15.KM.MITT.S5: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.6252							
< 8							
Relugolix	356	31 (8.7)	325 (91.3)	NE [NE;NE]	NE	0.888 [0.510;1.545]	0.6742
Leuprolide	185	21 (11.4)	164 (88.6)	344.0 [338.0;NE]			
>= 8							
Relugolix	341	24 (7.0)	317 (93.0)	357.0 [NE;NE]	NE	0.713 [0.361;1.410]	0.3312
Leuprolide	166	13 (7.8)	153 (92.2)	NE [NE;NE]			
Missing							
Relugolix	20	1 (5.0)	19 (95.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	0	6 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2INCT15.KM.MITT.S8: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.8901							
Asia (Excl. Korea)							
Relugolix	104	7 (6.7)	97 (93.3)	357.0 [NE;NE]	NE	0.874 [0.218;3.496]	0.8487
Leuprolide	53	3 (5.7)	50 (94.3)	NE [NE;NE]			
Rest of World							
Relugolix	613	49 (8.0)	564 (92.0)	NE [NE;NE]	NE	0.788 [0.503;1.236]	0.3005
Leuprolide	304	31 (10.2)	273 (89.8)	344.0 [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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5.1.4 Morbidität – supportive Endpunkte

5.1.4.1 Testosteronkonzentration

5.1.4.1.1 Initiale Kastration

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Table MOR.T2ITCAST.KM.MITT.S5: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Gleason Score at Study Entry, Interaction p-value: 0.0361							
< 8							
Relugolix	356	353 (99.2)	3 (0.8)	4.0 [NE;NE]	-23.0	10.378 [8.396;12.827]	<.0001
Leuprolide	185	181 (97.8)	4 (2.2)	27.0 [23.0;29.0]			
>= 8							
Relugolix	341	340 (99.7)	1 (0.3)	4.0 [4.0;5.0]	-24.0	7.840 [6.367;9.654]	<.0001
Leuprolide	166	163 (98.2)	3 (1.8)	28.0 [24.0;29.0]			
Missing							
Relugolix	20	20 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	6 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.T2ITCAST.KM.MITT.S2: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region I, Interaction p-value: 0.0411							
North and South America							
Relugolix	253	252 (99.6)	1 (0.4)	4.0 [4.0;5.0]	-23.0	10.295 [8.090;13.101]	<.0001
Leuprolide	126	125 (99.2)	1 (0.8)	27.0 [24.0;29.0]			
Europe							
Relugolix	271	268 (98.9)	3 (1.1)	4.0 [NE;NE]	-23.0	7.454 [5.947;9.343]	<.0001
Leuprolide	135	132 (97.8)	3 (2.2)	27.0 [22.0;29.0]			
Asia and Rest of World							
Relugolix	193	193 (100.0)	0	5.0 [4.0;5.0]	-24.0	10.843 [8.210;14.321]	<.0001
Leuprolide	96	93 (96.9)	3 (3.1)	29.0 [23.0;29.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2ITCAST.KM.MITT.S7: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.0584							
< 20 ng/mL							
Relugolix	428	425 (99.3)	3 (0.7)	4.0 [NE;NE]	-24.0	9.934 [8.186;12.055]	<.0001
Leuprolide	213	210 (98.6)	3 (1.4)	28.0 [26.0;29.0]			
>= 20 ng/mL							
Relugolix	289	288 (99.7)	1 (0.3)	5.0 [4.0;5.0]	-22.0	7.700 [6.152;9.636]	<.0001
Leuprolide	144	140 (97.2)	4 (2.8)	27.0 [22.0;29.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2ITCAST.KM.MITT.S4: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.2676							
Asian							
Relugolix	157	157 (100.0)	0	5.0 [4.0;5.0]	-24.0	10.633 [7.936;14.246]	<.0001
Leuprolide	88	85 (96.6)	3 (3.4)	29.0 [23.0;29.0]			
Black or African American							
Relugolix	34	34 (100.0)	0	5.0 [4.0;5.0]	-20.0	5.849 [3.201;10.689]	<.0001
Leuprolide	16	16 (100.0)	0	25.0 [21.0;29.0]			
White							
Relugolix	492	488 (99.2)	4 (0.8)	4.0 [NE;NE]	-23.0	8.799 [7.318;10.580]	<.0001
Leuprolide	234	230 (98.3)	4 (1.7)	27.0 [23.0;28.0]			
Others							
Relugolix	21	21 (100.0)	0	4.0 [3.0;6.0]	-23.0	11.611 [5.515;24.443]	<.0001
Leuprolide	11	11 (100.0)	0	27.0 [22.0;29.0]			
Not Reported							
Relugolix	13	13 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	8 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

Table MOR.T2ITCAST.KM.MITT.S3: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.4937							
Not Hispanic or Latino							
Relugolix	640	636 (99.4)	4 (0.6)	4.0 [4.0;5.0]	-23.0	8.832 [7.469;10.443]	<.0001
Leuprolide	312	305 (97.8)	7 (2.2)	27.0 [25.0;29.0]			
Hispanic or Latino							
Relugolix	64	64 (100.0)	0	4.0 [4.0;5.0]	-23.0	10.270 [6.705;15.731]	<.0001
Leuprolide	37	37 (100.0)	0	27.0 [22.0;29.0]			
Not Reported							
Relugolix	13	13 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	8 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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Table MOR.T2ITCAST.KM.MITT.S8: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.7887							
Asia (Excl. Korea)							
Relugolix	104	104 (100.0)	0	4.0 [4.0;5.0]	-22.0	8.604 [6.048;12.240]	<.0001
Leuprolide	53	53 (100.0)	0	26.0 [22.0;29.0]			
Rest of World							
Relugolix	613	609 (99.3)	4 (0.7)	4.0 [4.0;5.0]	-24.0	9.042 [7.636;10.708]	<.0001
Leuprolide	304	297 (97.7)	7 (2.3)	28.0 [26.0;29.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.T2ITCAST.KM.MITT.S1: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.7907							
<= 75 years old							
Relugolix	509	506 (99.4)	3 (0.6)	4.0 [4.0;5.0]	-24.0	8.844 [7.380;10.598]	<.0001
Leuprolide	254	251 (98.8)	3 (1.2)	28.0 [26.0;29.0]			
> 75 years old							
Relugolix	208	207 (99.5)	1 (0.5)	4.0 [NE;NE]	-22.0	9.193 [7.093;11.915]	<.0001
Leuprolide	103	99 (96.1)	4 (3.9)	26.0 [22.0;29.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.T2ITCAST.KM.MITT.S6: Time to Initial Castration Rate (Testosterone < 50 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: 0.9124							
< 250 ng/dL							
Relugolix	72	72 (100.0)	0	4.0 [NE;NE]	-17.0	9.376 [6.206;14.167]	<.0001
Leuprolide	39	38 (97.4)	1 (2.6)	21.0 [15.0;22.0]			
>= 250 ng/dL							
Relugolix	635	631 (99.4)	4 (0.6)	4.0 [4.0;5.0]	-25.0	9.157 [7.728;10.850]	<.0001
Leuprolide	307	301 (98.0)	6 (2.0)	29.0 [27.0;29.0]			
Missing							
Relugolix	10	10 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	11 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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5.1.4.1.2 Initiale profunde Kastration

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.T2IPCAST.KM.MITT.S6: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: 0.0177							
< 250 ng/dL							
Relugolix	72	72 (100.0)	0	7.0 [5.0;10.0]	-21.0	6.416 [4.296;9.582]	<.0001
Leuprolide	39	38 (97.4)	1 (2.6)	28.0 [27.0;29.0]			
>= 250 ng/dL							
Relugolix	635	620 (97.6)	15 (2.4)	15.0 [NE;NE]	-14.0	3.856 [3.328;4.468]	<.0001
Leuprolide	307	299 (97.4)	8 (2.6)	29.0 [29.0;30.0]			
Missing							
Relugolix	10	10 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	11 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.T2IPCAST.KM.MITT.S3: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.0548							
Not Hispanic or Latino							
Relugolix	640	626 (97.8)	14 (2.2)	15.0 [NE;NE]	-14.0	4.223 [3.641;4.899]	<.0001
Leuprolide	312	303 (97.1)	9 (2.9)	29.0 [NE;NE]			
Hispanic or Latino							
Relugolix	64	63 (98.4)	1 (1.6)	15.0 [10.0;15.0]	-14.0	2.766 [1.838;4.163]	<.0001
Leuprolide	37	37 (100.0)	0	29.0 [29.0;31.0]			
Not Reported							
Relugolix	13	13 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	8 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.T2IPCAST.KM.MITT.S4: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.0772							
Asian							
Relugolix	157	155 (98.7)	2 (1.3)	15.0 [NE;NE]	-14.0	5.127 [3.886;6.765]	<.0001
Leuprolide	88	84 (95.5)	4 (4.5)	29.0 [29.0;30.0]			
Black or African American							
Relugolix	34	32 (94.1)	2 (5.9)	14.0 [8.0;15.0]	-16.0	2.737 [1.499;4.997]	0.0010
Leuprolide	16	16 (100.0)	0	30.0 [29.0;55.0]			
White							
Relugolix	492	481 (97.8)	11 (2.2)	15.0 [NE;NE]	-14.0	3.860 [3.271;4.556]	<.0001
Leuprolide	234	229 (97.9)	5 (2.1)	29.0 [29.0;30.0]			
Others							
Relugolix	21	21 (100.0)	0	15.0 [8.0;15.0]	-14.0	6.979 [3.310;14.717]	<.0001
Leuprolide	11	11 (100.0)	0	29.0 [27.0;55.0]			
Not Reported							
Relugolix	13	13 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	8 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

Table MOR.T2IPCAST.KM.MITT.S2: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.0978							
North and South America							
Relugolix	253	247 (97.6)	6 (2.4)	15.0 [14.0;15.0]	-14.0	3.869 [3.103;4.825]	<.0001
Leuprolide	126	124 (98.4)	2 (1.6)	29.0 [29.0;30.0]			
Europe							
Relugolix	271	264 (97.4)	7 (2.6)	15.0 [NE;NE]	-14.0	3.624 [2.922;4.495]	<.0001
Leuprolide	135	132 (97.8)	3 (2.2)	29.0 [29.0;30.0]			
Asia and Rest of World							
Relugolix	193	191 (99.0)	2 (1.0)	15.0 [NE;NE]	-14.0	5.138 [3.958;6.671]	<.0001
Leuprolide	96	92 (95.8)	4 (4.2)	29.0 [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.T2IPCAST.KM.MITT.S7: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.2803							
< 20 ng/mL							
Relugolix	428	420 (98.1)	8 (1.9)	15.0 [NE;NE]	-14.0	4.225 [3.550;5.027]	<.0001
Leuprolide	213	209 (98.1)	4 (1.9)	29.0 [29.0;30.0]			
>= 20 ng/mL							
Relugolix	289	282 (97.6)	7 (2.4)	15.0 [NE;NE]	-14.0	3.653 [2.959;4.509]	<.0001
Leuprolide	144	139 (96.5)	5 (3.5)	29.0 [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2IPCAST.KM.MITT.S8: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.2804							
Asia (Excl. Korea)							
Relugolix	104	104 (100.0)	0	15.0 [NE;NE]	-14.0	4.776 [3.388;6.733]	<.0001
Leuprolide	53	52 (98.1)	1 (1.9)	29.0 [NE;NE]			
Rest of World							
Relugolix	613	598 (97.6)	15 (2.4)	15.0 [NE;NE]	-14.0	3.905 [3.369;4.528]	<.0001
Leuprolide	304	296 (97.4)	8 (2.6)	29.0 [29.0;30.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2IPCAST.KM.MITT.S5: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.4513							
< 8							
Relugolix	356	348 (97.8)	8 (2.2)	15.0 [NE;NE]	-14.0	3.765 [3.123;4.539]	<.0001
Leuprolide	185	180 (97.3)	5 (2.7)	29.0 [29.0;30.0]			
>= 8							
Relugolix	341	334 (97.9)	7 (2.1)	15.0 [NE;NE]	-14.0	4.163 [3.422;5.065]	<.0001
Leuprolide	166	162 (97.6)	4 (2.4)	29.0 [NE;NE]			
Missing							
Relugolix	20	20 (100.0)	0	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	6 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.T2IPCAST.KM.MITT.S1: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL), by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.5108							
<= 75 years old							
Relugolix	509	495 (97.2)	14 (2.8)	15.0 [NE;NE]	-14.0	3.899 [3.321;4.577]	<.0001
Leuprolide	254	249 (98.0)	5 (2.0)	29.0 [29.0;30.0]			
> 75 years old							
Relugolix	208	207 (99.5)	1 (0.5)	15.0 [NE;NE]	-14.0	4.291 [3.350;5.497]	<.0001
Leuprolide	103	99 (96.1)	4 (3.9)	29.0 [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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5.1.4.1.3 Anhaltende Kastration

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.T2STCW5.KM.MITT.S7: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.1609							
< 20 ng/mL							
Relugolix	428	12 (2.8)	416 (97.2)	NE [NE;NE]	NE	0.226 [0.114;0.450]	<.0001
Leuprolide	213	25 (11.7)	188 (88.3)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	289	12 (4.2)	277 (95.8)	NE [NE;NE]	NE	0.481 [0.216;1.071]	0.0730
Leuprolide	144	12 (8.3)	132 (91.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2STCW5.KM.MITT.S1: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.2195							
<= 75 years old							
Relugolix	509	20 (3.9)	489 (96.1)	NE [NE;NE]	NE	0.371 [0.207;0.665]	0.0009
Leuprolide	254	26 (10.2)	228 (89.8)	NE [NE;NE]			
> 75 years old							
Relugolix	208	4 (1.9)	204 (98.1)	NE [NE;NE]	NE	0.166 [0.053;0.521]	0.0021
Leuprolide	103	11 (10.7)	92 (89.3)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.T2STCW5.KM.MITT.S6: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: 0.2849							
< 250 ng/dL							
Relugolix	72	1 (1.4)	71 (98.6)	NE [NE;NE]	NE	0.099 [0.012;0.850]	0.0350
Leuprolide	39	5 (12.8)	34 (87.2)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	635	23 (3.6)	612 (96.4)	NE [NE;NE]	NE	0.332 [0.194;0.568]	<.0001
Leuprolide	307	32 (10.4)	275 (89.6)	NE [NE;NE]			
Missing							
Relugolix	10	0	10 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	0	11 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.T2STCW5.KM.MITT.S3: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.3804							
Not Hispanic or Latino							
Relugolix	640	20 (3.1)	620 (96.9)	NE [NE;NE]	NE	0.299 [0.170;0.524]	<.0001
Leuprolide	312	31 (9.9)	281 (90.1)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	4 (6.3)	60 (93.8)	NE [NE;NE]	NE	0.584 [0.146;2.334]	0.4464
Leuprolide	37	4 (10.8)	33 (89.2)	NE [NE;NE]			
Not Reported							
Relugolix	13	0	13 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	2 (25.0)	6 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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Table MOR.T2STCW5.KM.MITT.S5: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Gleason Score at Study Entry, Interaction p-value: 0.4287							
< 8							
Relugolix	356	9 (2.5)	347 (97.5)	NE [NE;NE]	NE	0.251 [0.113;0.559]	0.0007
Leuprolide	185	18 (9.7)	167 (90.3)	NE [NE;NE]			
>= 8							
Relugolix	341	15 (4.4)	326 (95.6)	NE [NE;NE]	NE	0.384 [0.194;0.763]	0.0063
Leuprolide	166	18 (10.8)	148 (89.2)	NE [NE;NE]			
Missing							
Relugolix	20	0	20 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	1 (16.7)	5 (83.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.T2STCW5.KM.MITT.S2: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region I, Interaction p-value: 0.7247							
North and South America							
Relugolix	253	10 (4.0)	243 (96.0)	NE [NE;NE]	NE	0.261 [0.121;0.566]	0.0007
Leuprolide	126	18 (14.3)	108 (85.7)	NE [NE;NE]			
Europe							
Relugolix	271	8 (3.0)	263 (97.0)	NE [NE;NE]	NE	0.426 [0.164;1.105]	0.0793
Leuprolide	135	9 (6.7)	126 (93.3)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	193	6 (3.1)	187 (96.9)	NE [NE;NE]	NE	0.284 [0.103;0.782]	0.0149
Leuprolide	96	10 (10.4)	86 (89.6)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2STCW5.KM.MITT.S4: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.7309							
Asian							
Relugolix	157	4 (2.5)	153 (97.5)	NE [NE;NE]	NE	0.212 [0.066;0.675]	0.0087
Leuprolide	88	10 (11.4)	78 (88.6)	NE [NE;NE]			
Black or African American							
Relugolix	34	2 (5.9)	32 (94.1)	NE [NE;NE]	NE	0.951 [0.086;10.495]	0.9676
Leuprolide	16	1 (6.3)	15 (93.8)	NE [NE;NE]			
White							
Relugolix	492	16 (3.3)	476 (96.7)	NE [NE;NE]	NE	0.316 [0.167;0.598]	0.0004
Leuprolide	234	23 (9.8)	211 (90.2)	NE [NE;NE]			
Others							
Relugolix	21	1 (4.8)	20 (95.2)	NE [NE;NE]	NE	0.239 [0.022;2.640]	0.2431
Leuprolide	11	2 (18.2)	9 (81.8)	NE [225.0;NE]			
Not Reported							
Relugolix	13	1 (7.7)	12 (92.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	1 (12.5)	7 (87.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

Table MOR.T2STCW5.KM.MITT.S8: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.7941							
Asia (Excl. Korea)							
Relugolix	104	2 (1.9)	102 (98.1)	NE [NE;NE]	NE	0.248 [0.045;1.353]	0.1073
Leuprolide	53	4 (7.5)	49 (92.5)	NE [NE;NE]			
Rest of World							
Relugolix	613	22 (3.6)	591 (96.4)	NE [NE;NE]	NE	0.314 [0.183;0.539]	<.0001
Leuprolide	304	33 (10.9)	271 (89.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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5.1.4.1.4 Anhaltende profunde Kastration

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Table MOR.T2SPCW5.KM.MITT.S7: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.0815							
< 20 ng/mL							
Relugolix	428	69 (16.1)	359 (83.9)	NE [NE;NE]	NE	0.380 [0.274;0.528]	<.0001
Leuprolide	213	74 (34.7)	139 (65.3)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	289	51 (17.6)	238 (82.4)	NE [NE;NE]	NE	0.612 [0.401;0.935]	0.0231
Leuprolide	144	37 (25.7)	107 (74.3)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2SPCW5.KM.MITT.S8: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region II, Interaction p-value: 0.2111							
Asia (Excl. Korea)							
Relugolix	104	20 (19.2)	84 (80.8)	NE [NE;NE]	NE	0.689 [0.343;1.385]	0.2957
Leuprolide	53	13 (24.5)	40 (75.5)	NE [NE;NE]			
Rest of World							
Relugolix	613	100 (16.3)	513 (83.7)	NE [NE;NE]	NE	0.426 [0.322;0.563]	<.0001
Leuprolide	304	98 (32.2)	206 (67.8)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2SPCW5.KM.MITT.S4: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.3344							
Asian							
Relugolix	157	26 (16.6)	131 (83.4)	NE [NE;NE]	NE	0.518 [0.297;0.902]	0.0202
Leuprolide	88	24 (27.3)	64 (72.7)	NE [NE;NE]			
Black or African American							
Relugolix	34	10 (29.4)	24 (70.6)	NE [NE;NE]	NE	0.650 [0.236;1.793]	0.4056
Leuprolide	16	6 (37.5)	10 (62.5)	NE [29.0;NE]			
White							
Relugolix	492	80 (16.3)	412 (83.7)	NE [NE;NE]	NE	0.461 [0.335;0.634]	<.0001
Leuprolide	234	71 (30.3)	163 (69.7)	NE [NE;NE]			
Others							
Relugolix	21	2 (9.5)	19 (90.5)	NE [NE;NE]	NE	0.118 [0.024;0.584]	0.0088
Leuprolide	11	6 (54.5)	5 (45.5)	225.0 [29.0;NE]			
Not Reported							
Relugolix	13	2 (15.4)	11 (84.6)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

Table MOR.T2SPCW5.KM.MITT.S1: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.4864							
<= 75 years old							
Relugolix	509	101 (19.8)	408 (80.2)	NE [NE;NE]	NE	0.474 [0.357;0.631]	<.0001
Leuprolide	254	89 (35.0)	165 (65.0)	NE [NE;NE]			
> 75 years old							
Relugolix	208	19 (9.1)	189 (90.9)	NE [NE;NE]	NE	0.373 [0.202;0.689]	0.0016
Leuprolide	103	22 (21.4)	81 (78.6)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2SPCW5.KM.MITT.S6: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: 0.5044							
< 250 ng/dL							
Relugolix	72	8 (11.1)	64 (88.9)	NE [NE;NE]	NE	0.341 [0.137;0.849]	0.0207
Leuprolide	39	11 (28.2)	28 (71.8)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	635	112 (17.6)	523 (82.4)	NE [NE;NE]	NE	0.472 [0.359;0.619]	<.0001
Leuprolide	307	97 (31.6)	210 (68.4)	NE [NE;NE]			
Missing							
Relugolix	10	0	10 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	3 (27.3)	8 (72.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.T2SPCW5.KM.MITT.S5: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Gleason Score at Study Entry, Interaction p-value: 0.5399							
< 8							
Relugolix	356	63 (17.7)	293 (82.3)	NE [NE;NE]	NE	0.488 [0.342;0.697]	<.0001
Leuprolide	185	58 (31.4)	127 (68.6)	NE [NE;NE]			
>= 8							
Relugolix	341	53 (15.5)	288 (84.5)	NE [NE;NE]	NE	0.414 [0.283;0.608]	<.0001
Leuprolide	166	52 (31.3)	114 (68.7)	NE [NE;NE]			
Missing							
Relugolix	20	4 (20.0)	16 (80.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	1 (16.7)	5 (83.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table MOR.T2SPCW5.KM.MITT.S2: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region I, Interaction p-value: 0.7320							
North and South America							
Relugolix	253	40 (15.8)	213 (84.2)	NE [NE;NE]	NE	0.403 [0.262;0.622]	<.0001
Leuprolide	126	42 (33.3)	84 (66.7)	NE [NE;NE]			
Europe							
Relugolix	271	48 (17.7)	223 (82.3)	NE [NE;NE]	NE	0.464 [0.308;0.701]	0.0003
Leuprolide	135	43 (31.9)	92 (68.1)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	193	32 (16.6)	161 (83.4)	NE [NE;NE]	NE	0.528 [0.315;0.886]	0.0157
Leuprolide	96	26 (27.1)	70 (72.9)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table MOR.T2SPCW5.KM.MITT.S3: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.7883							
Not Hispanic or Latino							
Relugolix	640	106 (16.6)	534 (83.4)	NE [NE;NE]	NE	0.472 [0.357;0.624]	<.0001
Leuprolide	312	93 (29.8)	219 (70.2)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	13 (20.3)	51 (79.7)	NE [NE;NE]	NE	0.528 [0.245;1.140]	0.1038
Leuprolide	37	13 (35.1)	24 (64.9)	NE [281.0;NE]			
Not Reported							
Relugolix	13	1 (7.7)	12 (92.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	5 (62.5)	3 (37.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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5.1.4.1.5 Wiederanstieg der Testosteronkonzentration

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.TG50SFU.BIN.MITT.S8: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.0358						
Asia (Excl. Korea)						
Relugolix	104	24 (23.1)	7.650	6.115	0.193	0.0014
Leuprolide	53	2 (3.8)	[1.733;33.762]	[1.502;24.900]	[0.097;0.289]	
Rest of World						
Relugolix	613	260 (42.4)	73.900	42.980	0.414	<.0001
Leuprolide	304	3 (1.0)	[23.436;233.025]	[13.887;133.019]	[0.374;0.455]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_BIN.SAS

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Table MOR.TG50SFU.BIN.MITT.S2: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Geographic Region I, Interaction p-value: 0.1207						
North and South America						
Relugolix	253	108 (42.7)	46.179	26.893	0.411	<.0001
Leuprolide	126	2 (1.6)	[11.173;190.873]	[6.751;107.139]	[0.346;0.476]	
Europe						
Relugolix	271	113 (41.7)	>99	>99	0.417	<.0001
Leuprolide	135	0	[NE;NE]	[NE;NE]	[0.358;0.476]	
Asia and Rest of World						
Relugolix	193	63 (32.6)	15.023	10.446	0.295	<.0001
Leuprolide	96	3 (3.1)	[4.578;49.304]	[3.367;32.402]	[0.220;0.370]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_BIN.SAS

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Table MOR.TG50SFU.BIN.MITT.S4: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Race, Interaction p-value: 0.1912						
Asian						
Relugolix	157	47 (29.9)	12.106	8.781	0.265	<.0001
Leuprolide	88	3 (3.4)	[3.643;40.233]	[2.815;27.391]	[0.184;0.346]	
Black or African American						
Relugolix	34	17 (50.0)	33.000	17.000	0.500	0.0003
Leuprolide	16	0	[1.833;594.052]	[1.086;266.128]	[0.332;0.668]	
White						
Relugolix	492	209 (42.5)	85.668	49.701	0.416	<.0001
Leuprolide	234	2 (0.9)	[21.056;348.547]	[12.456;198.308]	[0.371;0.461]	
Others						
Relugolix	21	7 (33.3)	11.897	8.182	0.333	0.0664
Leuprolide	11	0	[0.613;230.841]	[0.510;131.219]	[0.132;0.535]	
Not Reported						
Relugolix	13	4 (30.8)	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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Table MOR.TG50SFU.BIN.MITT.S5: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.4727						
< 8						
Relugolix	356	164 (46.1)	38.651	21.306	0.439	<.0001
Leuprolide	185	4 (2.2)	[14.043;106.379]	[8.030;56.533]	[0.383;0.495]	
>= 8						
Relugolix	341	114 (33.4)	82.863	55.496	0.328	<.0001
Leuprolide	166	1 (0.6)	[11.455;599.395]	[7.819;393.896]	[0.277;0.380]	
Missing						
Relugolix	20	6 (30.0)	NC	NC	NC	NC
Leuprolide	6	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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Table MOR.TG50SFU.BIN.MITT.S7: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.5062						
< 20 ng/mL						
Relugolix	428	211 (49.3)	40.450	21.001	0.470	<.0001
Leuprolide	213	5 (2.3)	[16.331;100.190]	[8.786;50.203]	[0.418;0.521]	
>= 20 ng/mL						
Relugolix	289	73 (25.3)	98.113	73.500	0.253	<.0001
Leuprolide	144	0	[6.031;1596.069]	[4.587;1177.739]	[0.203;0.303]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat.

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Table MOR.TG50SFU.BIN.MITT.S3: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Ethnicity, Interaction p-value: 0.7794						
Not Hispanic or Latino						
Relugolix	640	249 (38.9)	39.101	24.278	0.373	<.0001
Leuprolide	312	5 (1.6)	[15.932;95.963]	[10.122;58.231]	[0.333;0.413]	
Hispanic or Latino						
Relugolix	64	28 (43.8)	58.562	33.323	0.438	<.0001
Leuprolide	37	0	[3.446;995.248]	[2.094;530.315]	[0.316;0.559]	
Not Reported						
Relugolix	13	7 (53.8)	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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Table MOR.TG50SFU.BIN.MITT.S1: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.8188						
<= 75 years old						
Relugolix	509	227 (44.6)	50.310	28.319	0.430	<.0001
Leuprolide	254	4 (1.6)	[18.450;137.187]	[10.660;75.233]	[0.384;0.476]	
> 75 years old						
Relugolix	208	57 (27.4)	38.503	28.226	0.264	<.0001
Leuprolide	103	1 (1.0)	[5.248;282.512]	[3.964;200.973]	[0.201;0.328]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat.

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Table MOR.TG50SFU.BIN.MITT.S6: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.8754						
< 250 ng/dL						
Relugolix	72	21 (29.2)	32.981	23.562	0.292	<.0001
Leuprolide	39	0	[1.938;561.297]	[1.466;378.735]	[0.187;0.397]	
>= 250 ng/dL						
Relugolix	635	261 (41.1)	42.151	25.237	0.395	<.0001
Leuprolide	307	5 (1.6)	[17.175;103.444]	[10.527;60.499]	[0.354;0.436]	
Missing						
Relugolix	10	2 (20.0)	NC	NC	NC	NC
Leuprolide	11	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated.

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5.1.4.2 Prostataspezifisches-Antigen-Ansprechrate

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.PSAR50W3.BIN.MITT.S7: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.0523						
< 20 ng/mL						
Relugolix	428	328 (76.6)	19.257	5.266	0.621	<.0001
Leuprolide	213	31 (14.6)	[12.380;29.953]	[3.787;7.321]	[0.559;0.683]	
>= 20 ng/mL						
Relugolix	289	244 (84.4)	10.194	2.432	0.497	<.0001
Leuprolide	144	50 (34.7)	[6.385;16.274]	[1.933;3.058]	[0.409;0.585]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_BIN.SAS

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Table MOR.PSAR50W3.BIN.MITT.S2: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: 0.0653						
North and South America						
Relugolix	253	196 (77.5)	22.047	5.742	0.640	<.0001
Leuprolide	126	17 (13.5)	[12.220;39.777]	[3.672;8.979]	[0.561;0.719]	
Europe						
Relugolix	271	212 (78.2)	9.172	2.779	0.501	<.0001
Leuprolide	135	38 (28.1)	[5.714;14.723]	[2.107;3.665]	[0.410;0.591]	
Asia and Rest of World						
Relugolix	193	164 (85.0)	15.225	3.138	0.579	<.0001
Leuprolide	96	26 (27.1)	[8.366;27.708]	[2.248;4.380]	[0.477;0.681]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen.

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Table MOR.PSAR50W3.BIN.MITT.S6: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.1192						
< 250 ng/dL						
Relugolix	72	56 (77.8)	7.000	2.333	0.444	<.0001
Leuprolide	39	13 (33.3)	[2.941;16.661]	[1.472;3.699]	[0.268;0.621]	
>= 250 ng/dL						
Relugolix	635	508 (80.0)	14.892	3.778	0.588	<.0001
Leuprolide	307	65 (21.2)	[10.644;20.836]	[3.034;4.705]	[0.533;0.644]	
Missing						
Relugolix	10	8 (80.0)	NC	NC	NC	NC
Leuprolide	11	3 (27.3)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen; NC: Not calculated.

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Table MOR.PSAR50W3.BIN.MITT.S1: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.1561						
<= 75 years old						
Relugolix	509	417 (81.9)	15.665	3.651	0.595	<.0001
Leuprolide	254	57 (22.4)	[10.807;22.709]	[2.894;4.605]	[0.534;0.656]	
> 75 years old						
Relugolix	208	155 (74.5)	9.627	3.198	0.512	<.0001
Leuprolide	103	24 (23.3)	[5.537;16.738]	[2.233;4.581]	[0.411;0.613]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen.

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Table MOR.PSAR50W3.BIN.MITT.S4: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.1786						
Asian						
Relugolix	157	134 (85.4)	14.682	3.004	0.569	<.0001
Leuprolide	88	25 (28.4)	[7.737;27.859]	[2.143;4.212]	[0.460;0.679]	
Black or African American						
Relugolix	34	28 (82.4)	70.000	13.176	0.761	<.0001
Leuprolide	16	1 (6.3)	[7.695;636.786]	[1.963;88.458]	[0.586;0.936]	
White						
Relugolix	492	381 (77.4)	11.441	3.356	0.544	<.0001
Leuprolide	234	54 (23.1)	[7.900;16.570]	[2.643;4.261]	[0.478;0.609]	
Others						
Relugolix	21	17 (81.0)	42.500	8.905	0.719	0.0001
Leuprolide	11	1 (9.1)	[4.150;435.224]	[1.358;58.371]	[0.480;0.958]	
Not Reported						
Relugolix	13	12 (92.3)	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen; NC: Not calculated.

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Table MOR.PSAR50W3.BIN.MITT.S8: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.2419						
Asia (Excl. Korea)						
Relugolix	104	89 (85.6)	9.041	2.160	0.460	<.0001
Leuprolide	53	21 (39.6)	[4.161;19.645]	[1.535;3.039]	[0.312;0.608]	
Rest of World						
Relugolix	613	483 (78.8)	15.109	3.992	0.591	<.0001
Leuprolide	304	60 (19.7)	[10.728;21.280]	[3.171;5.026]	[0.535;0.646]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen.

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Table MOR.PSAR50W3.BIN.MITT.S3: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.2456						
Not Hispanic or Latino						
Relugolix	640	514 (80.3)	12.891	3.341	0.563	<.0001
Leuprolide	312	75 (24.0)	[9.317;17.835]	[2.733;4.085]	[0.506;0.619]	
Hispanic or Latino						
Relugolix	64	51 (79.7)	25.108	5.897	0.662	<.0001
Leuprolide	37	5 (13.5)	[8.175;77.115]	[2.586;13.449]	[0.514;0.810]	
Not Reported						
Relugolix	13	7 (53.8)	NC	NC	NC	NC
Leuprolide	8	1 (12.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen; NC: Not calculated.

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Table MOR.PSAR50W3.BIN.MITT.S5: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1, by Subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.3168						
< 8						
Relugolix	356	273 (76.7)	15.726	4.433	0.594	<.0001
Leuprolide	185	32 (17.3)	[9.994;24.746]	[3.218;6.107]	[0.524;0.664]	
>= 8						
Relugolix	341	282 (82.7)	11.413	2.802	0.532	<.0001
Leuprolide	166	49 (29.5)	[7.381;17.647]	[2.204;3.562]	[0.452;0.612]	
Missing						
Relugolix	20	17 (85.0)	NC	NC	NC	NC
Leuprolide	6	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen; NC: Not calculated.

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5.1.5 Gesundheitsbezogene Lebensqualität

5.1.5.1 Gesundheitsbezogene Lebensqualität (European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire C30)

5.1.5.1.1 Skala: Globaler Gesundheitszustand

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2GLBH15.KM.MITT.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.2762							
Asia (Excl. Korea)							
Relugolix	104	53 (51.0)	51 (49.0)	337.0 [251.0;NE]	-7.0	1.247 [0.770;2.021]	0.3691
Leuprolide	53	24 (45.3)	29 (54.7)	344.0 [253.0;NE]			
Rest of World							
Relugolix	613	293 (47.8)	320 (52.2)	338.0 [336.0;342.0]	1.0	0.934 [0.767;1.137]	0.4959
Leuprolide	304	150 (49.3)	154 (50.7)	337.0 [253.0;344.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITT.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.3212							
<= 75 years old							
Relugolix	509	245 (48.1)	264 (51.9)	338.0 [333.0;343.0]	-3.0	1.036 [0.832;1.291]	0.7514
Leuprolide	254	118 (46.5)	136 (53.5)	341.0 [260.0;NE]			
> 75 years old							
Relugolix	208	101 (48.6)	107 (51.4)	339.0 [253.0;345.0]	81.0	0.849 [0.612;1.177]	0.3259
Leuprolide	103	56 (54.4)	47 (45.6)	258.0 [171.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITT.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.4023							
< 20 ng/mL							
Relugolix	428	211 (49.3)	217 (50.7)	337.0 [257.0;342.0]	0.0	1.041 [0.823;1.316]	0.7403
Leuprolide	213	104 (48.8)	109 (51.2)	337.0 [255.0;NE]			
>= 20 ng/mL							
Relugolix	289	135 (46.7)	154 (53.3)	339.0 [335.0;NE]	2.0	0.887 [0.665;1.185]	0.4181
Leuprolide	144	70 (48.6)	74 (51.4)	337.0 [246.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4043							
Asian							
Relugolix	157	74 (47.1)	83 (52.9)	343.0 [255.0;NE]	8.0	0.915 [0.633;1.322]	0.6370
Leuprolide	88	46 (52.3)	42 (47.7)	335.0 [169.0;NE]			
Black or African American							
Relugolix	34	19 (55.9)	15 (44.1)	176.0 [166.0;NE]	-78.0	0.903 [0.395;2.063]	0.8082
Leuprolide	16	8 (50.0)	8 (50.0)	254.0 [30.0;NE]			
White							
Relugolix	492	237 (48.2)	255 (51.8)	338.0 [334.0;342.0]	-3.0	1.029 [0.820;1.291]	0.8053
Leuprolide	234	109 (46.6)	125 (53.4)	341.0 [253.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2GLBH15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.4043							
Others							
Relugolix	21	9 (42.9)	12 (57.1)	340.0 [176.0;NE]	175.0	0.445 [0.171;1.159]	0.0972
Leuprolide	11	8 (72.7)	3 (27.3)	165.0 [29.0;NE]			
Not Reported							
Relugolix	13	7 (53.8)	6 (46.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	3 (37.5)	5 (62.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITT.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.5196							
< 250 ng/dL							
Relugolix	72	34 (47.2)	38 (52.8)	338.0 [250.0;NE]	-3.0	0.805 [0.463;1.400]	0.4424
Leuprolide	39	20 (51.3)	19 (48.7)	341.0 [85.0;NE]			
>= 250 ng/dL							
Relugolix	635	306 (48.2)	329 (51.8)	338.0 [334.0;342.0]	1.0	0.976 [0.803;1.187]	0.8095
Leuprolide	307	150 (48.9)	157 (51.1)	337.0 [255.0;344.0]			
Missing							
Relugolix	10	6 (60.0)	4 (40.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	4 (36.4)	7 (63.6)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITT.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.6010							
Not Hispanic or Latino							
Relugolix	640	312 (48.8)	328 (51.3)	337.0 [334.0;342.0]	0.0	0.966 [0.796;1.171]	0.7219
Leuprolide	312	155 (49.7)	157 (50.3)	337.0 [253.0;344.0]			
Hispanic or Latino							
Relugolix	64	30 (46.9)	34 (53.1)	339.0 [175.0;NE]	NE	1.148 [0.618;2.134]	0.6621
Leuprolide	37	15 (40.5)	22 (59.5)	NE [92.0;NE]			
Not Reported							
Relugolix	13	4 (30.8)	9 (69.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITT.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.8217							
< 8							
Relugolix	356	176 (49.4)	180 (50.6)	337.0 [252.0;341.0]	2.0	1.027 [0.798;1.322]	0.8341
Leuprolide	185	92 (49.7)	93 (50.3)	335.0 [252.0;NE]			
>= 8							
Relugolix	341	162 (47.5)	179 (52.5)	340.0 [337.0;344.0]	-1.0	0.984 [0.749;1.293]	0.9099
Leuprolide	166	76 (45.8)	90 (54.2)	341.0 [334.0;344.0]			
Missing							
Relugolix	20	8 (40.0)	12 (60.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	6 (100.0)	0	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2GLBH15.KM.MITT.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.8438							
North and South America							
Relugolix	253	125 (49.4)	128 (50.6)	337.0 [253.0;340.0]	0.0	1.028 [0.758;1.394]	0.8607
Leuprolide	126	62 (49.2)	64 (50.8)	337.0 [252.0;NE]			
Europe							
Relugolix	271	129 (47.6)	142 (52.4)	341.0 [260.0;351.0]	-10.0	0.991 [0.731;1.345]	0.9554
Leuprolide	135	61 (45.2)	74 (54.8)	351.0 [246.0;NE]			
Asia and Rest of World							
Relugolix	193	92 (47.7)	101 (52.3)	338.0 [256.0;NE]	3.0	0.899 [0.639;1.266]	0.5434
Leuprolide	96	51 (53.1)	45 (46.9)	335.0 [170.0;344.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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5.1.5.1.2 Skala: Körperliche Funktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2PHYS15.KM.MITT.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.0219							
< 20 ng/mL							
Relugolix	428	106 (24.8)	322 (75.2)	NE [NE;NE]	NE	1.226 [0.862;1.742]	0.2570
Leuprolide	213	44 (20.7)	169 (79.3)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	289	71 (24.6)	218 (75.4)	NE [352.0;NE]	NE	0.674 [0.465;0.977]	0.0374
Leuprolide	144	46 (31.9)	98 (68.1)	NE [343.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PHYS15.KM.MITT.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.2708							
<= 75 years old							
Relugolix	509	127 (25.0)	382 (75.0)	NE [NE;NE]	NE	1.036 [0.762;1.408]	0.8233
Leuprolide	254	60 (23.6)	194 (76.4)	NE [NE;NE]			
> 75 years old							
Relugolix	208	50 (24.0)	158 (76.0)	NE [352.0;NE]	NE	0.762 [0.484;1.198]	0.2384
Leuprolide	103	30 (29.1)	73 (70.9)	NE [343.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PHYS15.KM.MITT.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.2899							
Asia (Excl. Korea)							
Relugolix	104	18 (17.3)	86 (82.7)	NE [344.0;NE]	NE	0.657 [0.322;1.341]	0.2487
Leuprolide	53	13 (24.5)	40 (75.5)	NE [344.0;NE]			
Rest of World							
Relugolix	613	159 (25.9)	454 (74.1)	352.0 [352.0;NE]	NE	0.992 [0.756;1.303]	0.9562
Leuprolide	304	77 (25.3)	227 (74.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PHYS15.KM.MITT.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.3431							
Not Hispanic or Latino							
Relugolix	640	156 (24.4)	484 (75.6)	NE [352.0;NE]	NE	0.916 [0.699;1.201]	0.5257
Leuprolide	312	79 (25.3)	233 (74.7)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	20 (31.3)	44 (68.8)	NE [NE;NE]	NE	1.370 [0.624;3.009]	0.4329
Leuprolide	37	9 (24.3)	28 (75.7)	NE [NE;NE]			
Not Reported							
Relugolix	13	1 (7.7)	12 (92.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	2 (25.0)	6 (75.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2PHYS15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.3840							
Asian							
Relugolix	157	32 (20.4)	125 (79.6)	NE [NE;NE]	NE	0.725 [0.424;1.239]	0.2389
Leuprolide	88	23 (26.1)	65 (73.9)	NE [344.0;NE]			
Black or African American							
Relugolix	34	11 (32.4)	23 (67.6)	NE [337.0;NE]	NE	1.078 [0.343;3.389]	0.8972
Leuprolide	16	4 (25.0)	12 (75.0)	NE [176.0;NE]			
White							
Relugolix	492	125 (25.4)	367 (74.6)	352.0 [352.0;NE]	NE	1.029 [0.752;1.407]	0.8605
Leuprolide	234	57 (24.4)	177 (75.6)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2PHYS15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.3840							
Others							
Relugolix	21	5 (23.8)	16 (76.2)	NE [NE;NE]	NE	0.400 [0.116;1.383]	0.1477
Leuprolide	11	5 (45.5)	6 (54.5)	NE [29.0;NE]			
Not Reported							
Relugolix	13	4 (30.8)	9 (69.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	1 (12.5)	7 (87.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2PHYS15.KM.MITT.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.4854							
North and South America							
Relugolix	253	77 (30.4)	176 (69.6)	NE [342.0;NE]	NE	1.108 [0.743;1.652]	0.6157
Leuprolide	126	35 (27.8)	91 (72.2)	NE [341.0;NE]			
Europe							
Relugolix	271	60 (22.1)	211 (77.9)	352.0 [352.0;NE]	NE	0.935 [0.603;1.450]	0.7650
Leuprolide	135	30 (22.2)	105 (77.8)	NE [NE;NE]			
Asia and Rest of World							
Relugolix	193	40 (20.7)	153 (79.3)	NE [NE;NE]	NE	0.748 [0.454;1.234]	0.2558
Leuprolide	96	25 (26.0)	71 (74.0)	NE [343.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2PHYS15.KM.MITT.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.5321							
< 250 ng/dL							
Relugolix	72	17 (23.6)	55 (76.4)	NE [NE;NE]	NE	1.215 [0.524;2.816]	0.6492
Leuprolide	39	8 (20.5)	31 (79.5)	NE [339.0;NE]			
>= 250 ng/dL							
Relugolix	635	157 (24.7)	478 (75.3)	NE [352.0;NE]	NE	0.917 [0.700;1.202]	0.5311
Leuprolide	307	79 (25.7)	228 (74.3)	NE [NE;NE]			
Missing							
Relugolix	10	3 (30.0)	7 (70.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	3 (27.3)	8 (72.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2PHYS15.KM.MITT.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.7043							
< 8							
Relugolix	356	84 (23.6)	272 (76.4)	352.0 [352.0;NE]	NE	0.991 [0.688;1.428]	0.9629
Leuprolide	185	44 (23.8)	141 (76.2)	NE [NE;NE]			
>= 8							
Relugolix	341	85 (24.9)	256 (75.1)	NE [NE;NE]	NE	0.897 [0.621;1.294]	0.5609
Leuprolide	166	43 (25.9)	123 (74.1)	NE [344.0;NE]			
Missing							
Relugolix	20	8 (40.0)	12 (60.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	3 (50.0)	3 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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5.1.5.1.3 Skala: Rollenfunktion

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Table QS.T2ROLE15.KM.MITT.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.0237							
Not Hispanic or Latino							
Relugolix	640	303 (47.3)	337 (52.7)	339.0 [336.0;344.0]	2.0	0.950 [0.782;1.153]	0.6034
Leuprolide	312	154 (49.4)	158 (50.6)	337.0 [259.0;343.0]			
Hispanic or Latino							
Relugolix	64	39 (60.9)	25 (39.1)	175.0 [169.0;255.0]	NE	2.029 [1.083;3.803]	0.0272
Leuprolide	37	13 (35.1)	24 (64.9)	NE [167.0;NE]			
Not Reported							
Relugolix	13	9 (69.2)	4 (30.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	5 (62.5)	3 (37.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITT.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline PSA Level, Interaction p-value: 0.1072							
< 20 ng/mL							
Relugolix	428	208 (48.6)	220 (51.4)	338.0 [260.0;344.0]	-4.0	1.159 [0.908;1.479]	0.2361
Leuprolide	213	94 (44.1)	119 (55.9)	342.0 [335.0;NE]			
>= 20 ng/mL							
Relugolix	289	143 (49.5)	146 (50.5)	337.0 [253.0;342.0]	80.0	0.856 [0.649;1.128]	0.2696
Leuprolide	144	78 (54.2)	66 (45.8)	257.0 [171.0;339.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITT.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.2773							
< 250 ng/dL							
Relugolix	72	37 (51.4)	35 (48.6)	267.0 [169.0;NE]	NE	1.393 [0.775;2.504]	0.2681
Leuprolide	39	16 (41.0)	23 (59.0)	NE [169.0;NE]			
>= 250 ng/dL							
Relugolix	635	308 (48.5)	327 (51.5)	337.0 [260.0;342.0]	0.0	0.989 [0.813;1.202]	0.9103
Leuprolide	307	150 (48.9)	157 (51.1)	337.0 [260.0;343.0]			
Missing							
Relugolix	10	6 (60.0)	4 (40.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	6 (54.5)	5 (45.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITT.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.3040							
< 8							
Relugolix	356	174 (48.9)	182 (51.1)	337.0 [254.0;344.0]	-5.0	1.157 [0.891;1.503]	0.2745
Leuprolide	185	83 (44.9)	102 (55.1)	342.0 [260.0;NE]			
>= 8							
Relugolix	341	168 (49.3)	173 (50.7)	339.0 [260.0;344.0]	2.0	0.953 [0.733;1.238]	0.7177
Leuprolide	166	84 (50.6)	82 (49.4)	337.0 [258.0;343.0]			
Missing							
Relugolix	20	9 (45.0)	11 (55.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	5 (83.3)	1 (16.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITT.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.4986							
<= 75 years old							
Relugolix	509	242 (47.5)	267 (52.5)	338.0 [333.0;344.0]	-1.0	1.063 [0.853;1.326]	0.5851
Leuprolide	254	117 (46.1)	137 (53.9)	339.0 [334.0;NE]			
> 75 years old							
Relugolix	208	109 (52.4)	99 (47.6)	255.0 [172.0;342.0]	-3.0	0.929 [0.672;1.284]	0.6550
Leuprolide	103	55 (53.4)	48 (46.6)	258.0 [170.0;342.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITT.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.8365							
Asia (Excl. Korea)							
Relugolix	104	50 (48.1)	54 (51.9)	344.0 [253.0;NE]	5.0	1.072 [0.659;1.745]	0.7788
Leuprolide	53	24 (45.3)	29 (54.7)	339.0 [197.0;NE]			
Rest of World							
Relugolix	613	301 (49.1)	312 (50.9)	337.0 [258.0;341.0]	0.0	1.015 [0.833;1.235]	0.8854
Leuprolide	304	148 (48.7)	156 (51.3)	337.0 [259.0;343.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.9020							
Asian							
Relugolix	157	76 (48.4)	81 (51.6)	339.0 [258.0;NE]	0.0	1.014 [0.696;1.479]	0.9412
Leuprolide	88	42 (47.7)	46 (52.3)	339.0 [253.0;NE]			
Black or African American							
Relugolix	34	18 (52.9)	16 (47.1)	337.0 [169.0;NE]	63.0	1.047 [0.437;2.509]	0.9176
Leuprolide	16	7 (43.8)	9 (56.3)	274.0 [85.0;NE]			
White							
Relugolix	492	234 (47.6)	258 (52.4)	339.0 [260.0;NE]	2.0	0.984 [0.786;1.231]	0.8865
Leuprolide	234	114 (48.7)	120 (51.3)	337.0 [258.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.9020							
Others							
Relugolix	21	15 (71.4)	6 (28.6)	171.0 [85.0;340.0]	-167.0	1.429 [0.554;3.685]	0.4599
Leuprolide	11	6 (54.5)	5 (45.5)	338.0 [29.0;NE]			
Not Reported							
Relugolix	13	8 (61.5)	5 (38.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	3 (37.5)	5 (62.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2ROLE15.KM.MITT.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.9636							
North and South America							
Relugolix	253	131 (51.8)	122 (48.2)	260.0 [175.0;339.0]	-75.0	1.043 [0.775;1.405]	0.7805
Leuprolide	126	65 (51.6)	61 (48.4)	335.0 [249.0;NE]			
Europe							
Relugolix	271	127 (46.9)	144 (53.1)	342.0 [258.0;NE]	0.0	1.039 [0.764;1.412]	0.8091
Leuprolide	135	60 (44.4)	75 (55.6)	342.0 [260.0;NE]			
Asia and Rest of World							
Relugolix	193	93 (48.2)	100 (51.8)	339.0 [260.0;344.0]	0.0	0.983 [0.692;1.397]	0.9251
Leuprolide	96	47 (49.0)	49 (51.0)	339.0 [256.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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5.1.5.1.4 Skala: Kognitive Funktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2COGN15.KM.MITT.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.0852							
Not Hispanic or Latino							
Relugolix	640	305 (47.7)	335 (52.3)	337.0 [330.0;NE]	63.0	0.907 [0.749;1.098]	0.3150
Leuprolide	312	161 (51.6)	151 (48.4)	274.0 [251.0;344.0]			
Hispanic or Latino							
Relugolix	64	37 (57.8)	27 (42.2)	175.0 [89.0;NE]	NE	1.559 [0.867;2.803]	0.1381
Leuprolide	37	16 (43.2)	21 (56.8)	NE [85.0;NE]			
Not Reported							
Relugolix	13	9 (69.2)	4 (30.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	5 (62.5)	3 (37.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITT.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.3199							
<= 75 years old							
Relugolix	509	251 (49.3)	258 (50.7)	336.0 [253.0;NE]	-1.0	1.021 [0.825;1.265]	0.8454
Leuprolide	254	127 (50.0)	127 (50.0)	337.0 [249.0;NE]			
> 75 years old							
Relugolix	208	100 (48.1)	108 (51.9)	337.0 [255.0;NE]	83.0	0.837 [0.602;1.164]	0.2897
Leuprolide	103	55 (53.4)	48 (46.6)	254.0 [169.0;344.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITT.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.3908							
< 20 ng/mL							
Relugolix	428	200 (46.7)	228 (53.3)	337.0 [330.0;NE]	0.0	0.903 [0.715;1.141]	0.3924
Leuprolide	213	109 (51.2)	104 (48.8)	337.0 [174.0;344.0]			
>= 20 ng/mL							
Relugolix	289	151 (52.2)	138 (47.8)	255.0 [172.0;341.0]	-79.0	1.059 [0.801;1.401]	0.6866
Leuprolide	144	73 (50.7)	71 (49.3)	334.0 [174.0;344.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.7667							
Asian							
Relugolix	157	85 (54.1)	72 (45.9)	253.0 [169.0;337.0]	0.0	1.085 [0.759;1.549]	0.6554
Leuprolide	88	47 (53.4)	41 (46.6)	253.0 [170.0;344.0]			
Black or African American							
Relugolix	34	18 (52.9)	16 (47.1)	252.0 [86.0;NE]	86.0	0.723 [0.325;1.610]	0.4271
Leuprolide	16	9 (56.3)	7 (43.8)	166.0 [29.0;NE]			
White							
Relugolix	492	229 (46.5)	263 (53.5)	338.0 [336.0;NE]	1.0	0.924 [0.739;1.155]	0.4875
Leuprolide	234	117 (50.0)	117 (50.0)	337.0 [253.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.7667							
Others							
Relugolix	21	12 (57.1)	9 (42.9)	251.0 [30.0;NE]	-87.0	1.124 [0.422;2.996]	0.8148
Leuprolide	11	6 (54.5)	5 (45.5)	338.0 [29.0;NE]			
Not Reported							
Relugolix	13	7 (53.8)	6 (46.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	3 (37.5)	5 (62.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITT.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Geographic Region I, Interaction p-value: 0.7764							
North and South America							
Relugolix	253	133 (52.6)	120 (47.4)	257.0 [174.0;337.0]	2.0	1.002 [0.747;1.344]	0.9913
Leuprolide	126	67 (53.2)	59 (46.8)	255.0 [169.0;NE]			
Europe							
Relugolix	271	118 (43.5)	153 (56.5)	350.0 [336.0;NE]	12.0	0.885 [0.653;1.201]	0.4333
Leuprolide	135	64 (47.4)	71 (52.6)	338.0 [253.0;NE]			
Asia and Rest of World							
Relugolix	193	100 (51.8)	93 (48.2)	255.0 [169.0;NE]	-79.0	1.029 [0.734;1.441]	0.8702
Leuprolide	96	51 (53.1)	45 (46.9)	334.0 [170.0;344.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITT.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.7810							
Asia (Excl. Korea)							
Relugolix	104	55 (52.9)	49 (47.1)	260.0 [164.0;NE]	-77.0	1.024 [0.653;1.606]	0.9190
Leuprolide	53	29 (54.7)	24 (45.3)	337.0 [92.0;344.0]			
Rest of World							
Relugolix	613	296 (48.3)	317 (51.7)	337.0 [256.0;343.0]	2.0	0.955 [0.785;1.161]	0.6427
Leuprolide	304	153 (50.3)	151 (49.7)	335.0 [252.0;342.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITT.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.8832							
< 250 ng/dL							
Relugolix	72	34 (47.2)	38 (52.8)	NE [168.0;NE]	NE	0.983 [0.566;1.708]	0.9511
Leuprolide	39	20 (51.3)	19 (48.7)	337.0 [92.0;NE]			
>= 250 ng/dL							
Relugolix	635	311 (49.0)	324 (51.0)	337.0 [254.0;342.0]	82.0	0.941 [0.777;1.139]	0.5318
Leuprolide	307	158 (51.5)	149 (48.5)	255.0 [174.0;344.0]			
Missing							
Relugolix	10	6 (60.0)	4 (40.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	4 (36.4)	7 (63.6)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2COGN15.KM.MITT.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.9060							
< 8							
Relugolix	356	164 (46.1)	192 (53.9)	337.0 [254.0;NE]	0.0	0.964 [0.746;1.246]	0.7788
Leuprolide	185	91 (49.2)	94 (50.8)	337.0 [174.0;NE]			
>= 8							
Relugolix	341	177 (51.9)	164 (48.1)	330.0 [246.0;342.0]	-5.0	0.985 [0.761;1.275]	0.9103
Leuprolide	166	86 (51.8)	80 (48.2)	335.0 [246.0;344.0]			
Missing							
Relugolix	20	10 (50.0)	10 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	5 (83.3)	1 (16.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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5.1.5.1.5 Skala: Emotionale Funktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2EMOT15.KM.MITT.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.0637							
Not Hispanic or Latino							
Relugolix	640	180 (28.1)	460 (71.9)	NE [350.0;NE]	NE	0.941 [0.731;1.211]	0.6354
Leuprolide	312	91 (29.2)	221 (70.8)	357.0 [NE;NE]			
Hispanic or Latino							
Relugolix	64	27 (42.2)	37 (57.8)	NE [253.0;NE]	NE	1.997 [0.939;4.248]	0.0723
Leuprolide	37	9 (24.3)	28 (75.7)	NE [339.0;NE]			
Not Reported							
Relugolix	13	4 (30.8)	9 (69.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	6 (75.0)	2 (25.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITT.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.1807							
<= 75 years old							
Relugolix	509	155 (30.5)	354 (69.5)	NE [NE;NE]	NE	1.077 [0.814;1.424]	0.6047
Leuprolide	254	72 (28.3)	182 (71.7)	NE [NE;NE]			
> 75 years old							
Relugolix	208	56 (26.9)	152 (73.1)	350.0 [350.0;NE]	-7.0	0.760 [0.496;1.164]	0.2072
Leuprolide	103	34 (33.0)	69 (67.0)	357.0 [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITT.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.4317							
< 20 ng/mL							
Relugolix	428	130 (30.4)	298 (69.6)	NE [NE;NE]	NE	1.050 [0.777;1.419]	0.7520
Leuprolide	213	63 (29.6)	150 (70.4)	357.0 [344.0;NE]			
>= 20 ng/mL							
Relugolix	289	81 (28.0)	208 (72.0)	NE [350.0;NE]	NE	0.867 [0.598;1.255]	0.4488
Leuprolide	144	43 (29.9)	101 (70.1)	NE [342.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITT.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.6770							
< 8							
Relugolix	356	106 (29.8)	250 (70.2)	NE [NE;NE]	NE	1.042 [0.749;1.449]	0.8073
Leuprolide	185	53 (28.6)	132 (71.4)	NE [NE;NE]			
>= 8							
Relugolix	341	100 (29.3)	241 (70.7)	350.0 [350.0;NE]	-7.0	0.942 [0.671;1.323]	0.7311
Leuprolide	166	50 (30.1)	116 (69.9)	357.0 [344.0;NE]			
Missing							
Relugolix	20	5 (25.0)	15 (75.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	3 (50.0)	3 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITT.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.8514							
Asia (Excl. Korea)							
Relugolix	104	21 (20.2)	83 (79.8)	NE [NE;NE]	NE	1.040 [0.490;2.210]	0.9183
Leuprolide	53	10 (18.9)	43 (81.1)	NE [344.0;NE]			
Rest of World							
Relugolix	613	190 (31.0)	423 (69.0)	350.0 [350.0;NE]	-7.0	0.964 [0.754;1.233]	0.7721
Leuprolide	304	96 (31.6)	208 (68.4)	357.0 [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITT.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.8526							
North and South America							
Relugolix	253	78 (30.8)	175 (69.2)	NE [343.0;NE]	NE	0.996 [0.680;1.459]	0.9852
Leuprolide	126	40 (31.7)	86 (68.3)	357.0 [340.0;NE]			
Europe							
Relugolix	271	82 (30.3)	189 (69.7)	350.0 [350.0;NE]	NE	0.899 [0.619;1.304]	0.5737
Leuprolide	135	42 (31.1)	93 (68.9)	NE [342.0;NE]			
Asia and Rest of World							
Relugolix	193	51 (26.4)	142 (73.6)	NE [344.0;NE]	NE	1.063 [0.655;1.728]	0.8038
Leuprolide	96	24 (25.0)	72 (75.0)	NE [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITT.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.8653							
< 250 ng/dL							
Relugolix	72	21 (29.2)	51 (70.8)	NE [339.0;NE]	NE	1.019 [0.491;2.114]	0.9595
Leuprolide	39	11 (28.2)	28 (71.8)	NE [337.0;NE]			
>= 250 ng/dL							
Relugolix	635	185 (29.1)	450 (70.9)	350.0 [350.0;NE]	-7.0	0.953 [0.742;1.224]	0.7077
Leuprolide	307	92 (30.0)	215 (70.0)	357.0 [344.0;NE]			
Missing							
Relugolix	10	5 (50.0)	5 (50.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	3 (27.3)	8 (72.7)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.9354							
Asian							
Relugolix	157	40 (25.5)	117 (74.5)	NE [NE;NE]	NE	0.876 [0.531;1.444]	0.6025
Leuprolide	88	25 (28.4)	63 (71.6)	NE [344.0;NE]			
Black or African American							
Relugolix	34	12 (35.3)	22 (64.7)	NE [336.0;NE]	NE	0.965 [0.340;2.740]	0.9471
Leuprolide	16	5 (31.3)	11 (68.8)	NE [166.0;NE]			
White							
Relugolix	492	149 (30.3)	343 (69.7)	350.0 [350.0;NE]	-7.0	1.047 [0.786;1.395]	0.7528
Leuprolide	234	68 (29.1)	166 (70.9)	357.0 [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2EMOT15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Race, Interaction p-value: 0.9354							
Others							
Relugolix	21	7 (33.3)	14 (66.7)	344.0 [337.0;NE]	5.0	0.868 [0.254;2.967]	0.8219
Leuprolide	11	4 (36.4)	7 (63.6)	339.0 [93.0;NE]			
Not Reported							
Relugolix	13	3 (23.1)	10 (76.9)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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5.1.5.1.6 Skala: Soziale Funktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2SOC15.KM.MITT.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Ethnicity, Interaction p-value: 0.0019							
Not Hispanic or Latino							
Relugolix	640	286 (44.7)	354 (55.3)	341.0 [338.0;NE]	4.0	0.859 [0.705;1.046]	0.1311
Leuprolide	312	150 (48.1)	162 (51.9)	337.0 [255.0;NE]			
Hispanic or Latino							
Relugolix	64	38 (59.4)	26 (40.6)	213.5 [169.0;NE]	NE	2.702 [1.346;5.423]	0.0052
Leuprolide	37	10 (27.0)	27 (73.0)	NE [339.0;NE]			
Not Reported							
Relugolix	13	5 (38.5)	8 (61.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	6 (75.0)	2 (25.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2SOC15.KM.MITT.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.1139							
<= 75 years old							
Relugolix	509	235 (46.2)	274 (53.8)	342.0 [337.0;NE]	NE	1.033 [0.824;1.295]	0.7787
Leuprolide	254	111 (43.7)	143 (56.3)	NE [337.0;NE]			
> 75 years old							
Relugolix	208	94 (45.2)	114 (54.8)	341.0 [337.0;NE]	81.0	0.747 [0.535;1.042]	0.0855
Leuprolide	103	55 (53.4)	48 (46.6)	260.0 [169.0;343.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITT.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.2050							
< 20 ng/mL							
Relugolix	428	202 (47.2)	226 (52.8)	341.0 [335.0;NE]	1.0	1.034 [0.811;1.317]	0.7873
Leuprolide	213	97 (45.5)	116 (54.5)	340.0 [274.0;NE]			
>= 20 ng/mL							
Relugolix	289	127 (43.9)	162 (56.1)	340.0 [337.0;NE]	3.0	0.808 [0.603;1.084]	0.1552
Leuprolide	144	69 (47.9)	75 (52.1)	337.0 [171.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.3641							
Asian							
Relugolix	157	51 (32.5)	106 (67.5)	NE [341.0;NE]	NE	0.775 [0.500;1.201]	0.2537
Leuprolide	88	33 (37.5)	55 (62.5)	NE [337.0;NE]			
Black or African American							
Relugolix	34	23 (67.6)	11 (32.4)	169.0 [84.0;336.0]	84.0	0.664 [0.330;1.337]	0.2519
Leuprolide	16	12 (75.0)	4 (25.0)	85.0 [30.0;166.0]			
White							
Relugolix	492	236 (48.0)	256 (52.0)	339.0 [260.0;344.0]	0.0	0.958 [0.766;1.198]	0.7061
Leuprolide	234	114 (48.7)	120 (51.3)	339.0 [254.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2SOC15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.3641							
Others							
Relugolix	21	11 (52.4)	10 (47.6)	339.0 [169.0;NE]	NE	2.122 [0.592;7.608]	0.2480
Leuprolide	11	3 (27.3)	8 (72.7)	NE [92.0;NE]			
Not Reported							
Relugolix	13	8 (61.5)	5 (38.5)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITT.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.4975							
< 8							
Relugolix	356	164 (46.1)	192 (53.9)	341.0 [334.0;NE]	2.0	0.983 [0.756;1.277]	0.8976
Leuprolide	185	85 (45.9)	100 (54.1)	339.0 [255.0;NE]			
>= 8							
Relugolix	341	151 (44.3)	190 (55.7)	341.0 [337.0;NE]	-1.0	0.862 [0.656;1.133]	0.2878
Leuprolide	166	78 (47.0)	88 (53.0)	342.0 [262.0;NE]			
Missing							
Relugolix	20	14 (70.0)	6 (30.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	3 (50.0)	3 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITT.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.5326							
North and South America							
Relugolix	253	139 (54.9)	114 (45.1)	253.0 [176.0;337.0]	-21.0	1.062 [0.793;1.424]	0.6857
Leuprolide	126	66 (52.4)	60 (47.6)	274.0 [169.0;NE]			
Europe							
Relugolix	271	125 (46.1)	146 (53.9)	344.0 [259.0;NE]	4.0	0.914 [0.676;1.235]	0.5580
Leuprolide	135	64 (47.4)	71 (52.6)	340.0 [246.0;NE]			
Asia and Rest of World							
Relugolix	193	65 (33.7)	128 (66.3)	NE [341.0;NE]	NE	0.805 [0.535;1.209]	0.2954
Leuprolide	96	36 (37.5)	60 (62.5)	344.0 [343.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITT.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.6575							
< 250 ng/dL							
Relugolix	72	37 (51.4)	35 (48.6)	339.0 [169.0;NE]	-3.0	1.064 [0.606;1.868]	0.8298
Leuprolide	39	18 (46.2)	21 (53.8)	342.0 [90.0;NE]			
>= 250 ng/dL							
Relugolix	635	286 (45.0)	349 (55.0)	341.0 [337.0;NE]	1.0	0.929 [0.760;1.136]	0.4738
Leuprolide	307	142 (46.3)	165 (53.7)	340.0 [267.0;NE]			
Missing							
Relugolix	10	6 (60.0)	4 (40.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	6 (54.5)	5 (45.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SOC15.KM.MITT.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.9116							
Asia (Excl. Korea)							
Relugolix	104	30 (28.8)	74 (71.2)	NE [341.0;NE]	NE	0.905 [0.493;1.661]	0.7476
Leuprolide	53	16 (30.2)	37 (69.8)	NE [344.0;NE]			
Rest of World							
Relugolix	613	299 (48.8)	314 (51.2)	337.0 [260.0;342.0]	0.0	0.938 [0.771;1.142]	0.5259
Leuprolide	304	150 (49.3)	154 (50.7)	337.0 [253.0;343.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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5.1.5.2 Gesundheitsbezogene Lebensqualität (European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire PR25)

5.1.5.2.1 Skala: Sexuelle Aktivität

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2SEXA15.KM.MITT.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Age Category, Interaction p-value: 0.2406							
<= 75 years old							
Relugolix	509	128 (25.1)	381 (74.9)	NE [NE;NE]	NE	0.803 [0.606;1.065]	0.1277
Leuprolide	254	78 (30.7)	176 (69.3)	NE [NE;NE]			
> 75 years old							
Relugolix	208	53 (25.5)	155 (74.5)	NE [NE;NE]	NE	1.127 [0.691;1.838]	0.6331
Leuprolide	103	23 (22.3)	80 (77.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITT.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.3353							
< 8							
Relugolix	356	82 (23.0)	274 (77.0)	NE [NE;NE]	NE	0.971 [0.675;1.397]	0.8758
Leuprolide	185	45 (24.3)	140 (75.7)	NE [NE;NE]			
>= 8							
Relugolix	341	92 (27.0)	249 (73.0)	NE [NE;NE]	NE	0.762 [0.546;1.064]	0.1109
Leuprolide	166	55 (33.1)	111 (66.9)	NE [NE;NE]			
Missing							
Relugolix	20	7 (35.0)	13 (65.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	1 (16.7)	5 (83.3)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2SEXA15.KM.MITT.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline Testosterone Level, Interaction p-value: 0.4992							
< 250 ng/dL							
Relugolix	72	14 (19.4)	58 (80.6)	NE [NE;NE]	NE	1.234 [0.474;3.210]	0.6672
Leuprolide	39	6 (15.4)	33 (84.6)	NE [NE;NE]			
>= 250 ng/dL							
Relugolix	635	165 (26.0)	470 (74.0)	NE [NE;NE]	NE	0.877 [0.678;1.133]	0.3154
Leuprolide	307	90 (29.3)	217 (70.7)	NE [NE;NE]			
Missing							
Relugolix	10	2 (20.0)	8 (80.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	5 (45.5)	6 (54.5)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2SEXA15.KM.MITT.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.5109							
Asia (Excl. Korea)							
Relugolix	104	12 (11.5)	92 (88.5)	NE [NE;NE]	NE	1.224 [0.431;3.474]	0.7043
Leuprolide	53	5 (9.4)	48 (90.6)	NE [NE;NE]			
Rest of World							
Relugolix	613	169 (27.6)	444 (72.4)	NE [NE;NE]	NE	0.854 [0.665;1.097]	0.2170
Leuprolide	304	96 (31.6)	208 (68.4)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITT.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.5213							
Not Hispanic or Latino							
Relugolix	640	150 (23.4)	490 (76.6)	NE [NE;NE]	NE	0.866 [0.662;1.134]	0.2950
Leuprolide	312	82 (26.3)	230 (73.7)	NE [NE;NE]			
Hispanic or Latino							
Relugolix	64	25 (39.1)	39 (60.9)	NE [251.0;NE]	NE	1.087 [0.573;2.062]	0.7984
Leuprolide	37	15 (40.5)	22 (59.5)	NE [176.0;NE]			
Not Reported							
Relugolix	13	6 (46.2)	7 (53.8)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITT.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.5540							
< 20 ng/mL							
Relugolix	428	112 (26.2)	316 (73.8)	NE [NE;NE]	NE	0.829 [0.612;1.124]	0.2281
Leuprolide	213	66 (31.0)	147 (69.0)	NE [NE;NE]			
>= 20 ng/mL							
Relugolix	289	69 (23.9)	220 (76.1)	NE [NE;NE]	NE	0.967 [0.644;1.452]	0.8708
Leuprolide	144	35 (24.3)	109 (75.7)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITT.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.6819							
North and South America							
Relugolix	253	70 (27.7)	183 (72.3)	NE [343.0;NE]	NE	0.906 [0.613;1.341]	0.6230
Leuprolide	126	39 (31.0)	87 (69.0)	NE [NE;NE]			
Europe							
Relugolix	271	78 (28.8)	193 (71.2)	NE [NE;NE]	NE	0.949 [0.648;1.390]	0.7882
Leuprolide	135	40 (29.6)	95 (70.4)	NE [343.0;NE]			
Asia and Rest of World							
Relugolix	193	33 (17.1)	160 (82.9)	NE [NE;NE]	NE	0.712 [0.415;1.221]	0.2171
Leuprolide	96	22 (22.9)	74 (77.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.8898							
Asian							
Relugolix	157	27 (17.2)	130 (82.8)	NE [NE;NE]	NE	0.727 [0.408;1.296]	0.2802
Leuprolide	88	20 (22.7)	68 (77.3)	NE [NE;NE]			
Black or African American							
Relugolix	34	15 (44.1)	19 (55.9)	343.0 [251.0;NE]	11.0	0.975 [0.398;2.393]	0.9564
Leuprolide	16	7 (43.8)	9 (56.3)	332.0 [90.0;NE]			
White							
Relugolix	492	127 (25.8)	365 (74.2)	NE [NE;NE]	NE	0.929 [0.689;1.252]	0.6282
Leuprolide	234	65 (27.8)	169 (72.2)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXA15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.8898							
Others							
Relugolix	21	8 (38.1)	13 (61.9)	NE [85.0;NE]	NE	0.790 [0.258;2.414]	0.6785
Leuprolide	11	5 (45.5)	6 (54.5)	NE [29.0;NE]			
Not Reported							
Relugolix	13	4 (30.8)	9 (69.2)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	4 (50.0)	4 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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5.1.5.2.2 Skala: Sexualfunktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2SEXF15.KM.MITT.S6: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Baseline Testosterone Level, Interaction p-value: 0.0775							
< 250 ng/dL							
Relugolix	72	7 (9.7)	65 (90.3)	338.0 [173.0;NE]	163.0	0.456 [0.159;1.302]	0.1422
Leuprolide	39	7 (17.9)	32 (82.1)	175.0 [29.0;NE]			
>= 250 ng/dL							
Relugolix	635	74 (11.7)	561 (88.3)	252.0 [169.0;258.0]	-7.0	1.250 [0.847;1.843]	0.2609
Leuprolide	307	39 (12.7)	268 (87.3)	259.0 [169.0;NE]			
Missing							
Relugolix	10	3 (30.0)	7 (70.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	11	2 (18.2)	9 (81.8)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SEXF15.KM.MITT.S8: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region II, Interaction p-value: 0.0841							
Asia (Excl. Korea)							
Relugolix	104	4 (3.8)	100 (96.2)	138.0 [29.0;NE]	NE	7.637 [0.849;68.664]	0.0696
Leuprolide	53	1 (1.9)	52 (98.1)	NE [337.0;NE]			
Rest of World							
Relugolix	613	80 (13.1)	533 (86.9)	253.0 [169.0;335.0]	0.0	1.074 [0.749;1.541]	0.6970
Leuprolide	304	47 (15.5)	257 (84.5)	253.0 [169.0;337.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXF15.KM.MITT.S7: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Baseline PSA Level, Interaction p-value: 0.3359							
< 20 ng/mL							
Relugolix	428	48 (11.2)	380 (88.8)	253.0 [170.0;NE]	-6.0	1.004 [0.633;1.594]	0.9849
Leuprolide	213	29 (13.6)	184 (86.4)	259.0 [165.0;NE]			
>= 20 ng/mL							
Relugolix	289	36 (12.5)	253 (87.5)	252.0 [87.0;258.0]	-1.0	1.432 [0.821;2.499]	0.2054
Leuprolide	144	19 (13.2)	125 (86.8)	253.0 [169.0;337.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXF15.KM.MITT.S3: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Ethnicity, Interaction p-value: 0.3716							
Not Hispanic or Latino							
Relugolix	640	73 (11.4)	567 (88.6)	253.0 [169.0;259.0]	-6.0	1.256 [0.849;1.860]	0.2542
Leuprolide	312	38 (12.2)	274 (87.8)	259.0 [172.0;338.0]			
Hispanic or Latino							
Relugolix	64	11 (17.2)	53 (82.8)	170.0 [85.0;NE]	1.0	0.817 [0.347;1.928]	0.6451
Leuprolide	37	10 (27.0)	27 (73.0)	169.0 [29.0;NE]			
Not Reported							
Relugolix	13	0	13 (100.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

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Table QS.T2SEXF15.KM.MITT.S1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR[2] [95% CI]**	**p-value[3]**
Age Category, Interaction p-value: 0.5484							
<= 75 years old							
Relugolix	509	75 (14.7)	434 (85.3)	252.0 [169.0;256.0]	-7.0	1.198 [0.813;1.765]	0.3610
Leuprolide	254	39 (15.4)	215 (84.6)	259.0 [169.0;337.0]			
> 75 years old							
Relugolix	208	9 (4.3)	199 (95.7)	NE [162.0;NE]	NE	0.881 [0.350;2.221]	0.7887
Leuprolide	103	9 (8.7)	94 (91.3)	253.0 [30.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.T2SEXF15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.6512							
Asian							
Relugolix	157	11 (7.0)	146 (93.0)	247.0 [29.0;NE]	-90.0	1.303 [0.414;4.096]	0.6508
Leuprolide	88	4 (4.5)	84 (95.5)	337.0 [29.0;NE]			
Black or African American							
Relugolix	34	7 (20.6)	27 (79.4)	341.0 [91.0;NE]	88.0	0.623 [0.209;1.857]	0.3963
Leuprolide	16	6 (37.5)	10 (62.5)	253.0 [29.0;NE]			
White							
Relugolix	492	61 (12.4)	431 (87.6)	252.0 [169.0;256.0]	-5.0	1.234 [0.820;1.859]	0.3137
Leuprolide	234	37 (15.8)	197 (84.2)	257.0 [169.0;338.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2SEXF15.KM.MITT.S4: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Race, Interaction p-value: 0.6512							
Others							
Relugolix	21	4 (19.0)	17 (81.0)	169.0 [34.0;NE]	NE	2.074 [0.231;18.582]	0.5144
Leuprolide	11	1 (9.1)	10 (90.9)	NE [29.0;NE]			
Not Reported							
Relugolix	13	1 (7.7)	12 (92.3)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	8	0	8 (100.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2SEXF15.KM.MITT.S5: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Gleason Score at Study Entry, Interaction p-value: 0.8075							
< 8							
Relugolix	356	51 (14.3)	305 (85.7)	253.0 [169.0;337.0]	-77.0	1.243 [0.770;2.007]	0.3731
Leuprolide	185	25 (13.5)	160 (86.5)	330.0 [165.0;NE]			
>= 8							
Relugolix	341	32 (9.4)	309 (90.6)	252.0 [169.0;338.0]	-5.0	1.134 [0.648;1.985]	0.6590
Leuprolide	166	20 (12.0)	146 (88.0)	257.0 [169.0;NE]			
Missing							
Relugolix	20	1 (5.0)	19 (95.0)	NC [NC;NC]	NC	NC [NC;NC]	NC
Leuprolide	6	3 (50.0)	3 (50.0)	NC [NC;NC]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NC: Not calculated; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.T2SEXF15.KM.MITT.S2: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score, by subgroup (mITT Population)

Study: HERO

Treatment	N	n (%)	Censored patients n (%)	Median time to 1st event [95% CI][1]	Median difference	HR[2] [95% CI]	p-value[3]
Geographic Region I, Interaction p-value: 0.9304							
North and South America							
Relugolix	253	40 (15.8)	213 (84.2)	252.0 [169.0;338.0]	-1.0	1.089 [0.661;1.796]	0.7373
Leuprolide	126	25 (19.8)	101 (80.2)	253.0 [169.0;337.0]			
Europe							
Relugolix	271	30 (11.1)	241 (88.9)	253.0 [85.0;337.0]	-4.0	1.261 [0.702;2.264]	0.4374
Leuprolide	135	18 (13.3)	117 (86.7)	257.0 [85.0;NE]			
Asia and Rest of World							
Relugolix	193	14 (7.3)	179 (92.7)	335.0 [87.0;NE]	-2.0	1.208 [0.435;3.355]	0.7175
Leuprolide	96	5 (5.2)	91 (94.8)	337.0 [87.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model with treatment group, subgroup and a subgroup-by-treatment interaction as covariates. 95% CIs are based on the approximation to the normal distribution. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
The interaction p-value is based on the subgroup-by-treatment interaction term in the Cox proportional hazards model used to compute the HR and 95% CI.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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5.1.6 Sicherheit

5.1.6.1 Gesamtrate jeglicher UE

Myovant Sciences, Inc.: HERO AMNOG

Table AE.TEAE.ANY.BIN.SAF.S3: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.0007						
Not Hispanic or Latino						
Relugolix	640	587 (91.7)	0.759	0.980	-0.019	0.3641
Leuprolide	312	292 (93.6)	[0.445;1.293]	[0.944;1.017]	[-0.053;0.016]	
Hispanic or Latino						
Relugolix	64	64 (100.0)	26.619	1.197	0.162	0.0018
Leuprolide	37	31 (83.8)	[1.453;487.577]	[1.034;1.385]	[0.043;0.281]	
Not Reported						
Relugolix	13	13 (100.0)	NC	NC	NC	NC
Leuprolide	8	7 (87.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAE.ANY.BIN.SAF.S5: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.0412						
< 8						
Relugolix	356	327 (91.9)	0.577	0.966	-0.033	0.2137
Leuprolide	185	176 (95.1)	[0.267;1.245]	[0.923;1.010]	[-0.075;0.009]	
>= 8						
Relugolix	341	317 (93.0)	1.606	1.043	0.038	0.1695
Leuprolide	166	148 (89.2)	[0.846;3.051]	[0.981;1.108]	[-0.016;0.093]	
Missing						
Relugolix	20	20 (100.0)	NC	NC	NC	NC
Leuprolide	6	6 (100.0)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAE.ANY.BIN.SAF.S7: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.2107						
< 20 ng/mL						
Relugolix	428	395 (92.3)	0.778	0.983	-0.016	0.5185
Leuprolide	213	200 (93.9)	[0.401;1.511]	[0.941;1.027]	[-0.057;0.025]	
>= 20 ng/mL						
Relugolix	289	269 (93.1)	1.448	1.031	0.028	0.3442
Leuprolide	144	130 (90.3)	[0.709;2.959]	[0.969;1.097]	[-0.029;0.085]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAE.ANY.BIN.SAF.S1: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.2181						
<= 75 years old						
Relugolix	509	470 (92.3)	1.200	1.015	0.014	0.5740
Leuprolide	254	231 (90.9)	[0.700;2.057]	[0.970;1.063]	[-0.028;0.056]	
> 75 years old						
Relugolix	208	194 (93.3)	0.560	0.970	-0.028	0.4405
Leuprolide	103	99 (96.1)	[0.180;1.746]	[0.920;1.023]	[-0.079;0.022]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAE.ANY.BIN.SAF.S2: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Geographic Region I, Interaction p-value: 0.2579						
North and South America						
Relugolix	253	243 (96.0)	1.647	1.026	0.024	0.3132
Leuprolide	126	118 (93.7)	[0.634;4.283]	[0.974;1.080]	[-0.025;0.073]	
Europe						
Relugolix	271	246 (90.8)	0.620	0.965	-0.033	0.3353
Leuprolide	135	127 (94.1)	[0.272;1.414]	[0.912;1.021]	[-0.086;0.020]	
Asia and Rest of World						
Relugolix	193	175 (90.7)	1.258	1.024	0.021	0.6780
Leuprolide	96	85 (88.5)	[0.569;2.782]	[0.941;1.115]	[-0.054;0.097]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAE.ANY.BIN.SAF.S4: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.5717						
Asian						
Relugolix	157	138 (87.9)	1.038	1.005	0.004	1.0000
Leuprolide	88	77 (87.5)	[0.469;2.294]	[0.911;1.108]	[-0.082;0.090]	
Black or African American						
Relugolix	34	33 (97.1)	4.714	1.109	0.096	0.2367
Leuprolide	16	14 (87.5)	[0.395;56.324]	[0.913;1.347]	[-0.076;0.267]	
White						
Relugolix	492	461 (93.7)	0.804	0.988	-0.012	0.6156
Leuprolide	234	222 (94.9)	[0.405;1.595]	[0.951;1.025]	[-0.047;0.024]	
Others						
Relugolix	21	19 (90.5)	0.950	0.995	-0.004	1.0000
Leuprolide	11	10 (90.9)	[0.076;11.803]	[0.789;1.256]	[-0.216;0.207]	
Not Reported						
Relugolix	13	13 (100.0)	NC	NC	NC	NC
Leuprolide	8	7 (87.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAE.ANY.BIN.SAF.S6: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.9149						
< 250 ng/dL						
Relugolix	72	68 (94.4)	0.919	0.995	-0.004	1.0000
Leuprolide	39	37 (94.9)	[0.161;5.256]	[0.908;1.091]	[-0.091;0.083]	
>= 250 ng/dL						
Relugolix	635	586 (92.3)	1.014	1.001	0.001	1.0000
Leuprolide	307	283 (92.2)	[0.610;1.686]	[0.962;1.042]	[-0.035;0.038]	
Missing						
Relugolix	10	10 (100.0)	NC	NC	NC	NC
Leuprolide	11	10 (90.9)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAE.ANY.BIN.SAF.S8: Proportion of Patients with at Least One Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.9315						
Asia (Excl. Korea)						
Relugolix	104	94 (90.4)	0.979	0.998	-0.002	1.0000
Leuprolide	53	48 (90.6)	[0.317;3.026]	[0.897;1.111]	[-0.099;0.095]	
Rest of World						
Relugolix	613	570 (93.0)	1.034	1.002	0.002	0.8920
Leuprolide	304	282 (92.8)	[0.607;1.763]	[0.965;1.041]	[-0.033;0.038]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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5.1.6.2 Häufige jegliche UE nach SOC und PT

Myovant Sciences, Inc.: HERO AMNOG

Table AE.TEAE.SPT.BIN.SAF.S8: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Diarrhoea

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.2870						
Asia (Excl. Korea)						
Relugolix	104	9 (8.7)	4.926	4.587	0.068	0.1660
Leuprolide	53	1 (1.9)	[0.607;39.967]	[0.597;35.250]	[0.002;0.133]	
Rest of World						
Relugolix	613	73 (11.9)	1.733	1.646	0.047	0.0290
Leuprolide	304	22 (7.2)	[1.053;2.851]	[1.043;2.597]	[0.008;0.086]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.TEAE.SPT.BIN.SAF.S5: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Diarrhoea

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.5788						
< 8						
Relugolix	356	42 (11.8)	2.116	1.984	0.059	0.0326
Leuprolide	185	11 (5.9)	[1.062;4.215]	[1.047;3.762]	[0.011;0.106]	
>= 8						
Relugolix	341	38 (11.1)	1.609	1.542	0.039	0.2043
Leuprolide	166	12 (7.2)	[0.818;3.169]	[0.828;2.871]	[-0.012;0.091]	
Missing						
Relugolix	20	2 (10.0)	NC	NC	NC	NC
Leuprolide	6	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.TEAE.SPT.BIN.SAF.S3: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Diarrhoea

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.5841						
Not Hispanic or Latino						
Relugolix	640	71 (11.1)	1.822	1.731	0.047	0.0251
Leuprolide	312	20 (6.4)	[1.088;3.052]	[1.074;2.789]	[0.010;0.083]	
Hispanic or Latino						
Relugolix	64	9 (14.1)	2.864	2.602	0.087	0.3199
Leuprolide	37	2 (5.4)	[0.584;14.038]	[0.594;11.403]	[-0.026;0.199]	
Not Reported						
Relugolix	13	2 (15.4)	NC	NC	NC	NC
Leuprolide	8	1 (12.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.TEAE.SPT.BIN.SAF.S2: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Diarrhoea

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: 0.6245						
North and South America						
Relugolix	253	42 (16.6)	1.730	1.609	0.063	0.1218
Leuprolide	126	13 (10.3)	[0.892;3.357]	[0.897;2.886]	[-0.007;0.133]	
Europe						
Relugolix	271	22 (8.1)	1.616	1.566	0.029	0.3141
Leuprolide	135	7 (5.2)	[0.672;3.883]	[0.686;3.573]	[-0.020;0.079]	
Asia and Rest of World						
Relugolix	193	18 (9.3)	3.189	2.984	0.062	0.0583
Leuprolide	96	3 (3.1)	[0.915;11.105]	[0.901;9.884]	[0.008;0.116]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each.
MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.TEAE.SPT.BIN.SAF.S6: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Diarrhoea

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.7381						
< 250 ng/dL						
Relugolix	72	8 (11.1)	1.500	1.444	0.034	0.7440
Leuprolide	39	3 (7.7)	[0.374;6.012]	[0.406;5.135]	[-0.077;0.145]	
>= 250 ng/dL						
Relugolix	635	72 (11.3)	1.938	1.832	0.051	0.0131
Leuprolide	307	19 (6.2)	[1.147;3.277]	[1.126;2.981]	[0.015;0.088]	
Missing						
Relugolix	10	2 (20.0)	NC	NC	NC	NC
Leuprolide	11	1 (9.1)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.TEAE.SPT.BIN.SAF.S1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Diarrhoea

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.7681						
<= 75 years old						
Relugolix	509	58 (11.4)	1.793	1.703	0.047	0.0397
Leuprolide	254	17 (6.7)	[1.021;3.148]	[1.013;2.861]	[0.006;0.088]	
> 75 years old						
Relugolix	208	24 (11.5)	2.109	1.981	0.057	0.1520
Leuprolide	103	6 (5.8)	[0.834;5.333]	[0.836;4.694]	[-0.006;0.120]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each.
MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.TEAE.SPT.BIN.SAF.S7: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Diarrhoea

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.9559						
< 20 ng/mL						
Relugolix	428	47 (11.0)	1.898	1.799	0.049	0.0603
Leuprolide	213	13 (6.1)	[1.003;3.591]	[0.996;3.252]	[0.005;0.092]	
>= 20 ng/mL						
Relugolix	289	35 (12.1)	1.846	1.744	0.052	0.1315
Leuprolide	144	10 (6.9)	[0.887;3.844]	[0.889;3.421]	[-0.004;0.108]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each.
MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Myovant Sciences, Inc.: HERO AMNOG

Table AE.TEAE.SPT.BIN.SAF.S4: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Gastrointestinal disorders, Preferred Term: Diarrhoea

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.9810						
Asian						
Relugolix	157	10 (6.4)	1.927	1.868	0.030	0.3878
Leuprolide	88	3 (3.4)	[0.516;7.198]	[0.528;6.610]	[-0.024;0.083]	
Black or African American						
Relugolix	34	5 (14.7)	2.586	2.353	0.085	0.6498
Leuprolide	16	1 (6.3)	[0.277;24.189]	[0.299;18.520]	[-0.083;0.253]	
White						
Relugolix	492	60 (12.2)	1.892	1.784	0.054	0.0277
Leuprolide	234	16 (6.8)	[1.065;3.363]	[1.051;3.027]	[0.010;0.097]	
Others						
Relugolix	21	5 (23.8)	1.406	1.310	0.056	1.0000
Leuprolide	11	2 (18.2)	[0.225;8.783]	[0.302;5.688]	[-0.236;0.348]	
Not Reported						
Relugolix	13	2 (15.4)	NC	NC	NC	NC
Leuprolide	8	1 (12.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

Table AE.TEAE.SPT.BIN.SAF.S6: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Vascular disorders, Preferred Term: Hypotension

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.2124						
< 250 ng/dL						
Relugolix	72	0	0.545	0.548	0.000	1.0000
Leuprolide	39	0	[0.011;27.988]	[0.011;27.095]		
>= 250 ng/dL						
Relugolix	635	13 (2.0)	13.337	13.075	0.020	0.0070
Leuprolide	307	0	[0.790;225.100]	[0.780;219.231]	[0.009;0.031]	
Missing						
Relugolix	10	0	NC	NC	NC	NC
Leuprolide	11	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

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Table AE.TEAE.SPT.BIN.SAF.S8: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Vascular disorders, Preferred Term: Hypotension

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.3593						
Asia (Excl. Korea)						
Relugolix	104	1 (1.0)	1.551	1.543	0.010	1.0000
Leuprolide	53	0	[0.062;38.718]	[0.064;37.240]	[-0.009;0.028]	
Rest of World						
Relugolix	613	12 (2.0)	12.656	12.419	0.020	0.0112
Leuprolide	304	0	[0.747;214.472]	[0.738;209.046]	[0.009;0.031]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each.
MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.TEAE.SPT.BIN.SAF.S5: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Vascular disorders, Preferred Term: Hypotension

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.4618						
< 8						
Relugolix	356	11 (3.1)	12.349	11.983	0.031	0.0193
Leuprolide	185	0	[0.724;210.734]	[0.710;202.224]	[0.013;0.049]	
>= 8						
Relugolix	341	2 (0.6)	2.452	2.442	0.006	1.0000
Leuprolide	166	0	[0.117;51.366]	[0.118;50.569]	[-0.002;0.014]	
Missing						
Relugolix	20	0	NC	NC	NC	NC
Leuprolide	6	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.TEAE.SPT.BIN.SAF.S1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Vascular disorders, Preferred Term: Hypotension

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: NC						
<= 75 years old						
Relugolix	509	9 (1.8)	NC [NC;NC]	NC [NC;NC]	NC [NC;NC]	NC
Leuprolide	254	0				
> 75 years old						
Relugolix	208	4 (1.9)	NC [NC;NC]	NC [NC;NC]	NC [NC;NC]	NC
Leuprolide	103	0				

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each.
MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

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Table AE.TEAE.SPT.BIN.SAF.S2: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Vascular disorders, Preferred Term: Hypotension

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: NC						
North and South America						
Relugolix	253	8 (3.2)	NC [NC;NC]	NC [NC;NC]	NC [NC;NC]	NC
Leuprolide	126	0				
Europe						
Relugolix	271	3 (1.1)	NC [NC;NC]	NC [NC;NC]	NC [NC;NC]	NC
Leuprolide	135	0				
Asia and Rest of World						
Relugolix	193	2 (1.0)	NC [NC;NC]	NC [NC;NC]	NC [NC;NC]	NC
Leuprolide	96	0				

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each.
MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

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Table AE.TEAE.SPT.BIN.SAF.S3: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Vascular disorders, Preferred Term: Hypotension

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: NC						
Not Hispanic or Latino						
Relugolix	640	9 (1.4)	NC	NC	NC	NC
Leuprolide	312	0	[NC;NC]	[NC;NC]	[NC;NC]	
Hispanic or Latino						
Relugolix	64	3 (4.7)	NC	NC	NC	NC
Leuprolide	37	0	[NC;NC]	[NC;NC]	[NC;NC]	
Not Reported						
Relugolix	13	1 (7.7)	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

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Myovant Sciences, Inc.: HERO AMNOG

Table AE.TEAE.SPT.BIN.SAF.S4: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Vascular disorders, Preferred Term: Hypotension

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: NC						
Asian						
Relugolix	157	1 (0.6)	NC	NC	NC	NC
Leuprolide	88	0	[NC;NC]	[NC;NC]	[NC;NC]	
Black or African American						
Relugolix	34	1 (2.9)	NC	NC	NC	NC
Leuprolide	16	0	[NC;NC]	[NC;NC]	[NC;NC]	
White						
Relugolix	492	9 (1.8)	NC	NC	NC	NC
Leuprolide	234	0	[NC;NC]	[NC;NC]	[NC;NC]	
Others						
Relugolix	21	0	NC	NC	NC	NC
Leuprolide	11	0	[NC;NC]	[NC;NC]	[NC;NC]	
Not Reported						
Relugolix	13	2 (15.4)	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

Table AE.TEAE.SPT.BIN.SAF.S7: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Vascular disorders, Preferred Term: Hypotension

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: NC						
< 20 ng/mL						
Relugolix	428	9 (2.1)	NC [NC;NC]	NC [NC;NC]	NC [NC;NC]	NC
Leuprolide	213	0				
>= 20 ng/mL						
Relugolix	289	4 (1.4)	NC [NC;NC]	NC [NC;NC]	NC [NC;NC]	NC
Leuprolide	144	0				

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each.
MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

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5.1.6.3 Gesamtrate der schweren UE (CTCAE-Grad ≥ 3)

Myovant Sciences, Inc.: HERO AMNOG

Table AE.G35TEAE.ANY.BIN.SAF.S3: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.0332						
Not Hispanic or Latino						
Relugolix	640	118 (18.4)	0.859	0.885	-0.024	0.3821
Leuprolide	312	65 (20.8)	[0.612;1.205]	[0.675;1.160]	[-0.078;0.030]	
Hispanic or Latino						
Relugolix	64	17 (26.6)	2.984	2.457	0.158	0.0764
Leuprolide	37	4 (10.8)	[0.920;9.679]	[0.894;6.754]	[0.010;0.305]	
Not Reported						
Relugolix	13	1 (7.7)	NC	NC	NC	NC
Leuprolide	8	1 (12.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

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Table AE.G35TEAE.ANY.BIN.SAF.S4: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.2256						
Asian						
Relugolix	157	26 (16.6)	0.829	0.857	-0.028	0.6027
Leuprolide	88	17 (19.3)	[0.422;1.630]	[0.493;1.490]	[-0.128;0.073]	
Black or African American						
Relugolix	34	6 (17.6)	0.643	0.706	-0.074	0.7067
Leuprolide	16	4 (25.0)	[0.153;2.699]	[0.231;2.157]	[-0.321;0.174]	
White						
Relugolix	492	96 (19.5)	0.939	0.951	-0.010	0.7656
Leuprolide	234	48 (20.5)	[0.637;1.384]	[0.698;1.296]	[-0.072;0.052]	
Others						
Relugolix	21	6 (28.6)	9.645	7.091	0.286	0.0711
Leuprolide	11	0	[0.492;189.109]	[0.436;115.345]	[0.092;0.479]	
Not Reported						
Relugolix	13	2 (15.4)	NC	NC	NC	NC
Leuprolide	8	1 (12.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

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Table AE.G35TEAE.ANY.BIN.SAF.S7: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.5755						
< 20 ng/mL						
Relugolix	428	71 (16.6)	1.047	1.039	0.006	0.9100
Leuprolide	213	34 (16.0)	[0.670;1.636]	[0.715;1.511]	[-0.054;0.067]	
>= 20 ng/mL						
Relugolix	289	65 (22.5)	0.871	0.900	-0.025	0.6296
Leuprolide	144	36 (25.0)	[0.545;1.389]	[0.631;1.283]	[-0.111;0.060]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.G35TEAE.ANY.BIN.SAF.S8: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.5980						
Asia (Excl. Korea)						
Relugolix	104	14 (13.5)	0.760	0.793	-0.035	0.6346
Leuprolide	53	9 (17.0)	[0.306;1.893]	[0.367;1.711]	[-0.156;0.085]	
Rest of World						
Relugolix	613	122 (19.9)	0.990	0.992	-0.002	1.0000
Leuprolide	304	61 (20.1)	[0.702;1.396]	[0.753;1.306]	[-0.057;0.053]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.G35TEAE.ANY.BIN.SAF.S5: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.6251						
< 8						
Relugolix	356	59 (16.6)	0.882	0.902	-0.018	0.6314
Leuprolide	185	34 (18.4)	[0.554;1.405]	[0.615;1.322]	[-0.086;0.050]	
>= 8						
Relugolix	341	74 (21.7)	1.037	1.029	0.006	0.9087
Leuprolide	166	35 (21.1)	[0.659;1.632]	[0.720;1.470]	[-0.070;0.082]	
Missing						
Relugolix	20	3 (15.0)	NC	NC	NC	NC
Leuprolide	6	1 (16.7)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.G35TEAE.ANY.BIN.SAF.S2: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: 0.6279						
North and South America						
Relugolix	253	61 (24.1)	1.165	1.125	0.027	0.6069
Leuprolide	126	27 (21.4)	[0.697;1.947]	[0.755;1.678]	[-0.062;0.116]	
Europe						
Relugolix	271	42 (15.5)	0.848	0.872	-0.023	0.5700
Leuprolide	135	24 (17.8)	[0.489;1.471]	[0.552;1.377]	[-0.100;0.055]	
Asia and Rest of World						
Relugolix	193	33 (17.1)	0.836	0.864	-0.027	0.6265
Leuprolide	96	19 (19.8)	[0.447;1.564]	[0.520;1.437]	[-0.123;0.069]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.G35TEAE.ANY.BIN.SAF.S6: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.7506						
< 250 ng/dL						
Relugolix	72	16 (22.2)	1.107	1.083	0.017	1.0000
Leuprolide	39	8 (20.5)	[0.426;2.878]	[0.510;2.302]	[-0.142;0.176]	
>= 250 ng/dL						
Relugolix	635	120 (18.9)	0.940	0.951	-0.010	0.7248
Leuprolide	307	61 (19.9)	[0.666;1.325]	[0.721;1.254]	[-0.064;0.044]	
Missing						
Relugolix	10	0	NC	NC	NC	NC
Leuprolide	11	1 (9.1)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.G35TEAE.ANY.BIN.SAF.S1: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.9048						
<= 75 years old						
Relugolix	509	92 (18.1)	0.947	0.956	-0.008	0.8427
Leuprolide	254	48 (18.9)	[0.643;1.394]	[0.698;1.310]	[-0.067;0.050]	
> 75 years old						
Relugolix	208	44 (21.2)	0.988	0.990	-0.002	1.0000
Leuprolide	103	22 (21.4)	[0.555;1.759]	[0.629;1.560]	[-0.099;0.095]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

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5.1.6.4 Häufige schwere UE (CTCAE-Grad ≥ 3) nach SOC und PT

Myovant Sciences, Inc.: HERO AMNOG

Table AE.G35TEAE.SPT.BIN.SAF.S: Frequent Grade 3 or Above Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: NA, Preferred Term: NA

Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
No SOCs or PTs meet the IQWiG frequent event rules in the overall Safety Population AND have a significant treatment effect (p-value <0.05) in the overall Safety Population for this endpoint.						

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NA: Not applicable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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5.1.6.5 Gesamtrate der SUE

Myovant Sciences, Inc.: HERO AMNOG

Table AE.STEAE.ANY.BIN.SAF.S3: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.2166						
Not Hispanic or Latino						
Relugolix	640	81 (12.7)	0.797	0.823	-0.027	0.2674
Leuprolide	312	48 (15.4)	[0.542;1.172]	[0.591;1.145]	[-0.075;0.020]	
Hispanic or Latino						
Relugolix	64	7 (10.9)	2.149	2.023	0.055	0.4799
Leuprolide	37	2 (5.4)	[0.422;10.934]	[0.443;9.237]	[-0.050;0.161]	
Not Reported						
Relugolix	13	1 (7.7)	NC	NC	NC	NC
Leuprolide	8	1 (12.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAE.ANY.BIN.SAF.S1: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.3689						
<= 75 years old						
Relugolix	509	60 (11.8)	0.961	0.966	-0.004	0.9058
Leuprolide	254	31 (12.2)	[0.605;1.526]	[0.643;1.450]	[-0.053;0.045]	
> 75 years old						
Relugolix	208	29 (13.9)	0.672	0.718	-0.055	0.2473
Leuprolide	103	20 (19.4)	[0.359;1.258]	[0.428;1.206]	[-0.144;0.035]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAE.ANY.BIN.SAF.S5: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.5039						
< 8						
Relugolix	356	42 (11.8)	0.942	0.949	-0.006	0.8893
Leuprolide	185	23 (12.4)	[0.548;1.621]	[0.589;1.528]	[-0.065;0.052]	
>= 8						
Relugolix	341	44 (12.9)	0.730	0.765	-0.040	0.2779
Leuprolide	166	28 (16.9)	[0.436;1.222]	[0.495;1.183]	[-0.107;0.028]	
Missing						
Relugolix	20	3 (15.0)	NC	NC	NC	NC
Leuprolide	6	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAE.ANY.BIN.SAF.S8: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.6271						
Asia (Excl. Korea)						
Relugolix	104	8 (7.7)	0.653	0.679	-0.036	0.5552
Leuprolide	53	6 (11.3)	[0.214;1.990]	[0.249;1.857]	[-0.136;0.063]	
Rest of World						
Relugolix	613	81 (13.2)	0.876	0.893	-0.016	0.5413
Leuprolide	304	45 (14.8)	[0.591;1.299]	[0.637;1.251]	[-0.064;0.032]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAE.ANY.BIN.SAF.S7: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.6276						
< 20 ng/mL						
Relugolix	428	47 (11.0)	0.928	0.936	-0.008	0.7913
Leuprolide	213	25 (11.7)	[0.554;1.554]	[0.593;1.477]	[-0.060;0.045]	
>= 20 ng/mL						
Relugolix	289	42 (14.5)	0.772	0.805	-0.035	0.4003
Leuprolide	144	26 (18.1)	[0.452;1.319]	[0.515;1.258]	[-0.110;0.040]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAE.ANY.BIN.SAF.S2: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: 0.7893						
North and South America						
Relugolix	253	34 (13.4)	0.995	0.996	-0.001	1.0000
Leuprolide	126	17 (13.5)	[0.532;1.861]	[0.580;1.712]	[-0.074;0.072]	
Europe						
Relugolix	271	34 (12.5)	0.825	0.847	-0.023	0.5374
Leuprolide	135	20 (14.8)	[0.455;1.496]	[0.507;1.413]	[-0.094;0.049]	
Asia and Rest of World						
Relugolix	193	21 (10.9)	0.715	0.746	-0.037	0.4440
Leuprolide	96	14 (14.6)	[0.346;1.477]	[0.397;1.401]	[-0.120;0.046]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAE.ANY.BIN.SAF.S4: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.8488						
Asian						
Relugolix	157	16 (10.2)	0.719	0.747	-0.034	0.4116
Leuprolide	88	12 (13.6)	[0.323;1.597]	[0.371;1.507]	[-0.120;0.051]	
Black or African American						
Relugolix	34	2 (5.9)	0.437	0.471	-0.066	0.5843
Leuprolide	16	2 (12.5)	[0.056;3.426]	[0.073;3.046]	[-0.246;0.114]	
White						
Relugolix	492	69 (14.0)	0.897	0.912	-0.014	0.6521
Leuprolide	234	36 (15.4)	[0.580;1.389]	[0.629;1.322]	[-0.069;0.042]	
Others						
Relugolix	21	1 (4.8)	1.683	1.636	0.048	1.0000
Leuprolide	11	0	[0.063;44.772]	[0.072;37.145]	[-0.043;0.139]	
Not Reported						
Relugolix	13	1 (7.7)	NC	NC	NC	NC
Leuprolide	8	1 (12.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAE.ANY.BIN.SAF.S6: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.8870						
< 250 ng/dL						
Relugolix	72	10 (13.9)	0.887	0.903	-0.015	1.0000
Leuprolide	39	6 (15.4)	[0.296;2.656]	[0.355;2.297]	[-0.154;0.124]	
>= 250 ng/dL						
Relugolix	635	78 (12.3)	0.815	0.838	-0.024	0.3531
Leuprolide	307	45 (14.7)	[0.549;1.210]	[0.596;1.178]	[-0.071;0.023]	
Missing						
Relugolix	10	1 (10.0)	NC	NC	NC	NC
Leuprolide	11	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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5.1.6.6 Gesamtrate der SUE ohne MACE-Events

Myovant Sciences, Inc.: HERO AMNOG

Table AE.STEAES1.ANY.BIN.SAF.S1: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.5237						
<= 75 years old						
Relugolix	509	51 (10.0)	1.067	1.060	0.006	0.8975
Leuprolide	254	24 (9.4)	[0.641;1.778]	[0.669;1.682]	[-0.039;0.050]	
> 75 years old						
Relugolix	208	27 (13.0)	0.811	0.836	-0.026	0.6012
Leuprolide	103	16 (15.5)	[0.415;1.584]	[0.472;1.480]	[-0.109;0.058]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAES1.ANY.BIN.SAF.S3: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.6020						
Not Hispanic or Latino						
Relugolix	640	72 (11.3)	0.942	0.949	-0.006	0.8284
Leuprolide	312	37 (11.9)	[0.618;1.436]	[0.654;1.377]	[-0.050;0.037]	
Hispanic or Latino						
Relugolix	64	5 (7.8)	1.483	1.445	0.024	1.0000
Leuprolide	37	2 (5.4)	[0.273;8.056]	[0.295;7.081]	[-0.074;0.122]	
Not Reported						
Relugolix	13	1 (7.7)	NC	NC	NC	NC
Leuprolide	8	1 (12.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAES1.ANY.BIN.SAF.S7: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.6740						
< 20 ng/mL						
Relugolix	428	42 (9.8)	1.050	1.045	0.004	1.0000
Leuprolide	213	20 (9.4)	[0.600;1.838]	[0.630;1.734]	[-0.044;0.052]	
>= 20 ng/mL						
Relugolix	289	36 (12.5)	0.882	0.897	-0.014	0.7613
Leuprolide	144	20 (13.9)	[0.490;1.587]	[0.539;1.492]	[-0.082;0.054]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAES1.ANY.BIN.SAF.S8: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.7381						
Asia (Excl. Korea)						
Relugolix	104	8 (7.7)	0.800	0.815	-0.017	0.7629
Leuprolide	53	5 (9.4)	[0.248;2.577]	[0.280;2.371]	[-0.111;0.076]	
Rest of World						
Relugolix	613	70 (11.4)	0.991	0.992	-0.001	1.0000
Leuprolide	304	35 (11.5)	[0.644;1.525]	[0.677;1.453]	[-0.045;0.043]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAES1.ANY.BIN.SAF.S5: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.7483						
< 8						
Relugolix	356	39 (11.0)	1.015	1.013	0.001	1.0000
Leuprolide	185	20 (10.8)	[0.573;1.796]	[0.609;1.686]	[-0.054;0.057]	
>= 8						
Relugolix	341	37 (10.9)	0.888	0.901	-0.012	0.7646
Leuprolide	166	20 (12.0)	[0.498;1.585]	[0.540;1.502]	[-0.071;0.048]	
Missing						
Relugolix	20	2 (10.0)	NC	NC	NC	NC
Leuprolide	6	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAES1.ANY.BIN.SAF.S2: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: 0.8553						
North and South America						
Relugolix	253	28 (11.1)	0.996	0.996	-0.000	1.0000
Leuprolide	126	14 (11.1)	[0.504;1.966]	[0.544;1.824]	[-0.068;0.067]	
Europe						
Relugolix	271	30 (11.1)	1.076	1.067	0.007	1.0000
Leuprolide	135	14 (10.4)	[0.550;2.104]	[0.586;1.945]	[-0.057;0.071]	
Asia and Rest of World						
Relugolix	193	20 (10.4)	0.809	0.829	-0.021	0.6909
Leuprolide	96	12 (12.5)	[0.378;1.733]	[0.423;1.624]	[-0.100;0.058]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAES1.ANY.BIN.SAF.S6: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.9481						
< 250 ng/dL						
Relugolix	72	9 (12.5)	0.971	0.975	-0.003	1.0000
Leuprolide	39	5 (12.8)	[0.301;3.130]	[0.351;2.708]	[-0.133;0.127]	
>= 250 ng/dL						
Relugolix	635	68 (10.7)	0.932	0.939	-0.007	0.7395
Leuprolide	307	35 (11.4)	[0.605;1.436]	[0.640;1.379]	[-0.050;0.036]	
Missing						
Relugolix	10	1 (10.0)	NC	NC	NC	NC
Leuprolide	11	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.STEAES1.ANY.BIN.SAF.S4: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.9653						
Asian						
Relugolix	157	15 (9.6)	0.824	0.841	-0.018	0.6647
Leuprolide	88	10 (11.4)	[0.353;1.921]	[0.395;1.791]	[-0.099;0.063]	
Black or African American						
Relugolix	34	2 (5.9)	0.937	0.941	-0.004	1.0000
Leuprolide	16	1 (6.3)	[0.079;11.168]	[0.092;9.632]	[-0.146;0.139]	
White						
Relugolix	492	60 (12.2)	1.022	1.019	0.002	1.0000
Leuprolide	234	28 (12.0)	[0.633;1.649]	[0.669;1.552]	[-0.048;0.053]	
Others						
Relugolix	21	0	0.535	0.545	0.000	1.0000
Leuprolide	11	0	[0.010;28.763]	[0.012;25.795]		
Not Reported						
Relugolix	13	1 (7.7)	NC	NC	NC	NC
Leuprolide	8	1 (12.5)	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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5.1.6.7 Häufige SUE nach SOC und PT

Myovant Sciences, Inc.: HERO AMNOG

Table AE.STEAE.SPT.BIN.SAF.S5: Frequent Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Nervous system disorders, Preferred Term: Any

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.0926						
< 8						
Relugolix	356	1 (0.3)	0.072	0.074	-0.035	0.0029
Leuprolide	185	7 (3.8)	[0.009;0.587]	[0.009;0.599]	[-0.063;-0.007]	
>= 8						
Relugolix	341	5 (1.5)	0.479	0.487	-0.015	0.3079
Leuprolide	166	5 (3.0)	[0.137;1.679]	[0.143;1.658]	[-0.044;0.014]	
Missing						
Relugolix	20	1 (5.0)	NC	NC	NC	NC
Leuprolide	6	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each.
MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.STEAE.SPT.BIN.SAF.S7: Frequent Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Nervous system disorders, Preferred Term: Any

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.2043						
< 20 ng/mL						
Relugolix	428	2 (0.5)	0.138	0.142	-0.028	0.0077
Leuprolide	213	7 (3.3)	[0.028;0.671]	[0.030;0.679]	[-0.053;-0.003]	
>= 20 ng/mL						
Relugolix	289	5 (1.7)	0.489	0.498	-0.017	0.3114
Leuprolide	144	5 (3.5)	[0.139;1.719]	[0.147;1.693]	[-0.051;0.016]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each.
MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.STEAE.SPT.BIN.SAF.S6: Frequent Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Nervous system disorders, Preferred Term: Any

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.6306						
< 250 ng/dL						
Relugolix	72	1 (1.4)	0.535	0.542	-0.012	1.0000
Leuprolide	39	1 (2.6)	[0.033;8.798]	[0.035;8.425]	[-0.068;0.045]	
>= 250 ng/dL						
Relugolix	635	6 (0.9)	0.257	0.264	-0.026	0.0073
Leuprolide	307	11 (3.6)	[0.094;0.701]	[0.098;0.706]	[-0.048;-0.004]	
Missing						
Relugolix	10	0	NC	NC	NC	NC
Leuprolide	11	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.STEAE.SPT.BIN.SAF.S1: Frequent Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Nervous system disorders, Preferred Term: Any

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.6888						
<= 75 years old						
Relugolix	509	4 (0.8)	0.244	0.250	-0.024	0.0253
Leuprolide	254	8 (3.1)	[0.073;0.817]	[0.076;0.821]	[-0.046;-0.001]	
> 75 years old						
Relugolix	208	3 (1.4)	0.362	0.371	-0.024	0.2254
Leuprolide	103	4 (3.9)	[0.080;1.650]	[0.085;1.629]	[-0.065;0.016]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each.
MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.STEAE.SPT.BIN.SAF.S3: Frequent Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Nervous system disorders, Preferred Term: Any

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.7768						
Not Hispanic or Latino						
Relugolix	640	7 (1.1)	0.303	0.310	-0.024	0.0192
Leuprolide	312	11 (3.5)	[0.116;0.788]	[0.121;0.793]	[-0.046;-0.002]	
Hispanic or Latino						
Relugolix	64	0	0.189	0.195	-0.027	0.3663
Leuprolide	37	1 (2.7)	[0.007;4.751]	[0.008;4.665]	[-0.079;0.025]	
Not Reported						
Relugolix	13	0	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.STEAE.SPT.BIN.SAF.S8: Frequent Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Nervous system disorders, Preferred Term: Any

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.9044						
Asia (Excl. Korea)						
Relugolix	104	1 (1.0)	0.248	0.255	-0.028	0.2635
Leuprolide	53	2 (3.8)	[0.022;2.795]	[0.024;2.746]	[-0.083;0.027]	
Rest of World						
Relugolix	613	6 (1.0)	0.291	0.298	-0.023	0.0160
Leuprolide	304	10 (3.3)	[0.105;0.807]	[0.109;0.811]	[-0.045;-0.002]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each.
MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Myovant Sciences, Inc.: HERO AMNOG

Table AE.STEAE.SPT.BIN.SAF.S4: Frequent Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Nervous system disorders, Preferred Term: Any

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.9083						
Asian						
Relugolix	157	1 (0.6)	0.182	0.187	-0.028	0.1335
Leuprolide	88	3 (3.4)	[0.019;1.773]	[0.020;1.769]	[-0.068;0.012]	
Black or African American						
Relugolix	34	0	0.150	0.162	-0.063	0.3200
Leuprolide	16	1 (6.3)	[0.006;3.886]	[0.007;3.770]	[-0.181;0.056]	
White						
Relugolix	492	6 (1.2)	0.349	0.357	-0.022	0.0778
Leuprolide	234	8 (3.4)	[0.120;1.017]	[0.125;1.016]	[-0.047;0.003]	
Others						
Relugolix	21	0	0.535	0.545	0.000	1.0000
Leuprolide	11	0	[0.010;28.763]	[0.012;25.795]		
Not Reported						
Relugolix	13	0	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

Table AE.STEAE.SPT.BIN.SAF.S2: Frequent Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term, by Subgroup (Safety Population)

Study: HERO

System Organ Class: Nervous system disorders, Preferred Term: Any

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: NC						
North and South America						
Relugolix	253	4 (1.6)	NC [NC;NC]	NC [NC;NC]	NC [NC;NC]	NC
Leuprolide	126	3 (2.4)				
Europe						
Relugolix	271	2 (0.7)	NC [NC;NC]	NC [NC;NC]	NC [NC;NC]	NC
Leuprolide	135	5 (3.7)				
Asia and Rest of World						
Relugolix	193	1 (0.5)	NC [NC;NC]	NC [NC;NC]	NC [NC;NC]	NC
Leuprolide	96	4 (4.2)				

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group in the overall Safety Population are considered. Further, only SOCs and PTs for which there is a significant treatment effect (p-value <0.05) in the overall Safety Population are presented. Events are sorted alphabetically by SOC and PT and then by ascending subgroup-by-treatment interaction p-value within each.
MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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5.1.6.8 Absetzen der Studienmedikation aufgrund von UE

Myovant Sciences, Inc.: HERO AMNOG

Table AE.TEAED.ANY.BIN.SAF.S8: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region II, Interaction p-value: 0.1745						
Asia (Excl. Korea)						
Relugolix	104	4 (3.8)	2.080	2.038	0.020	0.6633
Leuprolide	53	1 (1.9)	[0.227;19.090]	[0.234;17.786]	[-0.032;0.072]	
Rest of World						
Relugolix	613	22 (3.6)	23.166	22.353	0.036	0.0003
Leuprolide	304	0	[1.400;383.184]	[1.361;367.253]	[0.021;0.051]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAED.ANY.BIN.SAF.S4: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Race, Interaction p-value: 0.3019						
Asian						
Relugolix	157	6 (3.8)	3.457	3.363	0.027	0.4268
Leuprolide	88	1 (1.1)	[0.409;29.188]	[0.411;27.487]	[-0.010;0.064]	
Black or African American						
Relugolix	34	0	0.478	0.486	0.000	1.0000
Leuprolide	16	0	[0.009;25.178]	[0.010;23.447]		
White						
Relugolix	492	19 (3.9)	19.315	18.590	0.039	0.0008
Leuprolide	234	0	[1.161;321.290]	[1.127;306.572]	[0.022;0.056]	
Others						
Relugolix	21	0	0.535	0.545	0.000	1.0000
Leuprolide	11	0	[0.010;28.763]	[0.012;25.795]		
Not Reported						
Relugolix	13	1 (7.7)	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAED.ANY.BIN.SAF.S5: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Gleason Score at Study Entry, Interaction p-value: 0.4554						
< 8						
Relugolix	356	16 (4.5)	17.978	17.193	0.045	0.0020
Leuprolide	185	0	[1.072;301.364]	[1.037;284.981]	[0.023;0.066]	
>= 8						
Relugolix	341	10 (2.9)	4.985	4.868	0.023	0.1122
Leuprolide	166	1 (0.6)	[0.633;39.272]	[0.628;37.710]	[0.002;0.045]	
Missing						
Relugolix	20	0	NC	NC	NC	NC
Leuprolide	6	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAED.ANY.BIN.SAF.S7: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline PSA Level, Interaction p-value: 0.4840						
< 20 ng/mL						
Relugolix	428	16 (3.7)	17.080	16.462	0.037	0.0021
Leuprolide	213	0	[1.020;286.073]	[0.992;273.071]	[0.019;0.055]	
>= 20 ng/mL						
Relugolix	289	10 (3.5)	5.125	4.983	0.028	0.1095
Leuprolide	144	1 (0.7)	[0.650;40.435]	[0.644;38.546]	[0.003;0.053]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAED.ANY.BIN.SAF.S6: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Baseline Testosterone Level, Interaction p-value: 0.5857						
< 250 ng/dL						
Relugolix	72	3 (4.2)	3.978	3.836	0.042	0.5506
Leuprolide	39	0	[0.200;79.020]	[0.203;72.409]	[-0.004;0.088]	
>= 250 ng/dL						
Relugolix	635	23 (3.6)	11.500	11.120	0.033	0.0014
Leuprolide	307	1 (0.3)	[1.546;85.555]	[1.509;81.957]	[0.017;0.049]	
Missing						
Relugolix	10	0	NC	NC	NC	NC
Leuprolide	11	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAED.ANY.BIN.SAF.S2: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Geographic Region I, Interaction p-value: 0.8248						
North and South America						
Relugolix	253	11 (4.3)	11.998	11.500	0.043	0.0187
Leuprolide	126	0	[0.701;205.266]	[0.683;193.591]	[0.018;0.069]	
Europe						
Relugolix	271	7 (2.6)	7.684	7.500	0.026	0.1009
Leuprolide	135	0	[0.436;135.554]	[0.432;130.347]	[0.007;0.045]	
Asia and Rest of World						
Relugolix	193	8 (4.1)	4.108	3.979	0.031	0.2801
Leuprolide	96	1 (1.0)	[0.506;33.331]	[0.505;31.359]	[-0.004;0.066]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAED.ANY.BIN.SAF.S1: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Age Category, Interaction p-value: 0.8701						
<= 75 years old						
Relugolix	509	16 (3.1)	8.211	7.984	0.027	0.0165
Leuprolide	254	1 (0.4)	[1.083;62.267]	[1.065;59.868]	[0.010;0.044]	
> 75 years old						
Relugolix	208	10 (4.8)	10.950	10.450	0.048	0.0340
Leuprolide	103	0	[0.635;188.722]	[0.618;176.593]	[0.019;0.077]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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Table AE.TEAED.ANY.BIN.SAF.S3: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation, by Subgroup (Safety Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Ethnicity, Interaction p-value: 0.9188						
Not Hispanic or Latino						
Relugolix	640	20 (3.1)	10.032	9.750	0.028	0.0038
Leuprolide	312	1 (0.3)	[1.340;75.097]	[1.315;72.318]	[0.013;0.043]	
Hispanic or Latino						
Relugolix	64	6 (9.4)	8.333	7.600	0.094	0.0830
Leuprolide	37	0	[0.456;152.289]	[0.440;131.185]	[0.022;0.165]	
Not Reported						
Relugolix	13	0	NC	NC	NC	NC
Leuprolide	8	0	[NC;NC]	[NC;NC]	[NC;NC]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, subgroup and a subgroup-by-treatment interaction as covariates.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
The Interaction p-value is based on the subgroup-by-treatment interaction term in the logistic regression model used to compute the OR and 95% CI.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; NC: Not calculated.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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6 Ergebnisse der Teilpopulation d1) der Studie HERO

6.1 Ergebnisse zu Wirksamkeit und Sicherheit

6.1.1 Mortalität

6.1.1.1 Gesamtüberleben

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.OS.KM.MITTM1: Time to Overall Survival (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	14 (4.8)	276 (95.2)	NE [NE;NE]	NE	0.858 [0.359;2.049]	0.7298
Leuprolide	144	8 (5.6)	136 (94.4)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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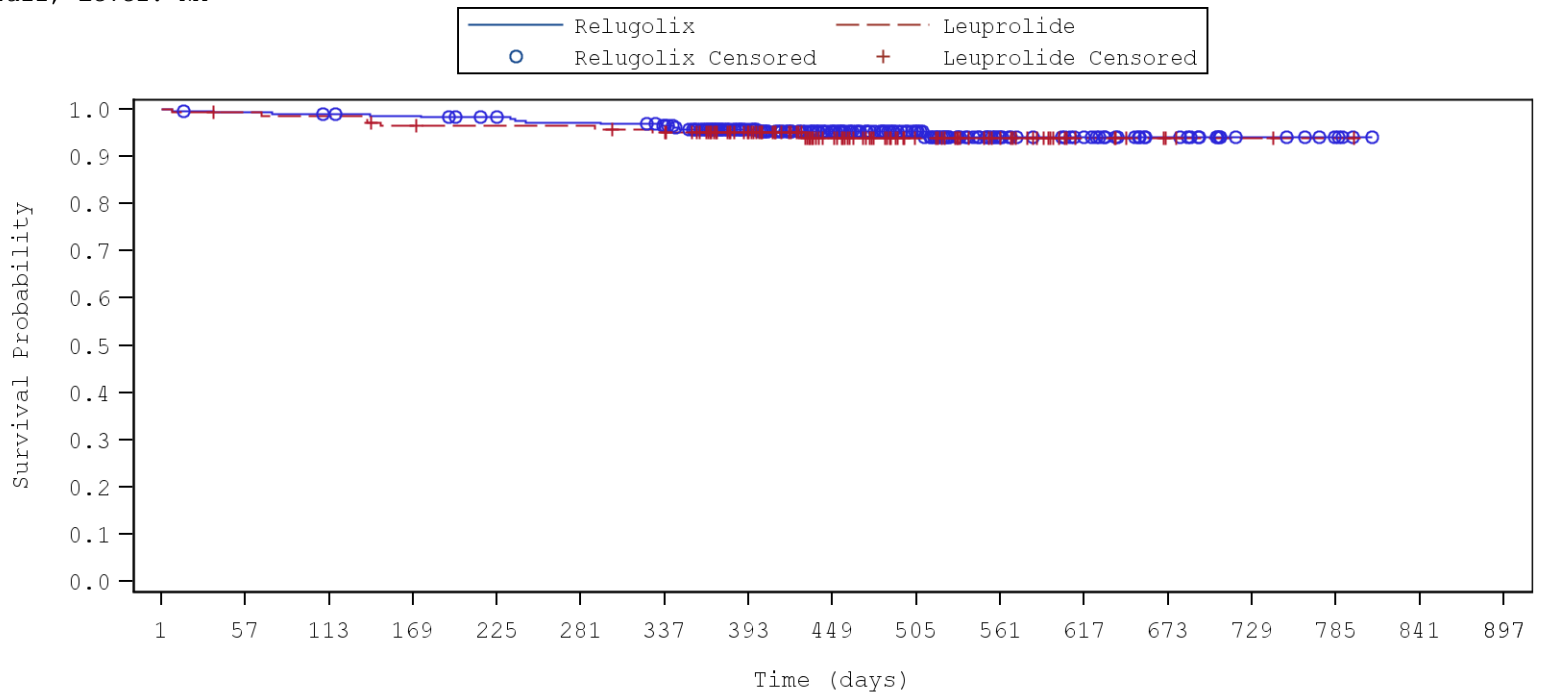
Myovant Sciences, Inc.: HERO AMNOG
Figure MOR.OS.KM.MITTM1: Kaplan-Meier Curves of Time to Overall Survival (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	287	285	283	279	275	268	199	141	91	47	32	18	8	4	0	0
Leuprolide	144	142	141	137	136	136	133	99	67	38	23	8	3	2	1	0	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 0.858 (0.359, 2.049)
P-value: 0.7298
Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (NE, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_MOR_KM.SAS
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6.1.2 Mortalität/ Morbidität

6.1.2.1 Major Adverse Cardiovascular Events

6.1.2.1.1 Hauptanalyse des kombinierten Endpunkts

Myovant Sciences, Inc.: HERO AMNOG

Table MC.T2MACE1.KM.SAFM1: Time to Pre-defined Major Adverse Cardiovascular Events (Safety Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	18 (6.2)	272 (93.8)	NE [NE;NE]	NE	0.895 [0.413;1.938]	0.7776
Leuprolide	144	10 (6.9)	134 (93.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Deaths due to all causes.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HR and 95% CI are based on a Cox proportional hazards model adjusting for treatment. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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6.1.2.1.2 Sensitivitätsanalyse des kombinierten Endpunkts

Myovant Sciences, Inc.: HERO AMNOG

Table MC.T2MACE2.KM.SAFM1: Time to Post-hoc Defined Major Adverse Cardiovascular Events (Safety Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	11 (3.8)	279 (96.2)	NE [NE;NE]	NE	0.778 [0.302;2.007]	0.6038
Leuprolide	144	7 (4.9)	137 (95.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group.
Search criteria for MACE events include Myocardial infarction SMQ (broad), Central nervous system haemorrhages and cerebrovascular conditions SMQ (broad), and Cardiovascular deaths.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HR and 95% CI are based on a Cox proportional hazards model adjusting for treatment. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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6.1.2.1.3 Einzelkomponenten

Myovant Sciences, Inc.: HERO AMNOG

Table MC.T2DTHALL.KM.SAFM1: Time to Adverse Events leading to Death (All Causes) (Safety Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	10 (3.4)	280 (96.6)	NE [NE;NE]	NE	0.715 [0.272;1.878]	0.4955
Leuprolide	144	7 (4.9)	137 (95.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HR and 95% CI are based on a Cox proportional hazards model adjusting for treatment. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Subject 205008 has a death date but no corresponding AE documented. The death (due to all causes) has been analysed using the death date (different to the CSR analysis).
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Myovant Sciences, Inc.: HERO AMNOG

Table MC.T2DTHCV.KM.SAFM1: Time to Cardiovascular Events (including MI and Stroke) leading to Death (Safety Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	3 (1.0)	287 (99.0)	NE [NE;NE]	NE	0.500 [0.101;2.478]	0.3962
Leuprolide	144	3 (2.1)	141 (97.9)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group.
Cardiovascular deaths are selected manually by medical experts.
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HR and 95% CI are based on a Cox proportional hazards model adjusting for treatment. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Table MC.T2NDMI.KM.SAFM1: Time to Non-deadly Myocardial Infarction (Safety Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	5 (1.7)	285 (98.3)	NE [NE;NE]	NE	1.246 [0.242;6.424]	0.7925
Leuprolide	144	2 (1.4)	142 (98.6)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group.
Non-deadly myocardial infarction includes non-fatal events in Myocardial infarction SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HR and 95% CI are based on a Cox proportional hazards model adjusting for treatment. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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Myovant Sciences, Inc.: HERO AMNOG

Table MC.T2NDSTRK.KM.SAFM1: Time to Non-deadly Stroke (Safety Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	3 (1.0)	287 (99.0)	NE [NE;NE]	NE	0.733 [0.122;4.387]	0.7337
Leuprolide	144	2 (1.4)	142 (98.6)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group.
Non-deadly stroke includes non-fatal events in Central Nervous System Haemorrhages and Cerebrovascular Conditions SMQ (broad).
Patients without an event are censored at the earliest date of ('Initiation of alternative therapies', 'End of AE reporting (Last exposure date + 30 days)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HR and 95% CI are based on a Cox proportional hazards model adjusting for treatment. The Exact method is used to handle tied event times. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MC_KM.SAS

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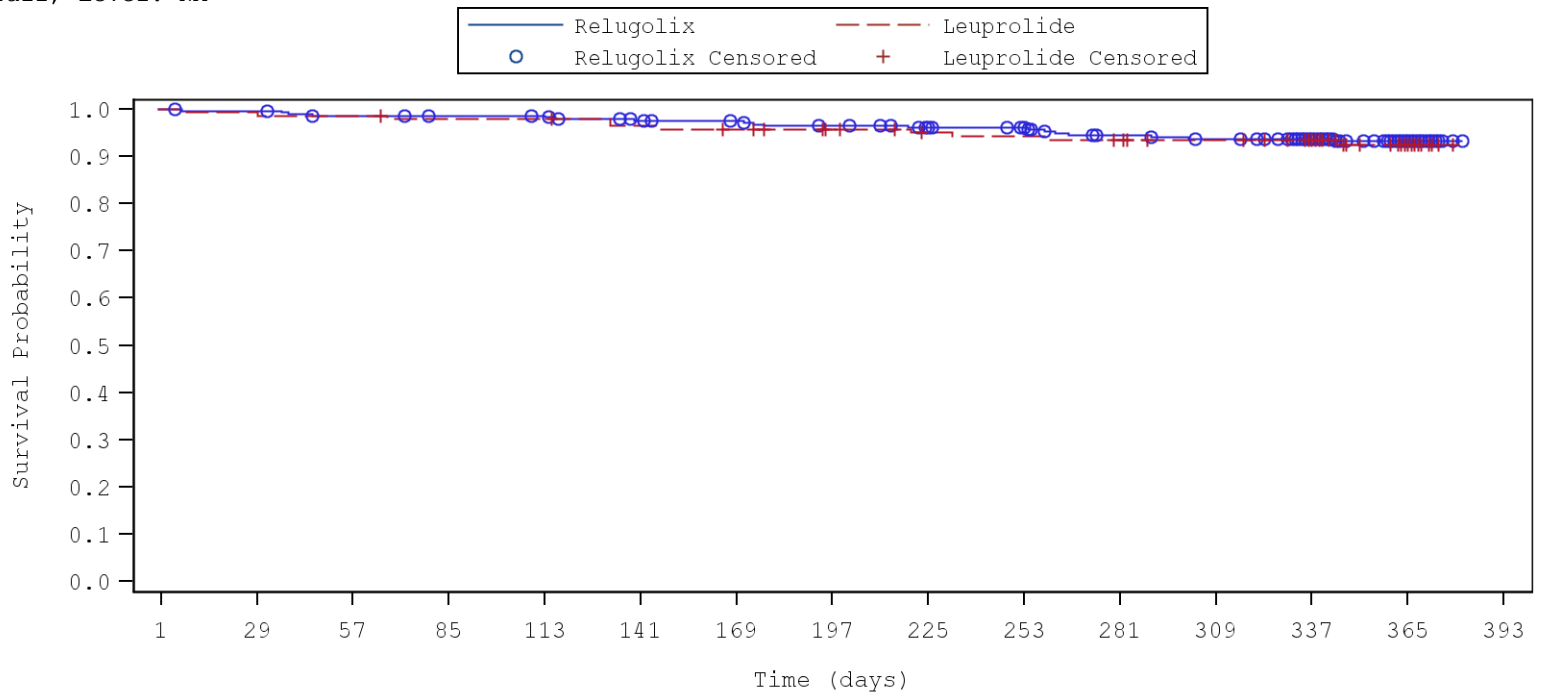
6.1.2.1.4 Kaplan-Meier-Kurven zum Endpunkt MACE

Myovant Sciences, Inc.: HERO AMNOG
Figure MC.T2MACE1.KM.SAFM1: Kaplan-Meier Curves of Time to Pre-defined Major Adverse Cardiovascular Events (Safety Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	288	282	280	279	271	268	263	257	253	243	239	219	135	0
Leuprolide	144	143	142	140	140	135	133	129	124	123	121	118	112	68	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 0.895 (0.413, 1.938)
P-value: 0.7776
Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (NE, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_MC_KM.SAS
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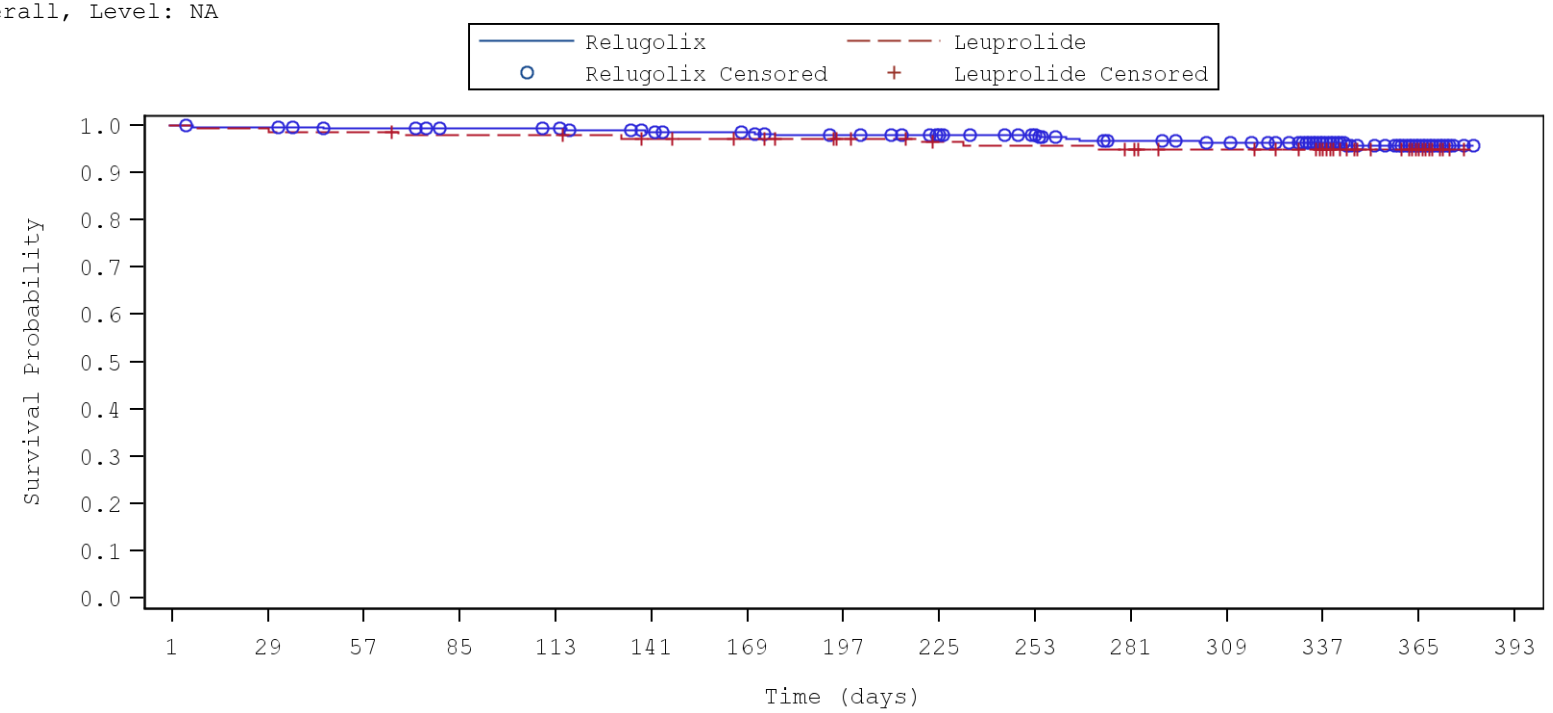
Myovant Sciences, Inc.: HERO AMNOG
Figure MC.T2MACE2.KM.SAFM1: Kaplan-Meier Curves of Time to Post-hoc Defined Major Adverse Cardiovascular Events (Safety Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	288	283	280	279	272	269	264	259	253	244	240	219	135	0
Leuprolide	144	143	142	140	140	135	133	129	124	123	121	118	112	68	0

Relugolix vs Leuprolide

Hazard Ratio (95% CI): 0.778 (0.302, 2.007)
P-value: 0.6038
Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (NE, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_MC_KM.SAS
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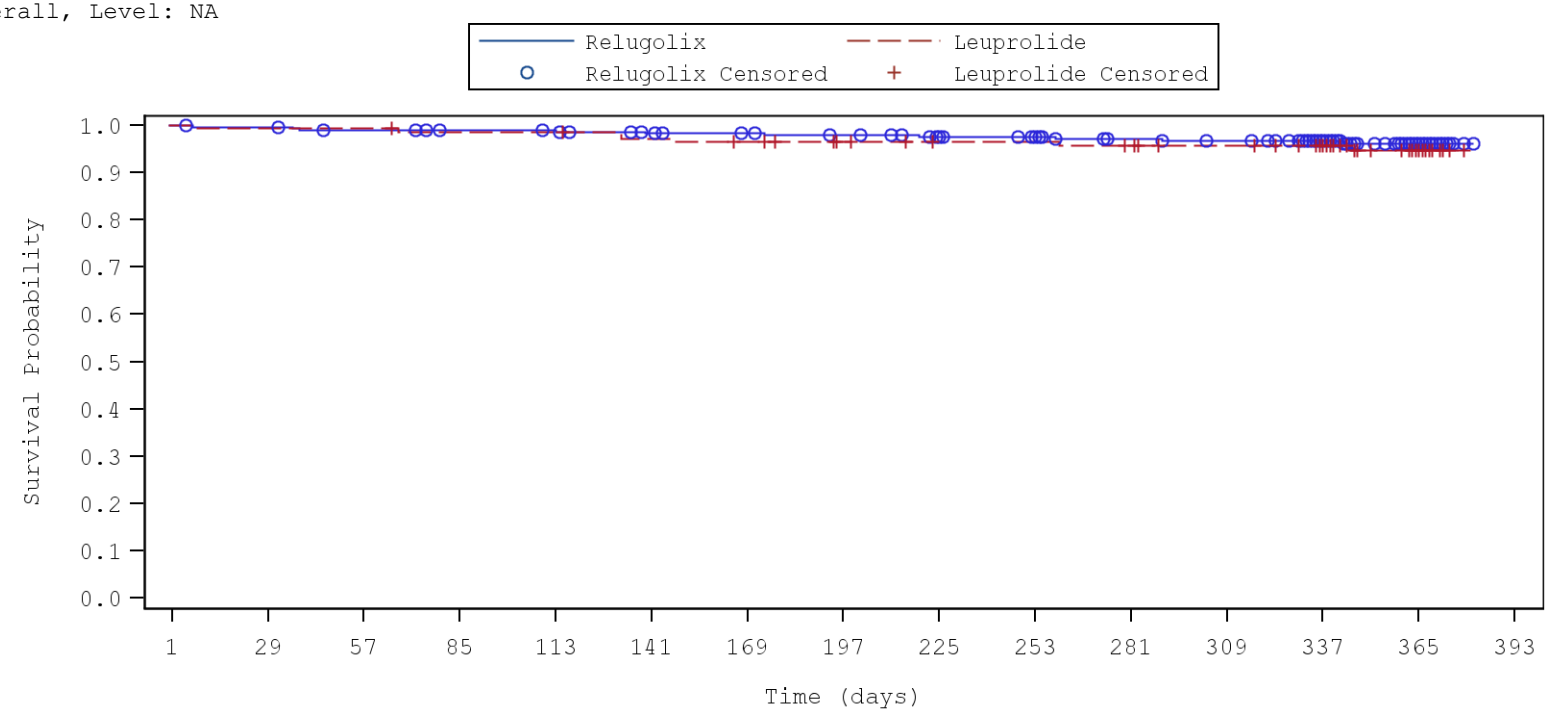
Myovant Sciences, Inc.: HERO AMNOG
Figure MC.T2DTHALL.KM.SAFM1: Kaplan-Meier Curves of Time to Adverse Events leading to Death (All Causes) (Safety Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	288	283	280	279	272	269	266	260	256	249	246	226	139	0
Leuprolide	144	143	143	141	141	136	134	130	126	126	124	121	115	70	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 0.715 (0.272, 1.878)
P-value: 0.4955
Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (NE, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_MC_KM.SAS
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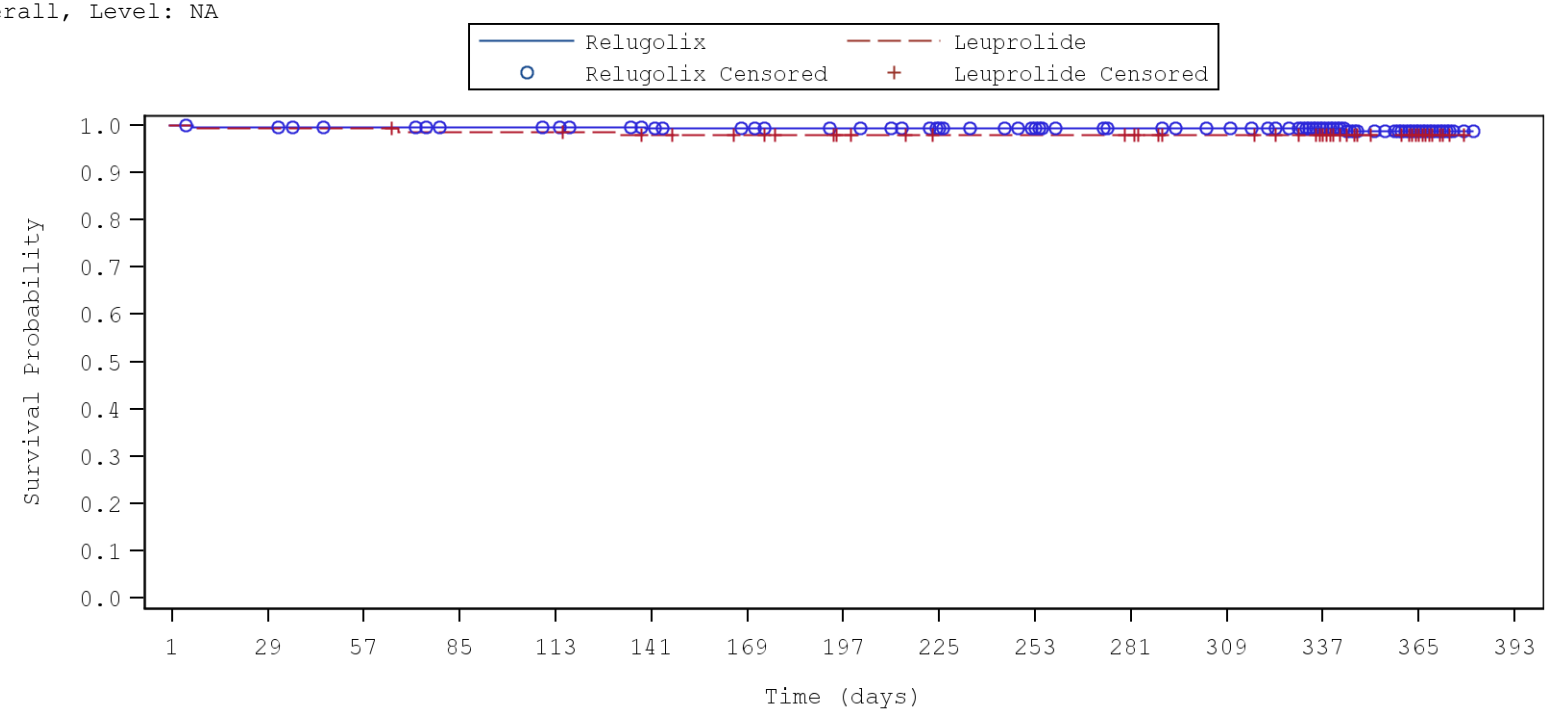
Myovant Sciences, Inc.: HERO AMNOG
Figure MC.T2DTHCV.KM.SAFM1: Kaplan-Meier Curves of Time to Cardiovascular Events (including MI and Stroke) leading to Death (Safety Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	288	284	280	279	273	270	267	262	256	250	247	226	139	0
Leuprolide	144	143	143	141	141	136	134	130	126	126	125	121	115	70	0

Relugolix vs Leuprolide

Hazard Ratio (95% CI): 0.500 (0.101, 2.478)
P-value: 0.3962

Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (NE, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_MC_KM.SAS
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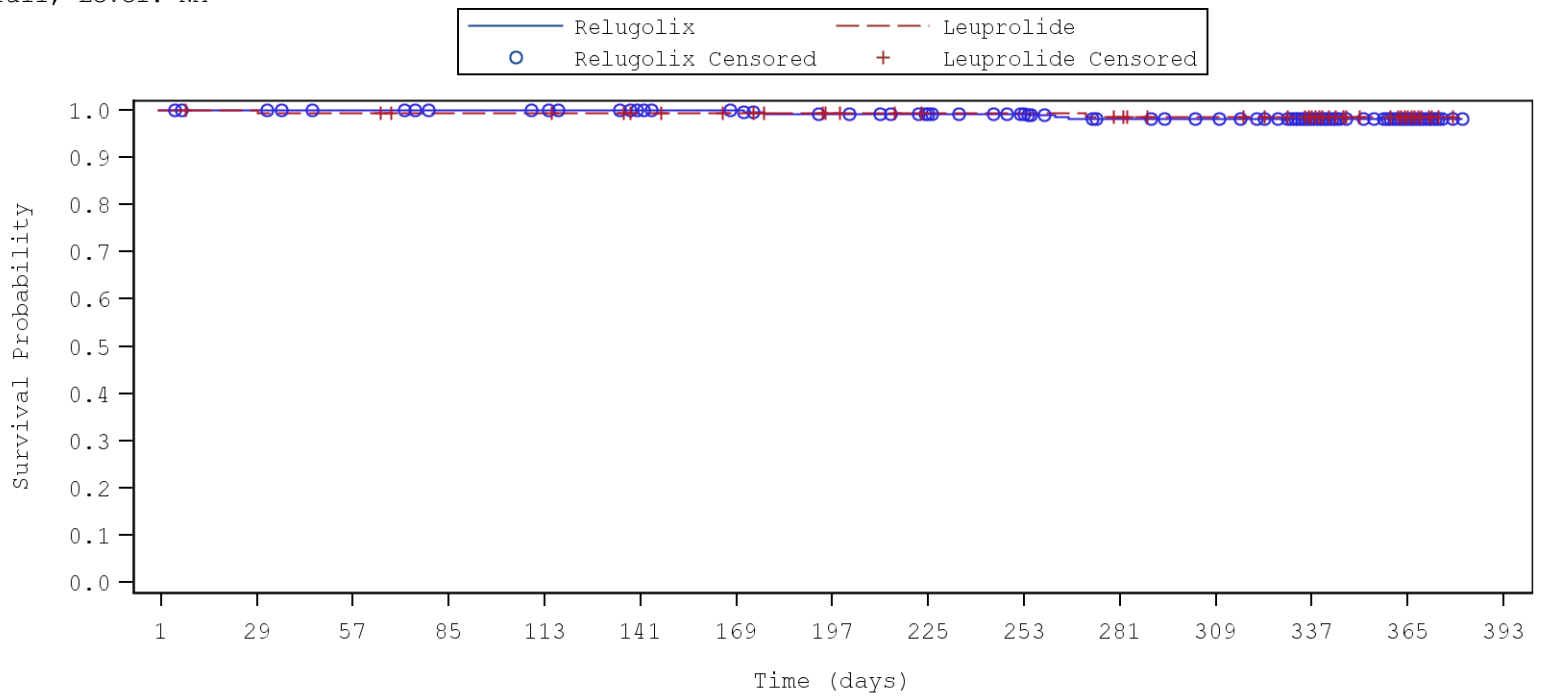
Myovant Sciences, Inc.: HERO AMNOG
Figure MC.T2NDMI.KM.SAFM1: Kaplan-Meier Curves of Time to Non-deadly Mycordial Infarction (Safety Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	288	284	280	279	273	270	265	260	254	245	242	221	137	0
Leuprolide	144	143	142	140	140	135	133	129	125	125	123	120	114	69	0

Relugolix vs Leuprolide

Hazard Ratio (95% CI): 1.246 (0.242, 6.424)
P-value: 0.7925

Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (NE, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_MC_KM.SAS
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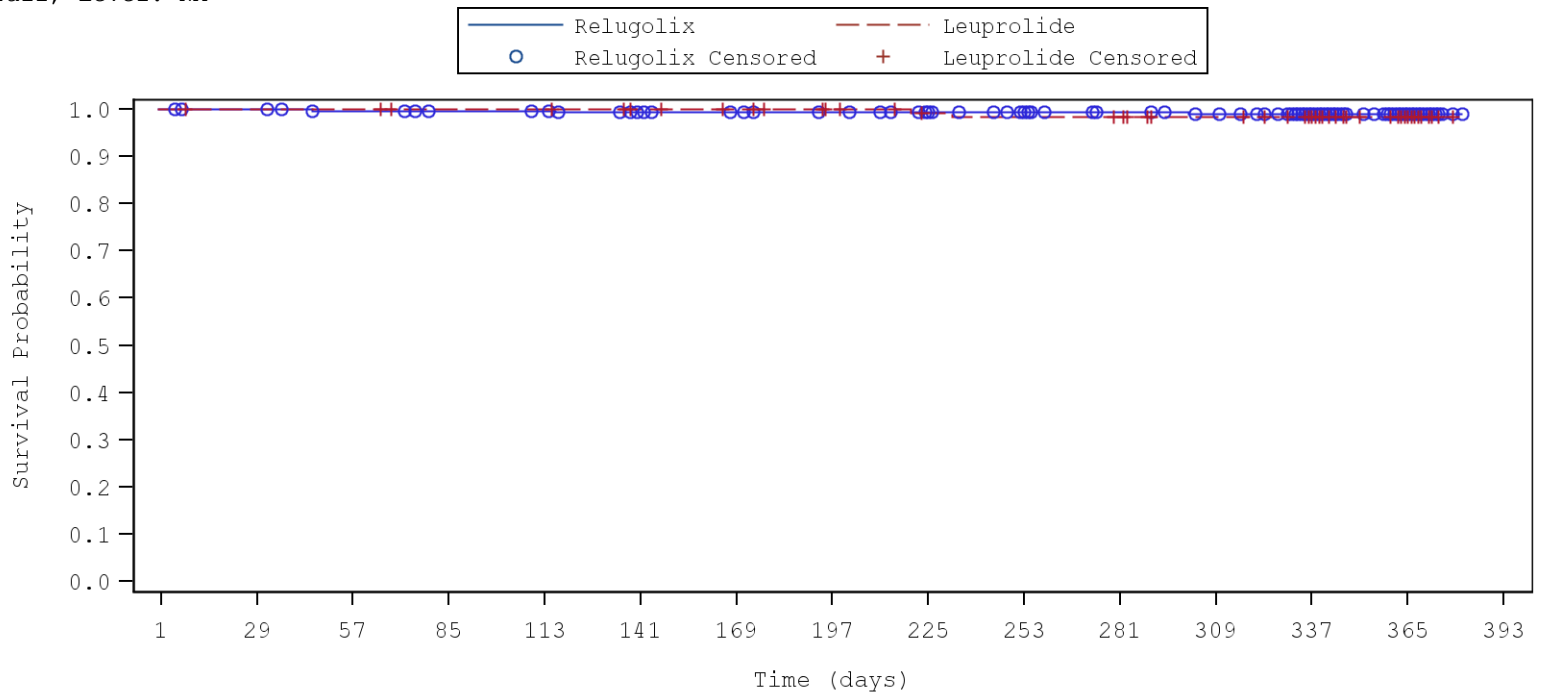
Myovant Sciences, Inc.: HERO AMNOG
Figure MC.T2NDSTRK.KM.SAFM1: Kaplan-Meier Curves of Time to Non-deadly Stroke (Safety Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	288	283	280	279	272	269	266	261	255	249	245	224	137	0
Leuprolide	144	143	143	141	141	136	134	130	125	124	123	119	113	69	0

Relugolix vs Leuprolide

Hazard Ratio (95% CI): 0.733 (0.122, 4.387)
P-value: 0.7337

Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (NE, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_MC_KM.SAS
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6.1.3 Morbidität

6.1.3.1 Gesundheitszustand (EuroQol-5-Dimension Visual Analog Scale)

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2EQ5D15.KM.MITTM1: Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	93 (32.1)	197 (67.9)	NE [344.0;NE]	NE	0.910 [0.643;1.287]	0.5944
Leuprolide	144	50 (34.7)	94 (65.3)	344.0 [343.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.EQ5DCHG.MM.MITTM1: Summary of Change from Baseline in EQ-5D VAS Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	288 (99.3)	79.03 (16.857)			
	Week 5 Day 1	278 (95.9)	79.74 (14.617)	276 (95.2) 0.24 (0.716)	0.69 [-1.61; 2.99] 0.5546	0.06 [-0.14; 0.26]
Leuprolide (N=144)	Baseline	144 (100.0)	79.60 (15.330)			
	Week 5 Day 1	143 (99.3)	79.51 (13.255)	143 (99.3) -0.45 (0.974)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	79.52 (15.086)	276 (95.2) -0.20 (0.801)	0.50 [-2.11; 3.11] 0.7054	0.04 [-0.16; 0.24]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	79.23 (15.358)	139 (96.5) -0.70 (1.105)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	78.39 (16.875)	269 (92.8) -1.39 (0.876)	-0.44 [-3.34; 2.46] 0.7651	-0.03 [-0.24; 0.18]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	79.31 (13.968)	131 (91.0) -0.95 (1.227)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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Table QS.EQ5DCHG.MM.MITTM1: Summary of Change from Baseline in EQ-5D VAS Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	78.58 (14.915)	247 (85.2) -1.70 (0.806)	0.32 [-2.33; 2.96] 0.8141	0.03 [-0.19; 0.24]
Leuprolide (N=144)	Week 37 Day 1	122 (84.7)	78.51 (12.792)	122 (84.7) -2.01 (1.121)		
Relugolix (N=290)	Week 49 Day 1	237 (81.7)	77.91 (15.712)	236 (81.4) -2.45 (0.896)	-0.60 [-3.59; 2.40] 0.6959	-0.04 [-0.27; 0.18]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	78.67 (13.817)	110 (76.4) -1.86 (1.273)		
Relugolix (N=290)	Overall	284 (97.9)	78.46 (13.250)	282 (97.2) -1.10 (0.627)	0.09 [-1.90; 2.09] 0.9258	0.01 [-0.19; 0.21]
Leuprolide (N=144)	Overall	143 (99.3)	78.90 (11.360)	143 (99.3) -1.19 (0.856)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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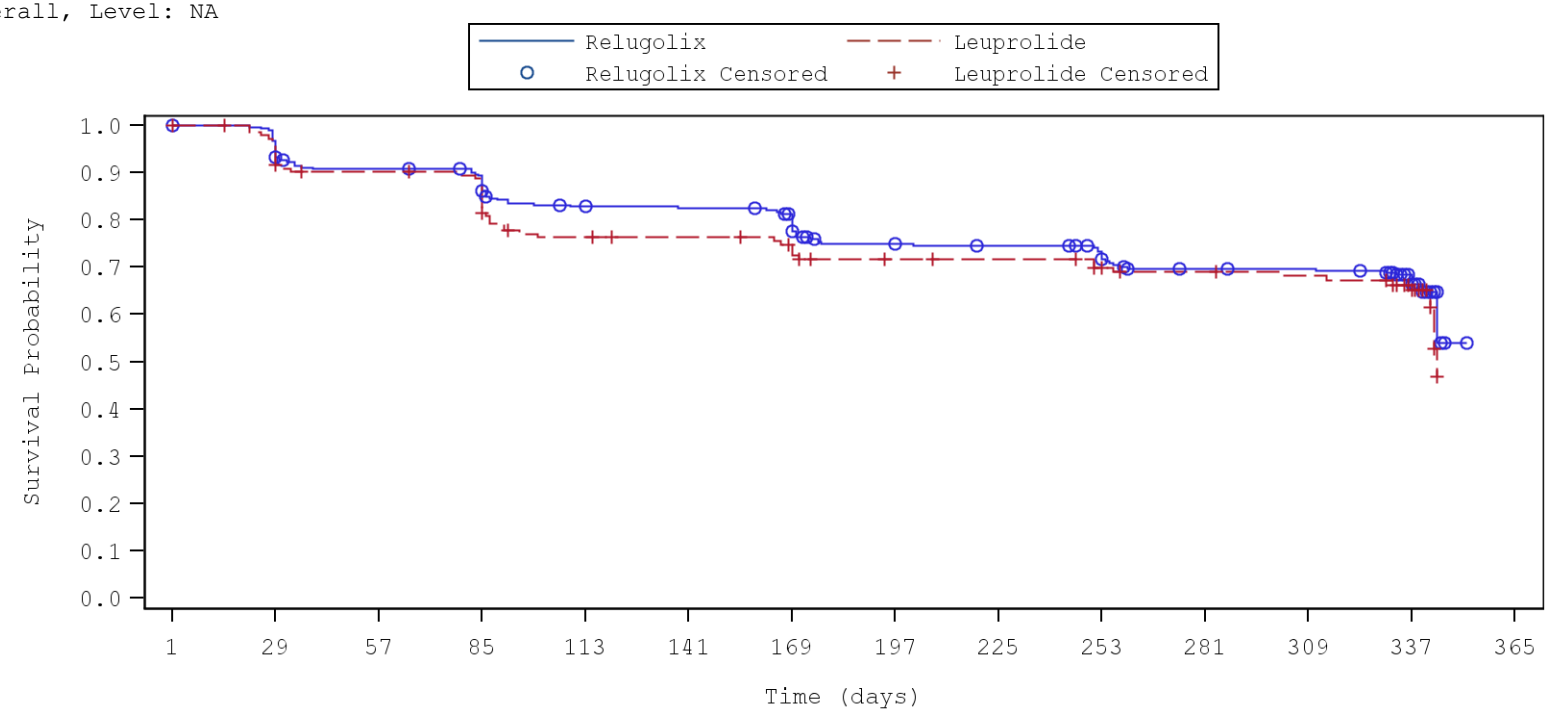
Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2EQ5D15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Decrease in EQ-5D VAS Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	273	253	247	226	224	218	194	190	184	170	169	128	0
Leuprolide	144	137	126	123	102	100	96	89	88	80	77	75	61	0

Relugolix vs Leuprolide

Hazard Ratio (95% CI): 0.910 (0.643, 1.287)
P-value: 0.5944

Relugolix Median (95% CI): NE (344.0, NE)
Leuprolide Median (95% CI): 344.0 (343.0, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_QS_KM.SAS
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6.1.3.2 Symptomatik (European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire C30)

6.1.3.2.1 Skala: Fatigue

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2FAT15.KM.MITTM1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	119 (41.0)	171 (59.0)	344.0 [338.0;NE]	1.0	0.952 [0.699;1.299]	0.7584
Leuprolide	144	61 (42.4)	83 (57.6)	343.0 [337.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.FATCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Fatigue Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	22.54 (20.905)			
	Week 5 Day 1	275 (94.8)	21.45 (19.612)	270 (93.1) 0.07 (0.983)	0.19 [-2.94; 3.33] 0.9028	0.01 [-0.19; 0.22]
Leuprolide (N=144)	Baseline	143 (99.3)	19.58 (18.970)			
	Week 5 Day 1	143 (99.3)	19.74 (17.564)	142 (98.6) -0.13 (1.331)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	24.75 (19.369)	273 (94.1) 3.60 (1.068)	-0.92 [-4.39; 2.54] 0.6004	-0.05 [-0.26; 0.15]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	24.30 (20.833)	138 (95.8) 4.52 (1.471)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	26.42 (21.482)	266 (91.7) 5.48 (1.130)	0.53 [-3.17; 4.23] 0.7781	0.03 [-0.18; 0.24]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	24.00 (19.723)	131 (91.0) 4.95 (1.570)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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Table QS.FATCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Fatigue Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	24.96 (21.257)	244 (84.1) 4.94 (1.247)	-0.95 [-5.06; 3.17] 0.6511	-0.05 [-0.27; 0.17]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	24.72 (20.190)	120 (83.3) 5.89 (1.741)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	24.86 (20.148)	232 (80.0) 5.11 (1.237)	-0.72 [-4.83; 3.39] 0.7316	-0.04 [-0.27; 0.19]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	24.34 (20.164)	110 (76.4) 5.83 (1.744)		
Relugolix (N=290)	Overall	284 (97.9)	24.95 (17.308)	279 (96.2) 3.84 (0.905)	-0.37 [-3.26; 2.51] 0.7996	-0.02 [-0.22; 0.18]
Leuprolide (N=144)	Overall	143 (99.3)	23.77 (17.157)	142 (98.6) 4.21 (1.238)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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6.1.3.2.2 Skala: Schmerz

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2PAIN15.KM.MITTM1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	148 (51.0)	142 (49.0)	292.0 [178.0;339.0]	-45.0	1.140 [0.859;1.514]	0.3652
Leuprolide	144	72 (50.0)	72 (50.0)	337.0 [253.0;343.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat.

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Table QS.PAINCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Pain Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	20.60 (25.243)			
	Week 5 Day 1	275 (94.8)	15.82 (19.557)	270 (93.1) -3.87 (1.038)	0.60 [-2.71; 3.92] 0.7221	0.04 [-0.17; 0.24]
Leuprolide (N=144)	Baseline	143 (99.3)	19.23 (24.411)			
	Week 5 Day 1	143 (99.3)	14.69 (20.507)	142 (98.6) -4.47 (1.405)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	16.31 (20.606)	273 (94.1) -3.36 (1.142)	-0.21 [-3.93; 3.50] 0.9107	-0.01 [-0.22; 0.19]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	15.95 (22.511)	138 (95.8) -3.14 (1.576)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	19.14 (23.790)	266 (91.7) -0.27 (1.286)	2.48 [-1.77; 6.73] 0.2516	0.12 [-0.09; 0.33]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	15.39 (22.228)	131 (91.0) -2.75 (1.797)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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Table QS.PAINCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Pain Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	16.47 (20.807)	244 (84.1) -2.29 (1.258)	0.21 [-3.94; 4.35] 0.9226	0.01 [-0.21; 0.23]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	15.56 (21.251)	120 (83.3) -2.50 (1.756)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	18.15 (22.364)	232 (80.0) -0.69 (1.340)	-0.52 [-5.00; 3.95] 0.8177	-0.03 [-0.25; 0.20]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	17.73 (21.091)	110 (76.4) -0.17 (1.895)		
Relugolix (N=290)	Overall	284 (97.9)	17.47 (17.627)	279 (96.2) -2.10 (0.930)	0.51 [-2.46; 3.48] 0.7356	0.03 [-0.17; 0.23]
Leuprolide (N=144)	Overall	143 (99.3)	16.44 (18.763)	142 (98.6) -2.61 (1.274)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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6.1.3.2.3 Skala: Übelkeit und Erbrechen

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2NAUS15.KM.MITTM1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	73 (25.2)	217 (74.8)	NE [NE;NE]	NE	1.023 [0.683;1.532]	0.9135
Leuprolide	144	35 (24.3)	109 (75.7)	NE [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.NAUSCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Nausea and Vomitting Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	2.70 (8.203)			
	Week 5 Day 1	275 (94.8)	2.42 (7.547)	270 (93.1) -0.11 (0.472)	-1.33 [-2.86; 0.21] 0.0894	-0.18 [-0.38; 0.03]
Leuprolide (N=144)	Baseline	143 (99.3)	3.26 (9.539)			
	Week 5 Day 1	143 (99.3)	3.96 (10.270)	142 (98.6) 1.22 (0.644)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	2.71 (7.880)	273 (94.1) 0.22 (0.470)	0.19 [-1.36; 1.73] 0.8137	0.02 [-0.18; 0.23]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	2.76 (9.106)	138 (95.8) 0.03 (0.651)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	2.90 (8.181)	266 (91.7) 0.56 (0.525)	-0.86 [-2.61; 0.88] 0.3305	-0.11 [-0.31; 0.10]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	3.69 (10.995)	131 (91.0) 1.42 (0.735)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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Table QS.NAUSCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Nausea and Vomitting Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	2.76 (8.887)	244 (84.1) 0.56 (0.571)	-0.15 [-2.06; 1.76] 0.8740	-0.02 [-0.24; 0.20]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	3.06 (8.364)	120 (83.3) 0.72 (0.804)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	1.62 (5.187)	232 (80.0) -0.61 (0.412)	-1.73 [-3.09; -0.36] 0.0133	-0.29 [-0.51; -0.06]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	3.64 (8.562)	110 (76.4) 1.12 (0.582)		
Relugolix (N=290)	Overall	284 (97.9)	2.68 (5.603)	279 (96.2) 0.12 (0.343)	-0.78 [-1.87; 0.32] 0.1635	-0.10 [-0.30; 0.10]
Leuprolide (N=144)	Overall	143 (99.3)	3.68 (8.446)	142 (98.6) 0.90 (0.470)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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6.1.3.2.4 Skala: Atemnot

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2DYSP15.KM.MITTM1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	101 (34.8)	189 (65.2)	NE [344.0;NE]	NE	0.652 [0.479;0.889]	0.0069
Leuprolide	144	68 (47.2)	76 (52.8)	339.0 [260.0;343.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.DYSPCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Dyspnoea Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	10.33 (18.874)			
	Week 5 Day 1	275 (94.8)	8.85 (16.313)	270 (93.1) -1.26 (0.884)	-3.13 [-5.94; -0.32] 0.0291	-0.23 [-0.43; -0.02]
Leuprolide (N=144)	Baseline	143 (99.3)	9.79 (18.903)			
	Week 5 Day 1	143 (99.3)	11.89 (20.328)	142 (98.6) 1.87 (1.194)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	11.43 (18.867)	273 (94.1) 1.33 (1.075)	-4.03 [-7.54; -0.52] 0.0247	-0.24 [-0.44; -0.03]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	15.11 (23.475)	138 (95.8) 5.36 (1.487)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	14.20 (21.702)	266 (91.7) 3.96 (1.200)	-1.55 [-5.52; 2.43] 0.4451	-0.08 [-0.29; 0.13]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	15.01 (23.099)	131 (91.0) 5.50 (1.678)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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Table QS.DYSPCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Dyspnoea Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	13.98 (21.251)	244 (84.1) 4.58 (1.240)	-1.88 [-6.00; 2.24] 0.3706	-0.10 [-0.32; 0.12]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	15.28 (22.824)	120 (83.3) 6.46 (1.738)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	13.42 (19.541)	232 (80.0) 3.90 (1.279)	-5.04 [-9.34; -0.75] 0.0214	-0.26 [-0.49; -0.03]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	16.67 (24.210)	110 (76.4) 8.94 (1.816)		
Relugolix (N=290)	Overall	284 (97.9)	12.39 (15.856)	279 (96.2) 2.50 (0.862)	-3.13 [-5.89; -0.36] 0.0268	-0.18 [-0.38; 0.02]
Leuprolide (N=144)	Overall	143 (99.3)	15.34 (20.290)	142 (98.6) 5.63 (1.184)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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6.1.3.2.5 Skala: Appetitlosigkeit

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2APPT15.KM.MITTM1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	71 (24.5)	219 (75.5)	NE [344.0;NE]	NE	1.078 [0.712;1.632]	0.7231
Leuprolide	144	33 (22.9)	111 (77.1)	NE [342.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.APPTCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Appetite Loss Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	11.85 (22.686)			
	Week 5 Day 1	275 (94.8)	5.70 (14.091)	270 (93.1) -5.22 (0.949)	-4.24 [-7.32; -1.16] 0.0071	-0.28 [-0.48; -0.08]
Leuprolide (N=144)	Baseline	143 (99.3)	10.96 (21.221)			
	Week 5 Day 1	143 (99.3)	9.79 (20.870)	142 (98.6) -0.98 (1.294)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	6.26 (16.574)	273 (94.1) -4.31 (0.920)	0.65 [-2.36; 3.66] 0.6708	0.04 [-0.16; 0.25]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	5.76 (16.015)	138 (95.8) -4.96 (1.272)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	6.91 (15.261)	266 (91.7) -3.60 (0.900)	0.30 [-2.65; 3.26] 0.8403	0.02 [-0.19; 0.23]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	5.85 (15.733)	131 (91.0) -3.90 (1.254)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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Table QS.APPTCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Appetite Loss Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	7.12 (17.188)	244 (84.1) -3.06 (1.027)	0.52 [-2.88; 3.93] 0.7629	0.03 [-0.18; 0.25]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	6.11 (14.959)	120 (83.3) -3.58 (1.439)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	6.21 (15.033)	232 (80.0) -3.91 (1.039)	-2.65 [-6.14; 0.84] 0.1367	-0.17 [-0.40; 0.05]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	8.18 (17.596)	110 (76.4) -1.27 (1.479)		
Relugolix (N=290)	Overall	284 (97.9)	6.95 (12.110)	279 (96.2) -4.02 (0.672)	-1.08 [-3.21; 1.04] 0.3171	-0.07 [-0.27; 0.13]
Leuprolide (N=144)	Overall	143 (99.3)	8.25 (14.949)	142 (98.6) -2.94 (0.916)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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6.1.3.2.6 Skala: Schlaflosigkeit

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2INSO15.KM.MITTM1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	134 (46.2)	156 (53.8)	338.0 [254.0;NE]	-1.0	1.020 [0.760;1.369]	0.8948
Leuprolide	144	68 (47.2)	76 (52.8)	339.0 [256.0;344.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.INSOCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Insomnia Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	21.36 (27.267)			
	Week 5 Day 1	275 (94.8)	22.55 (25.646)	270 (93.1) 1.42 (1.324)	3.08 [-1.19; 7.34] 0.1569	0.15 [-0.06; 0.35]
Leuprolide (N=144)	Baseline	143 (99.3)	20.51 (24.995)			
	Week 5 Day 1	143 (99.3)	18.88 (23.590)	142 (98.6) -1.65 (1.801)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	24.43 (27.819)	273 (94.1) 3.35 (1.477)	0.25 [-4.59; 5.09] 0.9191	0.01 [-0.19; 0.21]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	23.50 (26.146)	138 (95.8) 3.10 (2.045)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	24.69 (27.707)	266 (91.7) 3.85 (1.470)	1.51 [-3.34; 6.35] 0.5410	0.07 [-0.14; 0.27]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	21.63 (24.433)	131 (91.0) 2.34 (2.053)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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Table QS.INSOCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Insomnia Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	23.79 (25.156)	244 (84.1) 3.44 (1.417)	0.53 [-4.12; 5.19] 0.8221	0.02 [-0.19; 0.24]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	22.50 (23.336)	120 (83.3) 2.91 (1.977)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	22.60 (24.937)	232 (80.0) 2.56 (1.468)	0.12 [-4.77; 5.01] 0.9611	0.01 [-0.22; 0.23]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	21.82 (22.772)	110 (76.4) 2.44 (2.079)		
Relugolix (N=290)	Overall	284 (97.9)	23.97 (21.674)	279 (96.2) 2.92 (1.054)	1.10 [-2.24; 4.43] 0.5182	0.05 [-0.15; 0.25]
Leuprolide (N=144)	Overall	143 (99.3)	22.33 (19.235)	142 (98.6) 1.83 (1.439)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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6.1.3.2.7 Skala: Diarrhoe

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2DIAR15.KM.MITTM1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	68 (23.4)	222 (76.6)	NE [NE;NE]	NE	0.759 [0.520;1.107]	0.1526
Leuprolide	144	45 (31.3)	99 (68.8)	NE [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.DIARCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Diarrhoea Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	5.75 (14.087)			
	Week 5 Day 1	275 (94.8)	6.18 (14.457)	270 (93.1) 0.02 (0.818)	0.32 [-2.34; 2.97] 0.8142	0.02 [-0.18; 0.23]
Leuprolide (N=144)	Baseline	143 (99.3)	5.59 (14.794)			
	Week 5 Day 1	143 (99.3)	5.59 (16.304)	142 (98.6) -0.29 (1.114)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	6.26 (14.502)	273 (94.1) 0.33 (0.798)	-0.44 [-3.05; 2.17] 0.7405	-0.03 [-0.24; 0.17]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	6.71 (14.568)	138 (95.8) 0.77 (1.104)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	6.30 (14.566)	266 (91.7) 0.38 (0.902)	-0.56 [-3.56; 2.43] 0.7118	-0.04 [-0.25; 0.17]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	6.62 (15.146)	131 (91.0) 0.94 (1.264)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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Table QS.DIARCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Diarrhoea Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	5.65 (13.890)	244 (84.1) 0.23 (0.988)	-2.06 [-5.36; 1.23] 0.2193	-0.14 [-0.35; 0.08]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	7.78 (17.677)	120 (83.3) 2.29 (1.389)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	5.65 (14.295)	232 (80.0) 0.16 (0.879)	1.44 [-1.50; 4.38] 0.3369	0.11 [-0.12; 0.34]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	4.55 (13.146)	110 (76.4) -1.28 (1.248)		
Relugolix (N=290)	Overall	284 (97.9)	6.07 (10.899)	279 (96.2) 0.22 (0.588)	-0.26 [-2.13; 1.60] 0.7830	-0.02 [-0.22; 0.18]
Leuprolide (N=144)	Overall	143 (99.3)	6.27 (10.661)	142 (98.6) 0.48 (0.804)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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6.1.3.2.8 Skala: Obstipation

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2CONS15.KM.MITTM1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	98 (33.8)	192 (66.2)	NE [NE;NE]	NE	0.923 [0.661;1.290]	0.6398
Leuprolide	144	54 (37.5)	90 (62.5)	NE [339.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.CONSCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Constipation Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	12.56 (22.652)			
	Week 5 Day 1	275 (94.8)	9.33 (18.395)	270 (93.1) -2.31 (1.050)	-2.92 [-6.29; 0.45] 0.0889	-0.18 [-0.38; 0.03]
Leuprolide (N=144)	Baseline	143 (99.3)	13.99 (23.541)			
	Week 5 Day 1	143 (99.3)	13.05 (22.737)	142 (98.6) 0.61 (1.426)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	11.07 (20.008)	273 (94.1) -0.03 (1.118)	-1.07 [-4.71; 2.57] 0.5638	-0.06 [-0.26; 0.14]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	13.67 (21.163)	138 (95.8) 1.04 (1.546)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	10.99 (20.289)	266 (91.7) 0.23 (1.230)	-4.48 [-8.54; -0.42] 0.0308	-0.23 [-0.44; -0.02]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	16.54 (23.885)	131 (91.0) 4.71 (1.721)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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Table QS.CONSCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Constipation Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	11.29 (20.948)	244 (84.1) 0.97 (1.300)	-5.04 [-9.35; -0.73] 0.0220	-0.25 [-0.47; -0.04]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	16.67 (24.445)	120 (83.3) 6.01 (1.821)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	10.45 (20.720)	232 (80.0) 0.33 (1.347)	-3.47 [-7.98; 1.05] 0.1320	-0.17 [-0.40; 0.05]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	14.55 (23.256)	110 (76.4) 3.80 (1.913)		
Relugolix (N=290)	Overall	284 (97.9)	11.03 (15.972)	279 (96.2) -0.16 (0.887)	-3.39 [-6.22; -0.57] 0.0186	-0.18 [-0.38; 0.02]
Leuprolide (N=144)	Overall	143 (99.3)	15.30 (19.904)	142 (98.6) 3.24 (1.216)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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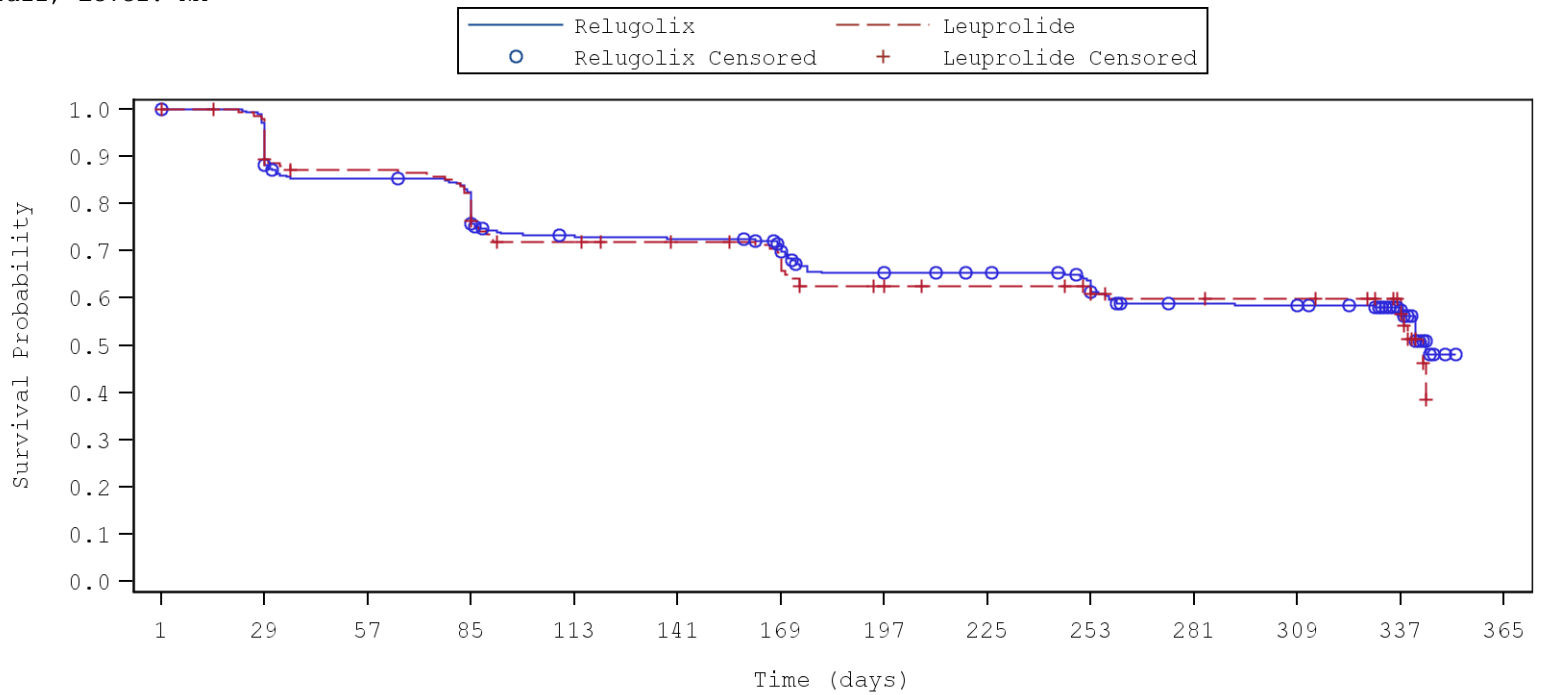
6.1.3.2.9 Kaplan-Meier-Kurven zu Time-to-Event-Analysen des EORTC-QLQ-C30 (Morbidität)

Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2FAT15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Fatigue Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	271	236	227	198	196	189	168	165	158	142	141	104	0
Leuprolide	144	138	121	114	96	93	89	78	76	73	68	67	54	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 0.952 (0.699, 1.299)
P-value: 0.7584
Relugolix Median (95% CI): 344.0 (338.0, NE)
Leuprolide Median (95% CI): 343.0 (337.0, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_QS_KM.SAS
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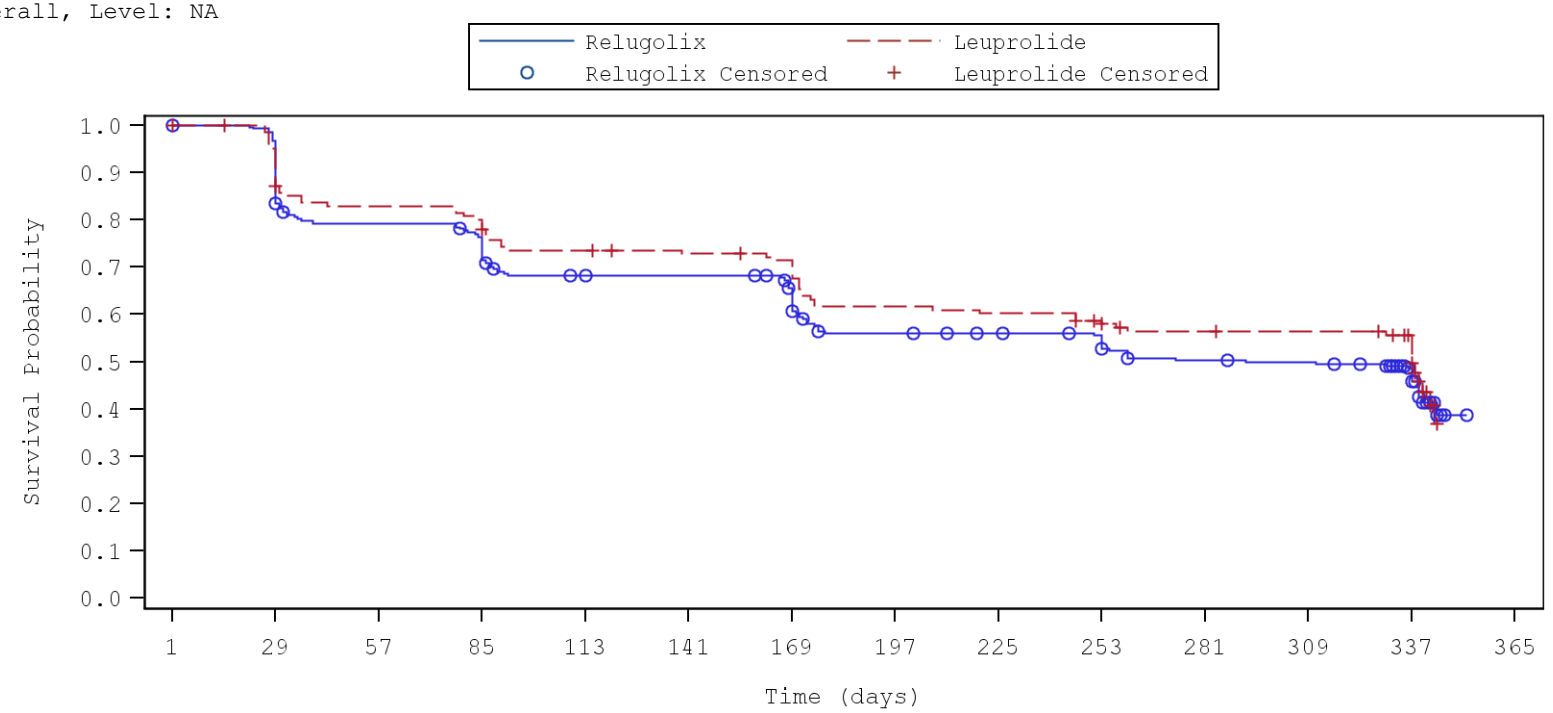
Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2PAIN15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Pain Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	270	219	210	185	184	173	143	140	137	122	120	91	0
Leuprolide	144	134	116	112	102	99	96	83	81	75	69	68	57	0

Relugolix vs Leuprolide

Hazard Ratio (95% CI): 1.140 (0.859, 1.514)
P-value: 0.3652

Relugolix Median (95% CI): 292.0 (178.0, 339.0)
Leuprolide Median (95% CI): 337.0 (253.0, 343.0)

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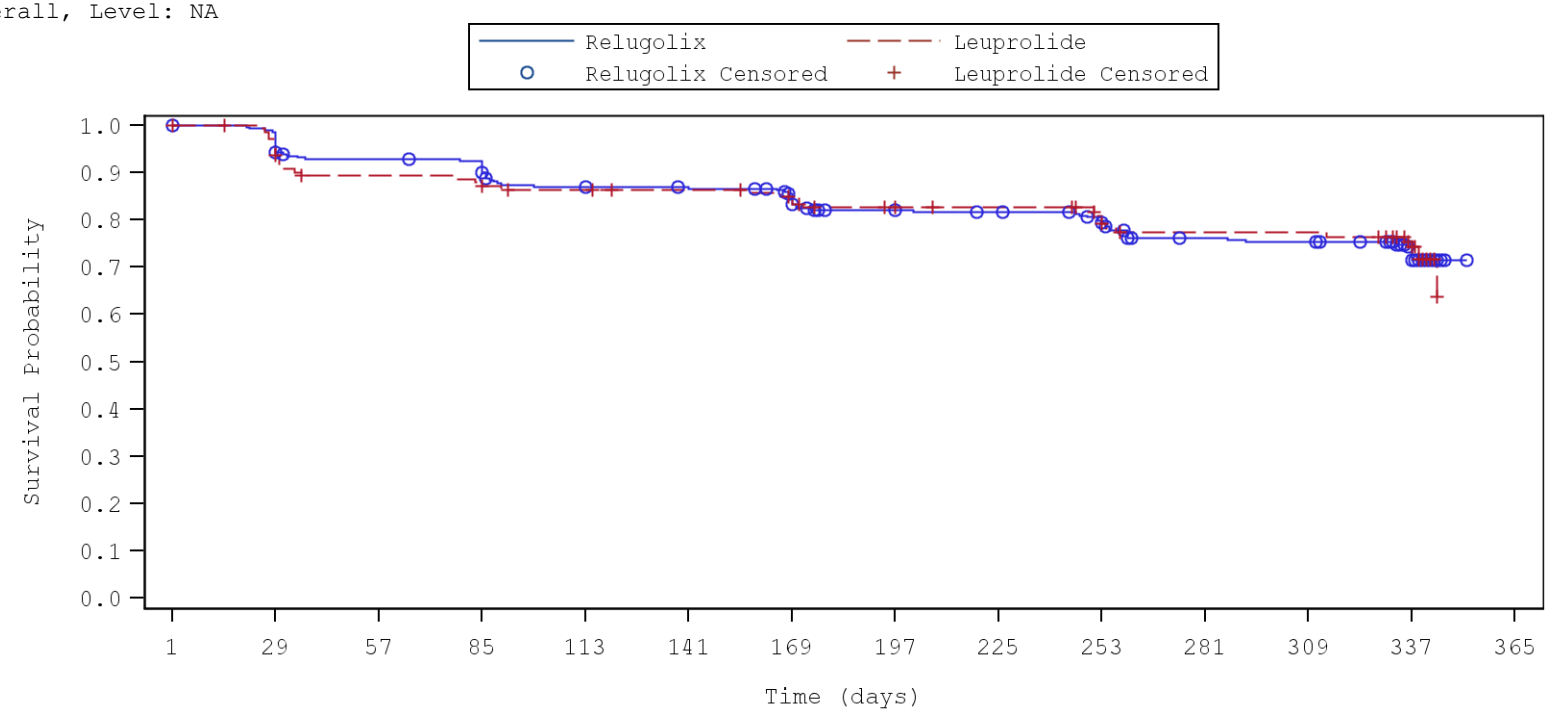
Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2NAUS15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Nausea and Vomitting Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	275	257	255	238	236	228	212	208	200	183	181	133	0
Leuprolide	144	137	124	122	116	114	110	104	102	93	86	86	67	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 1.023 (0.683, 1.532)
P-value: 0.9135
Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (344.0, NE)

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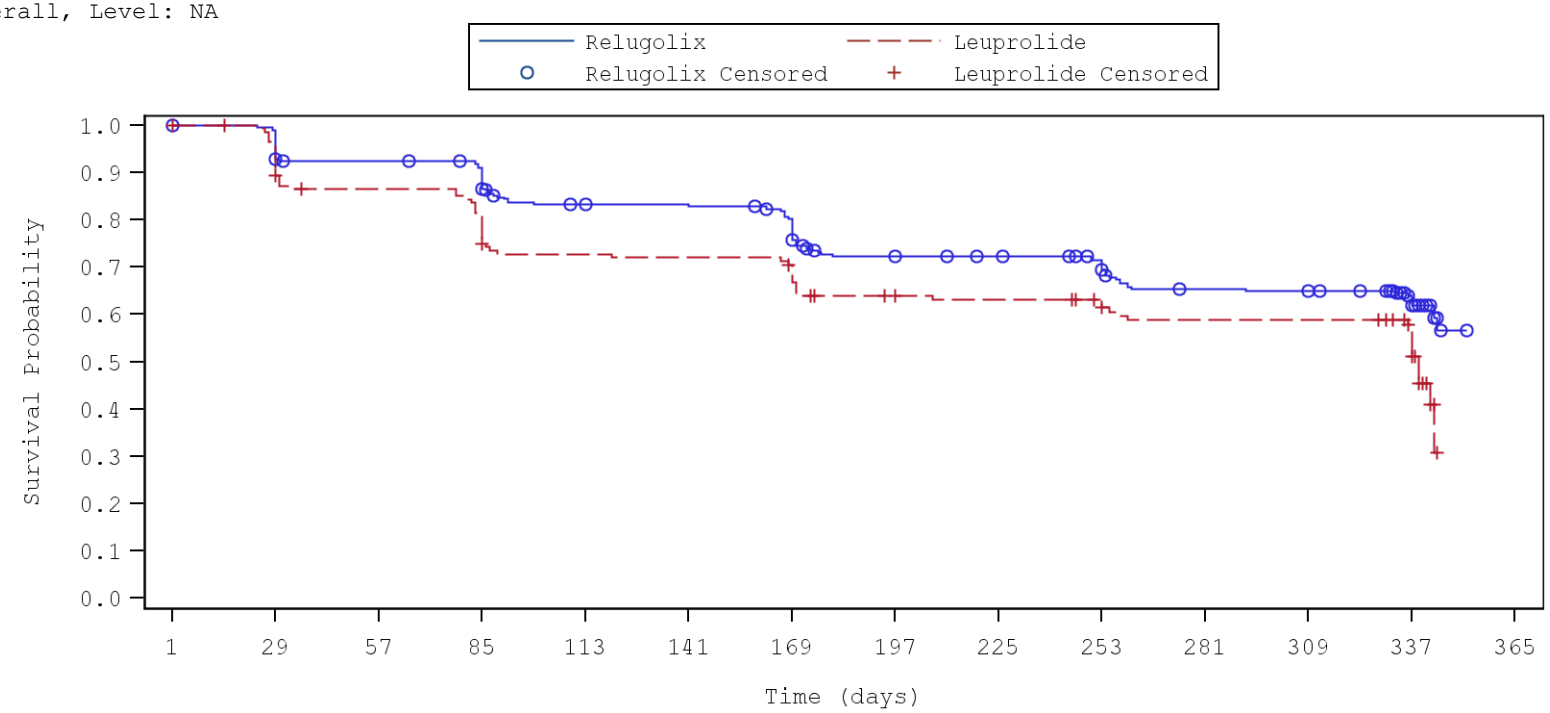
Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2DYSP15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Dyspnoea Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	276	255	249	224	223	213	186	183	177	158	157	117	0
Leuprolide	144	135	120	112	99	98	95	83	81	74	68	68	52	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 0.652 (0.479, 0.889)
P-value: 0.0069
Relugolix Median (95% CI): NE (344.0, NE)
Leuprolide Median (95% CI): 339.0 (260.0, 343.0)

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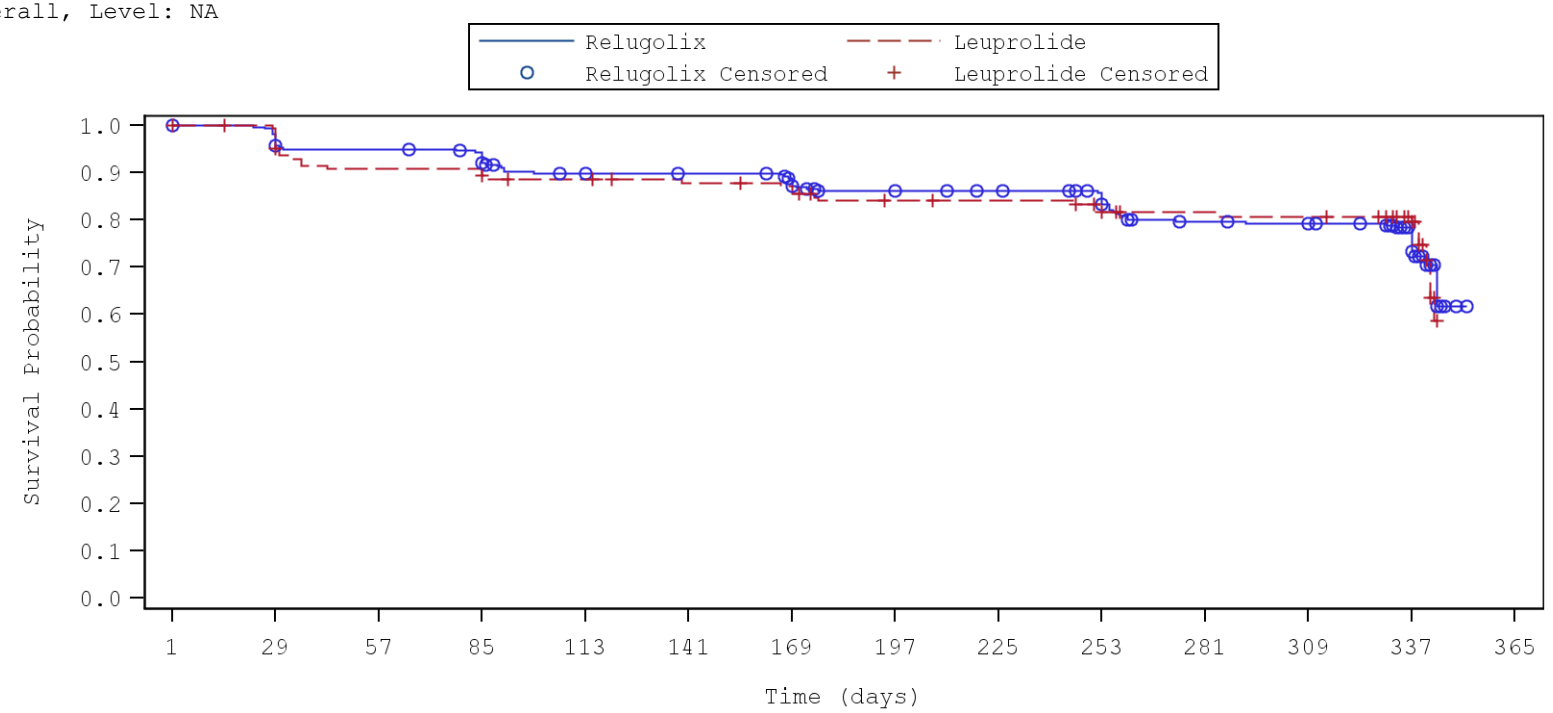
Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2APPT15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Appetite Loss Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	274	264	260	243	241	235	221	218	213	192	190	140	0
Leuprolide	144	140	127	127	120	117	115	108	107	100	95	94	75	0

Relugolix vs Leuprolide

Hazard Ratio (95% CI): 1.078 (0.712, 1.632)
P-value: 0.7231
Relugolix Median (95% CI): NE (344.0, NE)
Leuprolide Median (95% CI): NE (342.0, NE)

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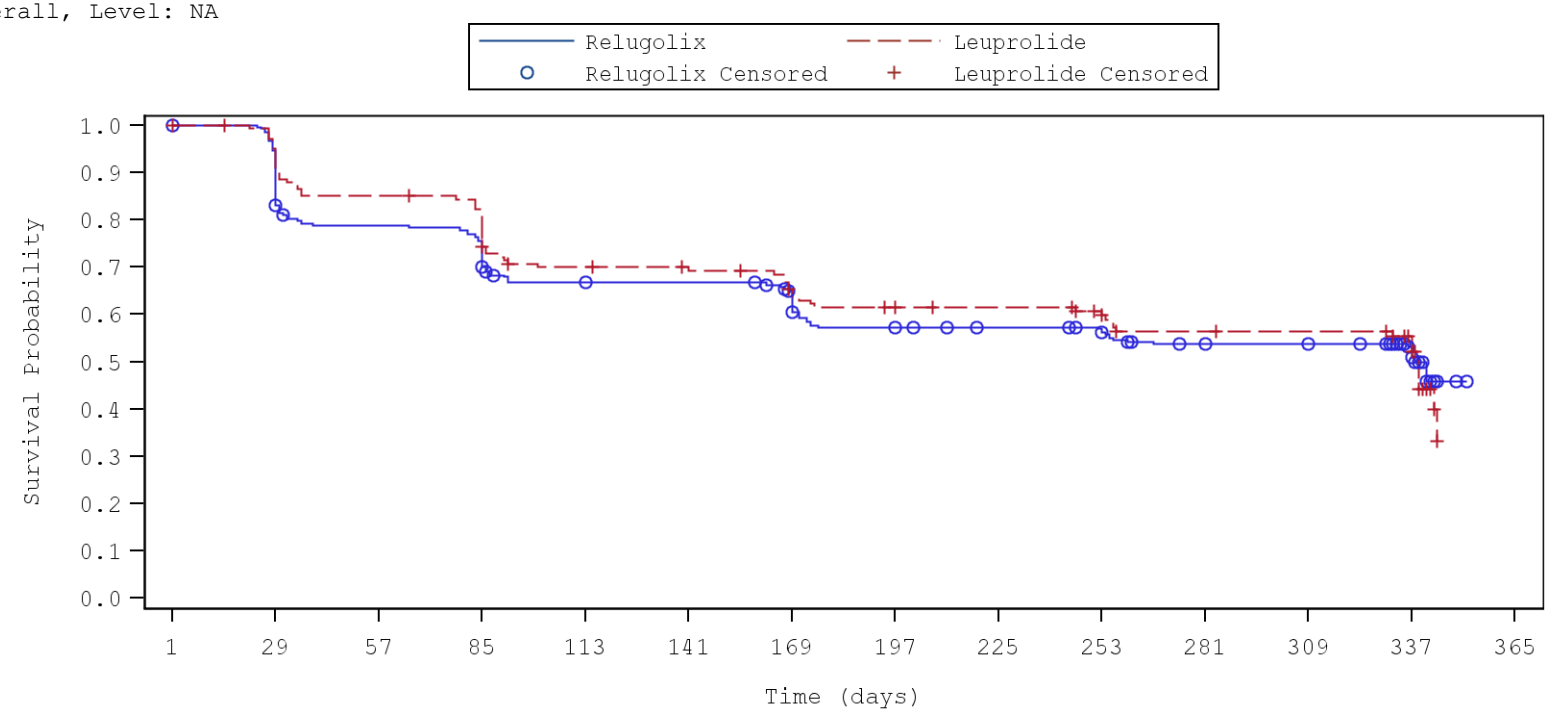
Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2INSO15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Insomnia Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	264	218	209	181	180	171	149	145	142	130	129	97	0
Leuprolide	144	134	120	115	94	92	84	78	76	71	64	63	51	0

Relugolix vs Leuprolide

Hazard Ratio (95% CI): 1.020 (0.760, 1.369)
P-value: 0.8948

Relugolix Median (95% CI): 338.0 (254.0, NE)
Leuprolide Median (95% CI): 339.0 (256.0, 344.0)

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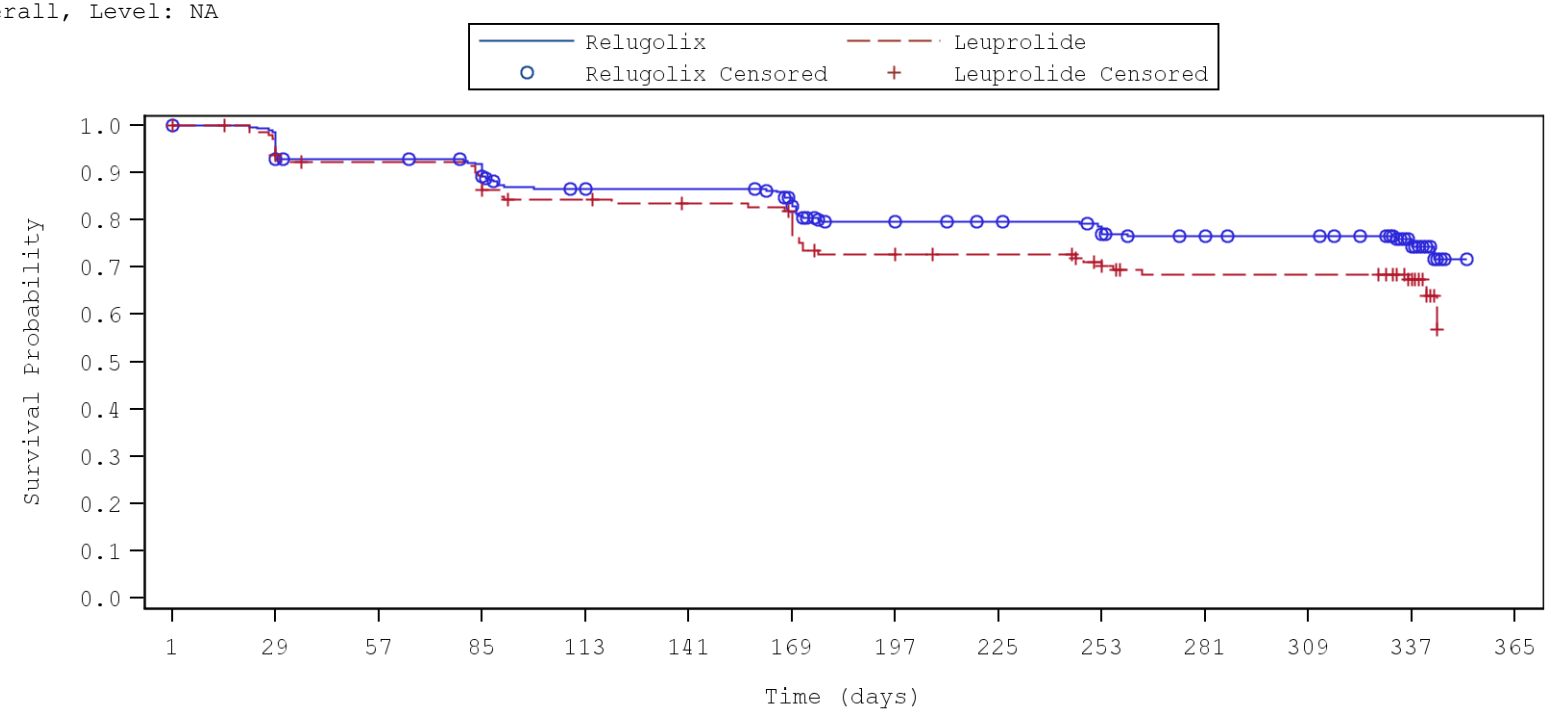
Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2DIAR15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Diarrhoea Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	275	256	251	232	231	222	203	200	195	183	181	136	0
Leuprolide	144	137	128	124	113	110	107	94	92	84	77	77	59	0

Relugolix vs Leuprolide

Hazard Ratio (95% CI): 0.759 (0.520, 1.107)
P-value: 0.1526

Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (344.0, NE)

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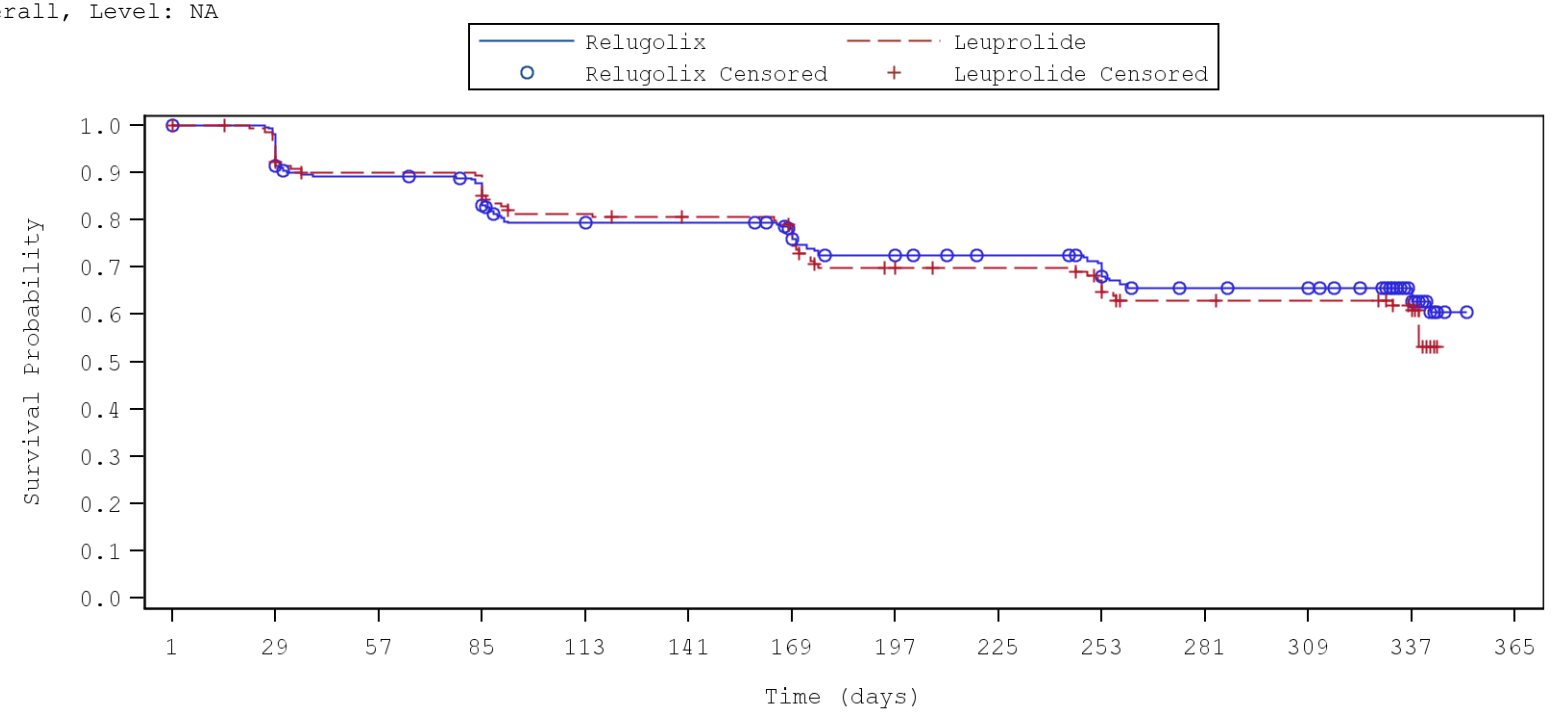
Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2CONS15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Increase in EORTC-QLQ-C30 Constipation Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	274	246	240	214	213	206	186	181	175	159	158	116	0
Leuprolide	144	135	125	124	109	106	103	88	86	79	70	69	54	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 0.923 (0.661, 1.290)
P-value: 0.6398
Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (339.0, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_QS_KM.SAS
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6.1.3.3 Symptomatik (European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire PR25)

6.1.3.3.1 Skala: Miktionsbeschwerden

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2URIN15.KM.MITTM1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	86 (29.7)	204 (70.3)	NE [NE;NE]	NE	1.273 [0.855;1.894]	0.2349
Leuprolide	144	34 (23.6)	110 (76.4)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.URINCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-PR25 Urinary Symptoms Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	283 (97.6)	21.89 (17.118)			
	Week 5 Day 1	272 (93.8)	19.93 (16.431)	266 (91.7) -0.81 (0.810)	0.60 [-1.97; 3.18] 0.6457	0.05 [-0.16; 0.25]
Leuprolide (N=144)	Baseline	143 (99.3)	22.99 (17.028)			
	Week 5 Day 1	143 (99.3)	20.31 (15.776)	142 (98.6) -1.41 (1.093)		
Relugolix (N=290)	Week 13 Day 1	275 (94.8)	19.30 (17.319)	270 (93.1) -1.60 (0.881)	0.66 [-2.19; 3.51] 0.6516	0.05 [-0.16; 0.25]
Leuprolide (N=144)	Week 13 Day 1	138 (95.8)	19.26 (16.676)	138 (95.8) -2.26 (1.211)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	20.45 (17.477)	265 (91.4) -0.15 (0.932)	1.66 [-1.39; 4.71] 0.2851	0.11 [-0.10; 0.32]
Leuprolide (N=144)	Week 25 Day 1	130 (90.3)	19.74 (16.533)	130 (90.3) -1.81 (1.297)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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Table QS.URINCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-PR25 Urinary Symptoms Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	18.70 (16.726)	243 (83.8) -1.31 (0.945)	1.65 [-1.44; 4.74] 0.2941	0.12 [-0.10; 0.33]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	18.02 (16.510)	120 (83.3) -2.96 (1.312)		
Relugolix (N=290)	Week 49 Day 1	235 (81.0)	19.06 (15.503)	230 (79.3) -0.43 (0.926)	2.38 [-0.66; 5.43] 0.1249	0.17 [-0.05; 0.40]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	18.33 (16.174)	110 (76.4) -2.81 (1.295)		
Relugolix (N=290)	Overall	284 (97.9)	19.91 (14.691)	278 (95.9) -0.86 (0.742)	1.39 [-0.97; 3.75] 0.2471	0.10 [-0.10; 0.30]
Leuprolide (N=144)	Overall	143 (99.3)	19.59 (14.552)	142 (98.6) -2.25 (1.014)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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6.1.3.3.2 Skala: Darmfunktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2BOWE15.KM.MITTM1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	51 (17.6)	239 (82.4)	NE [NE;NE]	NE	0.889 [0.565;1.399]	0.6115
Leuprolide	144	30 (20.8)	114 (79.2)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.BOWECHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-PR25 Bowel Symptoms Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	283 (97.6)	4.92 (8.883)			
	Week 5 Day 1	272 (93.8)	3.80 (6.894)	266 (91.7) -0.54 (0.366)	0.13 [-1.02; 1.29] 0.8204	0.02 [-0.18; 0.23]
Leuprolide (N=144)	Baseline	143 (99.3)	4.14 (8.027)			
	Week 5 Day 1	143 (99.3)	3.38 (6.351)	142 (98.6) -0.67 (0.491)		
Relugolix (N=290)	Week 13 Day 1	275 (94.8)	4.12 (7.581)	270 (93.1) -0.11 (0.443)	-0.95 [-2.39; 0.50] 0.1974	-0.13 [-0.34; 0.07]
Leuprolide (N=144)	Week 13 Day 1	138 (95.8)	4.89 (8.527)	138 (95.8) 0.84 (0.610)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	5.22 (10.101)	265 (91.4) 1.07 (0.515)	0.47 [-1.24; 2.18] 0.5901	0.06 [-0.15; 0.27]
Leuprolide (N=144)	Week 25 Day 1	130 (90.3)	4.42 (6.975)	130 (90.3) 0.60 (0.722)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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Table QS.BOWECHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-PR25 Bowel Symptoms Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	4.60 (8.271)	243 (83.8) 0.71 (0.513)	-0.49 [-2.19; 1.21] 0.5725	-0.06 [-0.28; 0.15]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	4.79 (7.765)	120 (83.3) 1.19 (0.717)		
Relugolix (N=290)	Week 49 Day 1	235 (81.0)	5.14 (7.961)	230 (79.3) 1.24 (0.530)	-0.86 [-2.63; 0.91] 0.3407	-0.11 [-0.34; 0.11]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	5.61 (8.967)	110 (76.4) 2.10 (0.749)		
Relugolix (N=290)	Overall	284 (97.9)	4.66 (6.829)	278 (95.9) 0.47 (0.354)	-0.34 [-1.47; 0.79] 0.5573	-0.05 [-0.25; 0.16]
Leuprolide (N=144)	Overall	143 (99.3)	4.71 (6.331)	142 (98.6) 0.81 (0.485)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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6.1.3.3.3 Skala: Nebenwirkungen der Hormontherapie

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2HRMN15.KM.MITTM1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	152 (52.4)	138 (47.6)	258.0 [248.0;337.0]	-79.0	1.055 [0.798;1.394]	0.7080
Leuprolide	144	74 (51.4)	70 (48.6)	337.0 [246.0;342.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.HRMNCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	283 (97.6)	8.44 (9.172)			
	Week 5 Day 1	272 (93.8)	11.85 (10.131)	266 (91.7) 3.78 (0.571)	2.20 [0.39; 4.01] 0.0172	0.25 [0.05; 0.45]
Leuprolide (N=144)	Baseline	143 (99.3)	7.81 (9.046)			
	Week 5 Day 1	143 (99.3)	9.60 (9.938)	142 (98.6) 1.58 (0.768)		
Relugolix (N=290)	Week 13 Day 1	275 (94.8)	14.91 (11.098)	270 (93.1) 6.78 (0.631)	-0.97 [-3.01; 1.07] 0.3503	-0.10 [-0.30; 0.11]
Leuprolide (N=144)	Week 13 Day 1	138 (95.8)	15.82 (11.370)	138 (95.8) 7.75 (0.867)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	17.20 (13.160)	265 (91.4) 9.24 (0.751)	0.65 [-1.83; 3.13] 0.6073	0.05 [-0.15; 0.26]
Leuprolide (N=144)	Week 25 Day 1	130 (90.3)	16.75 (11.657)	130 (90.3) 8.59 (1.049)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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Table QS.HRMNCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	18.12 (12.448)	243 (83.8) 10.45 (0.783)	0.20 [-2.39; 2.79] 0.8813	0.02 [-0.20; 0.23]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	18.33 (13.115)	120 (83.3) 10.25 (1.093)		
Relugolix (N=290)	Week 49 Day 1	235 (81.0)	17.23 (11.459)	230 (79.3) 10.17 (0.763)	-0.92 [-3.46; 1.62] 0.4762	-0.08 [-0.31; 0.15]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	19.60 (13.222)	110 (76.4) 11.09 (1.074)		
Relugolix (N=290)	Overall	284 (97.9)	16.10 (10.131)	278 (95.9) 8.08 (0.568)	0.23 [-1.59; 2.05] 0.8033	0.02 [-0.18; 0.22]
Leuprolide (N=144)	Overall	143 (99.3)	15.33 (9.800)	142 (98.6) 7.85 (0.780)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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6.1.3.3.4 Skala: Inkontinenzhilfe

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2INCT15.KM.MITTM1: Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	26 (9.0)	264 (91.0)	NE [344.0;NE]	NE	1.219 [0.584;2.545]	0.5974
Leuprolide	144	10 (6.9)	134 (93.1)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.INCTCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-PR25 Incontinence aid use Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	123 (42.4)	9.21 (20.602)			
	Week 5 Day 1	108 (37.2)	7.41 (16.641)	78 (26.9) -0.50 (1.875)	1.62 [-4.29; 7.53] 0.5882	0.10 [-0.26; 0.46]
Leuprolide (N=144)	Baseline	57 (39.6)	9.94 (21.790)			
	Week 5 Day 1	61 (42.4)	7.10 (18.373)	46 (31.9) -2.12 (2.421)		
Relugolix (N=290)	Week 13 Day 1	123 (42.4)	7.86 (17.639)	86 (29.7) 0.70 (1.675)	3.71 [-1.98; 9.40] 0.1996	0.25 [-0.13; 0.62]
Leuprolide (N=144)	Week 13 Day 1	55 (38.2)	6.06 (14.474)	39 (27.1) -3.01 (2.431)		
Relugolix (N=290)	Week 25 Day 1	113 (39.0)	11.50 (23.892)	78 (26.9) 5.38 (2.442)	9.63 [1.41; 17.84] 0.0220	0.44 [0.05; 0.82]
Leuprolide (N=144)	Week 25 Day 1	55 (38.2)	4.85 (13.484)	40 (27.8) -4.25 (3.434)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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Table QS.INCTCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-PR25 Incontinence aid use Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	106 (36.6)	9.12 (20.332)	74 (25.5) 0.82 (1.927)	4.41 [-2.29; 11.11] 0.1952	0.26 [-0.15; 0.67]
Leuprolide (N=144)	Week 37 Day 1	49 (34.0)	6.12 (14.709)	32 (22.2) -3.59 (2.860)		
Relugolix (N=290)	Week 49 Day 1	112 (38.6)	7.14 (15.126)	70 (24.1) -0.97 (1.719)	3.26 [-2.61; 9.13] 0.2750	0.23 [-0.19; 0.65]
Leuprolide (N=144)	Week 49 Day 1	47 (32.6)	4.26 (11.244)	31 (21.5) -4.22 (2.495)		
Relugolix (N=290)	Overall	182 (62.8)	7.81 (15.362)	108 (37.2) 1.08 (1.373)	4.53 [0.02; 9.03] 0.0490	0.27 [-0.07; 0.60]
Leuprolide (N=144)	Overall	90 (62.5)	5.44 (12.486)	50 (34.7) -3.44 (1.932)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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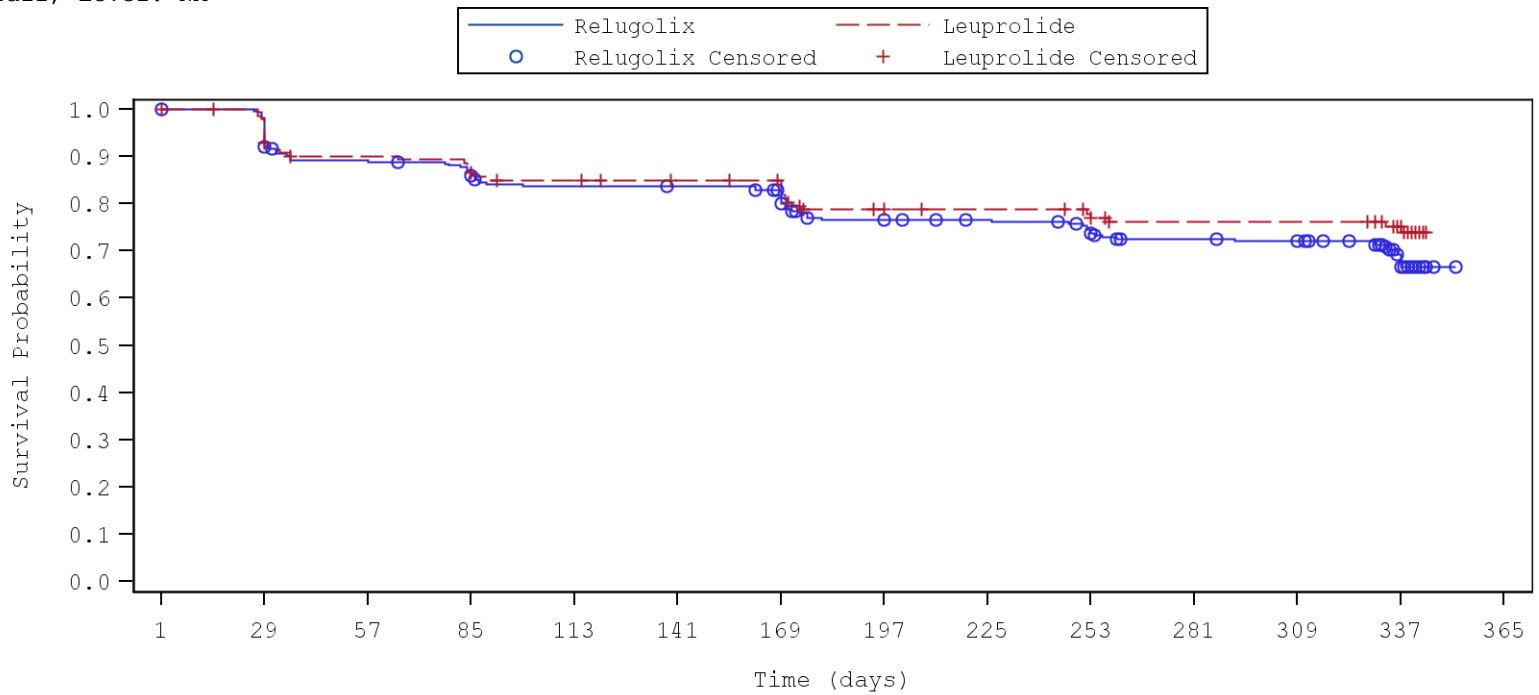
6.1.3.3.5 Kaplan-Meier-Kurven zu Time-to-Event-Analysen des EORTC-QLQ-PR25 (Morbidität)

Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2URIN15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Urinary Symptoms Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	273	245	238	227	226	221	198	194	187	176	174	124	0
Leuprolide	144	138	125	122	114	111	109	97	95	90	84	84	66	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 1.273 (0.855, 1.894)
P-value: 0.2349

Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (NE, NE)

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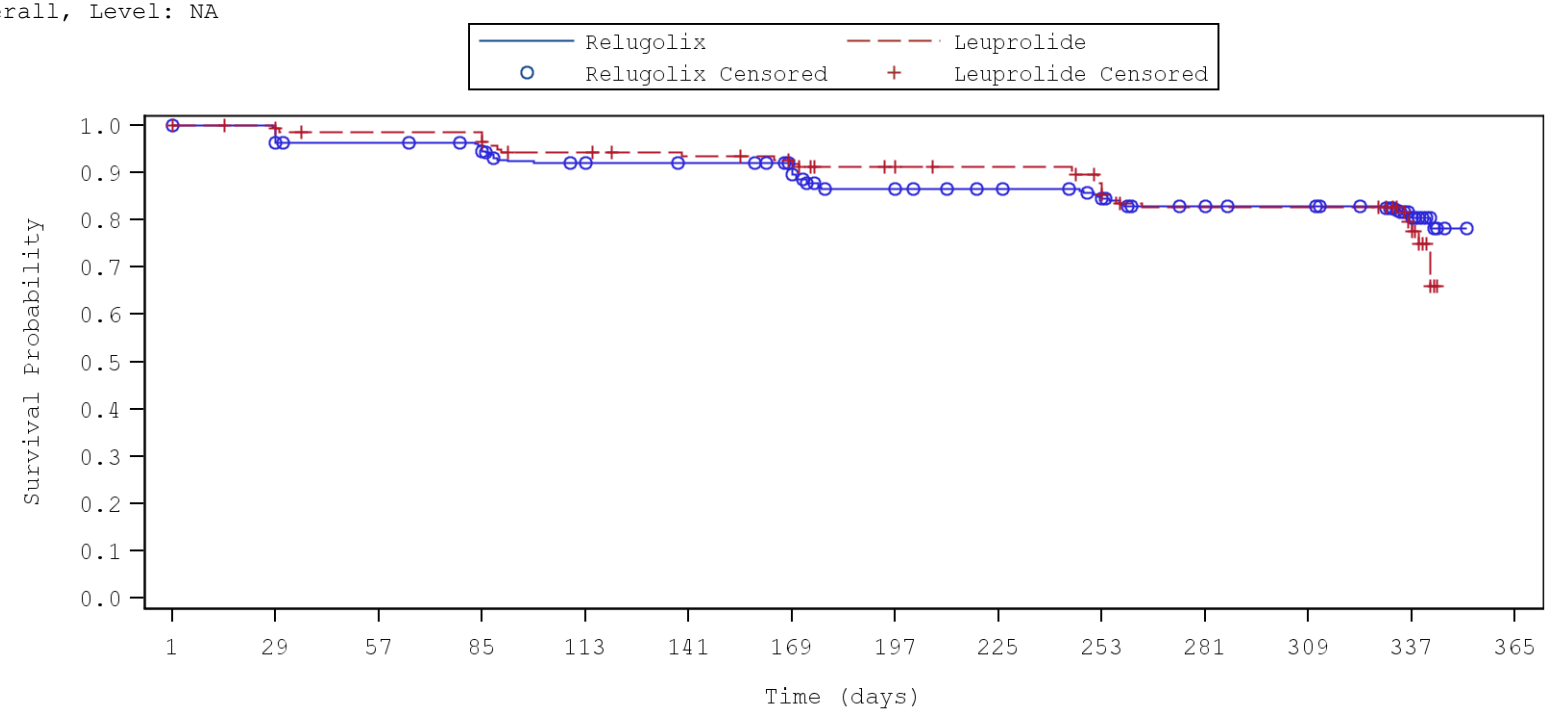
Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2BOWE15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Bowel Symptoms Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	277	265	261	247	245	241	221	217	210	198	196	145	0
Leuprolide	144	141	137	137	127	124	121	115	113	103	94	94	73	0

Relugolix vs Leuprolide

Hazard Ratio (95% CI): 0.889 (0.565, 1.399)
P-value: 0.6115

Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (NE, NE)

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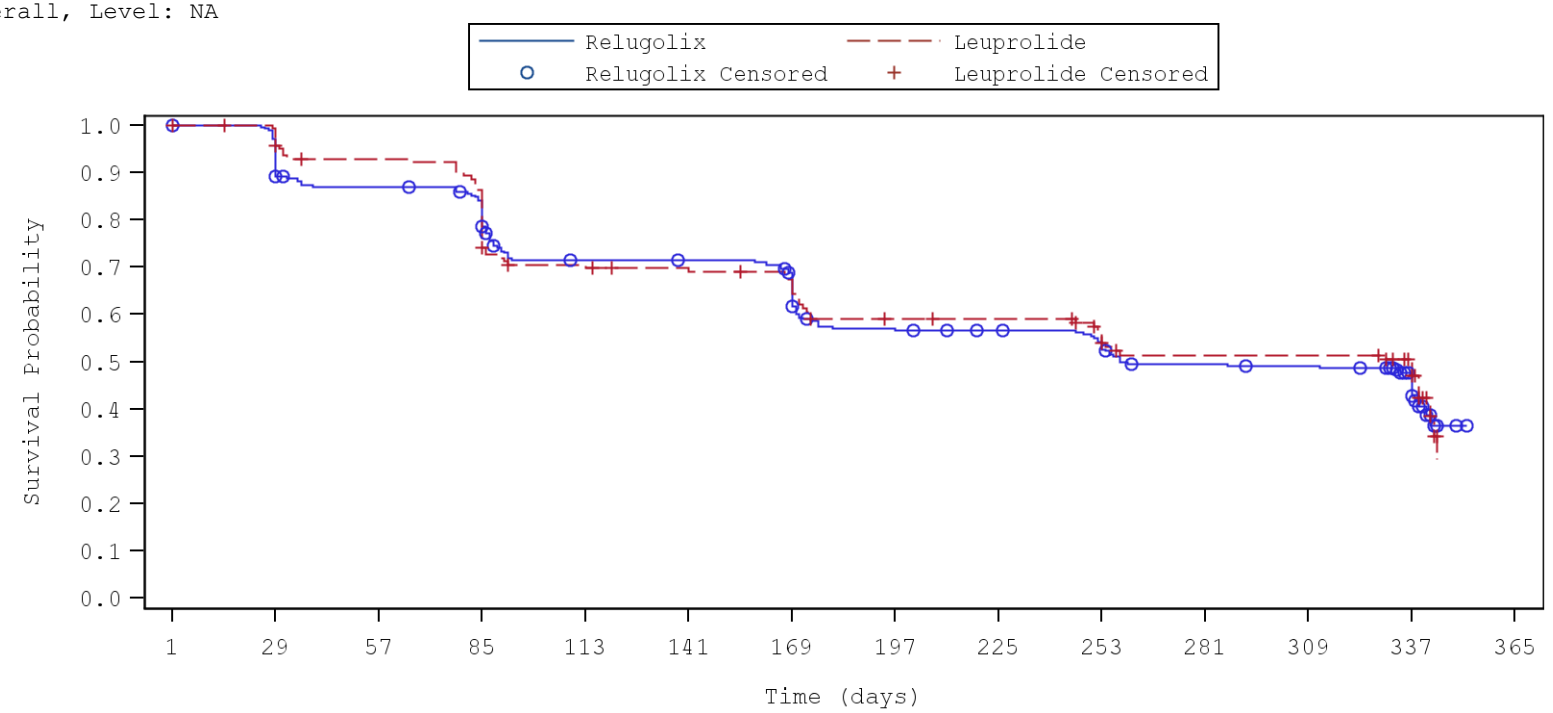
Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2HRMN15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Hormonal Treatment-related Symptoms Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	270	239	229	191	190	181	147	143	136	122	120	88	0
Leuprolide	144	140	129	120	95	92	88	75	74	67	59	59	44	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 1.055 (0.798, 1.394)
P-value: 0.7080
Relugolix Median (95% CI): 258.0 (248.0, 337.0)
Leuprolide Median (95% CI): 337.0 (246.0, 342.0)

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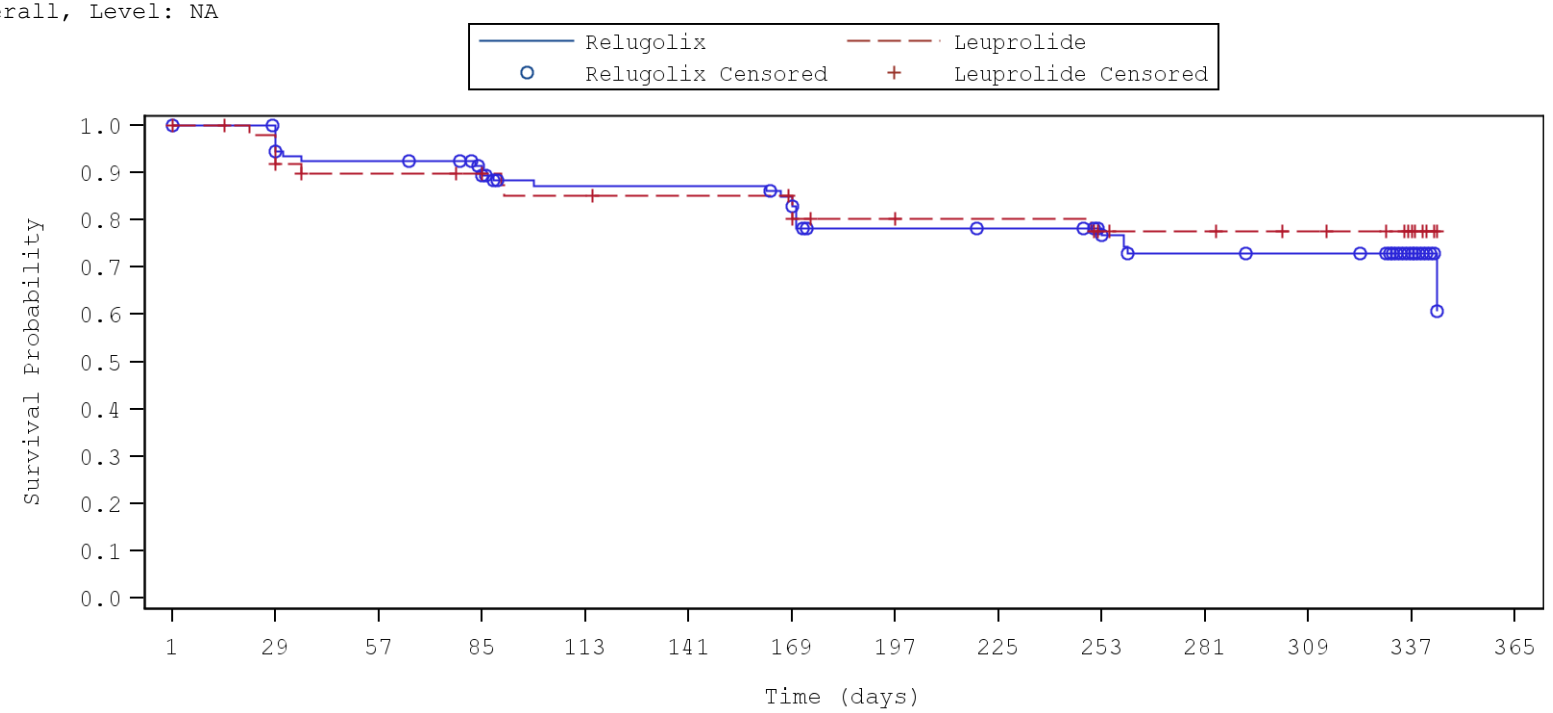
Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2INCT15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Increase in EORTC-QLQ-PR25 Incontinence aid use Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	107	94	89	80	80	77	65	64	61	54	53	40	0
Leuprolide	144	48	41	40	37	36	35	31	30	27	26	24	18	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 1.219 (0.584, 2.545)
P-value: 0.5974
Relugolix Median (95% CI): NE (344.0, NE)
Leuprolide Median (95% CI): NE (NE, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_QS_KM.SAS
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6.1.4 Morbidität – supportive Endpunkte

6.1.4.1 Testosteronkonzentration

6.1.4.1.1 Initiale Kastration

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.T2ITCAST.KM.MITTM1: Time to Initial Castration Rate (Testosterone < 50 ng/dL) (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	288 (99.3)	2 (0.7)	5.0 [4.0;5.0]	-22.0	9.371 [7.024;12.502]	<.0001
Leuprolide	144	139 (96.5)	5 (3.5)	27.0 [24.0;29.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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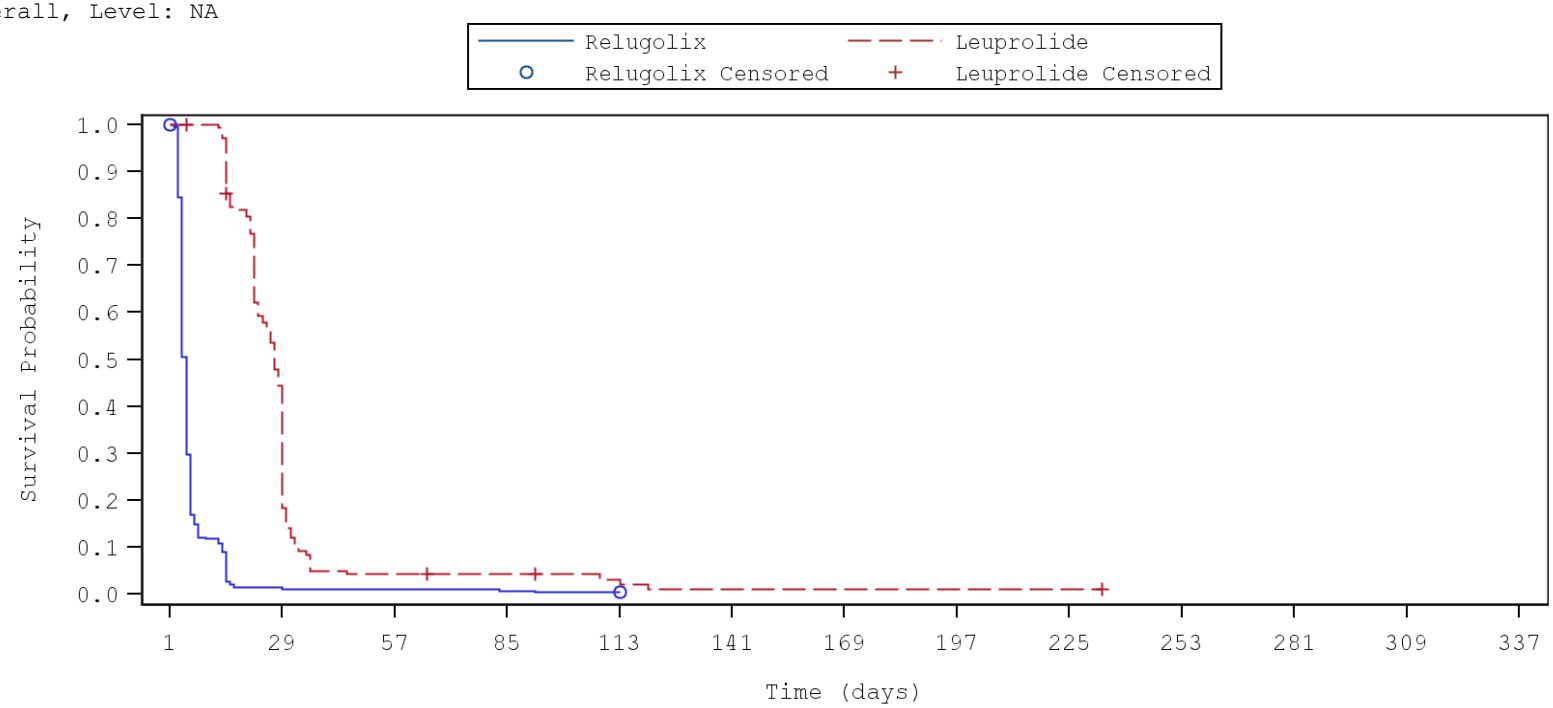
Myovant Sciences, Inc.: HERO AMNOG
Figure MOR.T2ITCAST.KM.MITTM1: Kaplan-Meier Curves of Time to Initial Castration (Testosterone < 50 ng/dL) (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	4	3	2	1	0	0	0	0	0	0	0
Leuprolide	144	63	6	5	3	1	1	1	1	0	0	0	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 9.371 (7.024, 12.502)
P-value: <.0001
Relugolix Median (95% CI): 5.0 (4.0, 5.0)
Leuprolide Median (95% CI): 27.0 (24.0, 29.0)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_MOR_KM.SAS
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6.1.4.1.2 Initiale profunde Kastration

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.T2IPCAST.KM.MITTM1: Time to Initial Profound Castration Rate (Testosterone < 20 ng/dL) (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	282 (97.2)	8 (2.8)	15.0 [NE;NE]	-14.0	5.087 [4.014;6.445]	<.0001
Leuprolide	144	138 (95.8)	6 (4.2)	29.0 [29.0;30.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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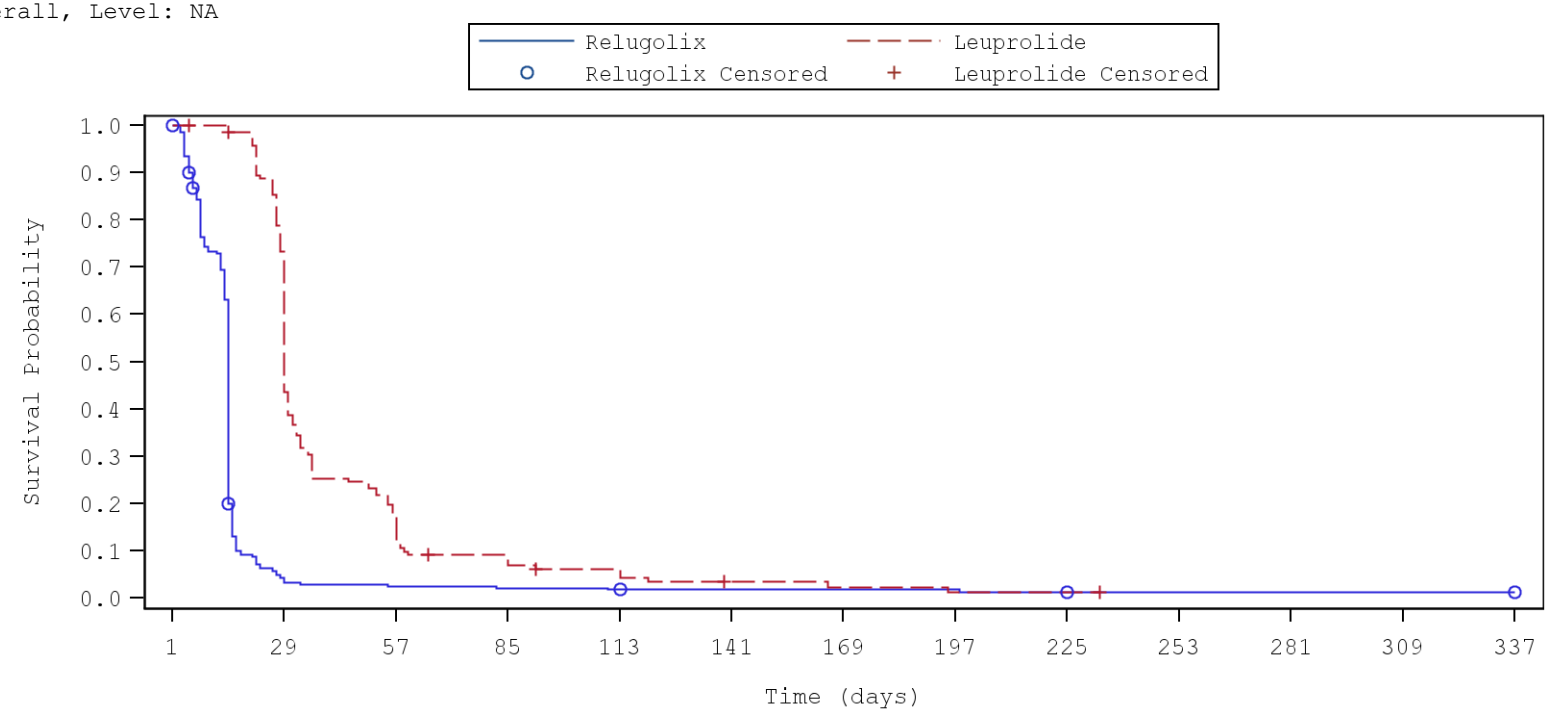
Myovant Sciences, Inc.: HERO AMNOG
Figure MOR.T2IPCAST.KM.MITTM1: Kaplan-Meier Curves of Time to Initial Profound Castration (Testosterone < 20 ng/dL) (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	12	7	6	5	4	4	4	3	2	2	2	2
Leuprolide	144	104	25	12	7	3	2	1	1	0	0	0	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 5.087 (4.014, 6.445)
P-value: <.0001
Relugolix Median (95% CI): 15.0 (NE, NE)
Leuprolide Median (95% CI): 29.0 (29.0, 30.0)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_MOR_KM.SAS
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6.1.4.1.3 Anhaltende Kastration

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.T2STCW5.KM.MITTM1: Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337 (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	9 (3.1)	281 (96.9)	NE [NE;NE]	NE	0.266 [0.117;0.602]	0.0015
Leuprolide	144	16 (11.1)	128 (88.9)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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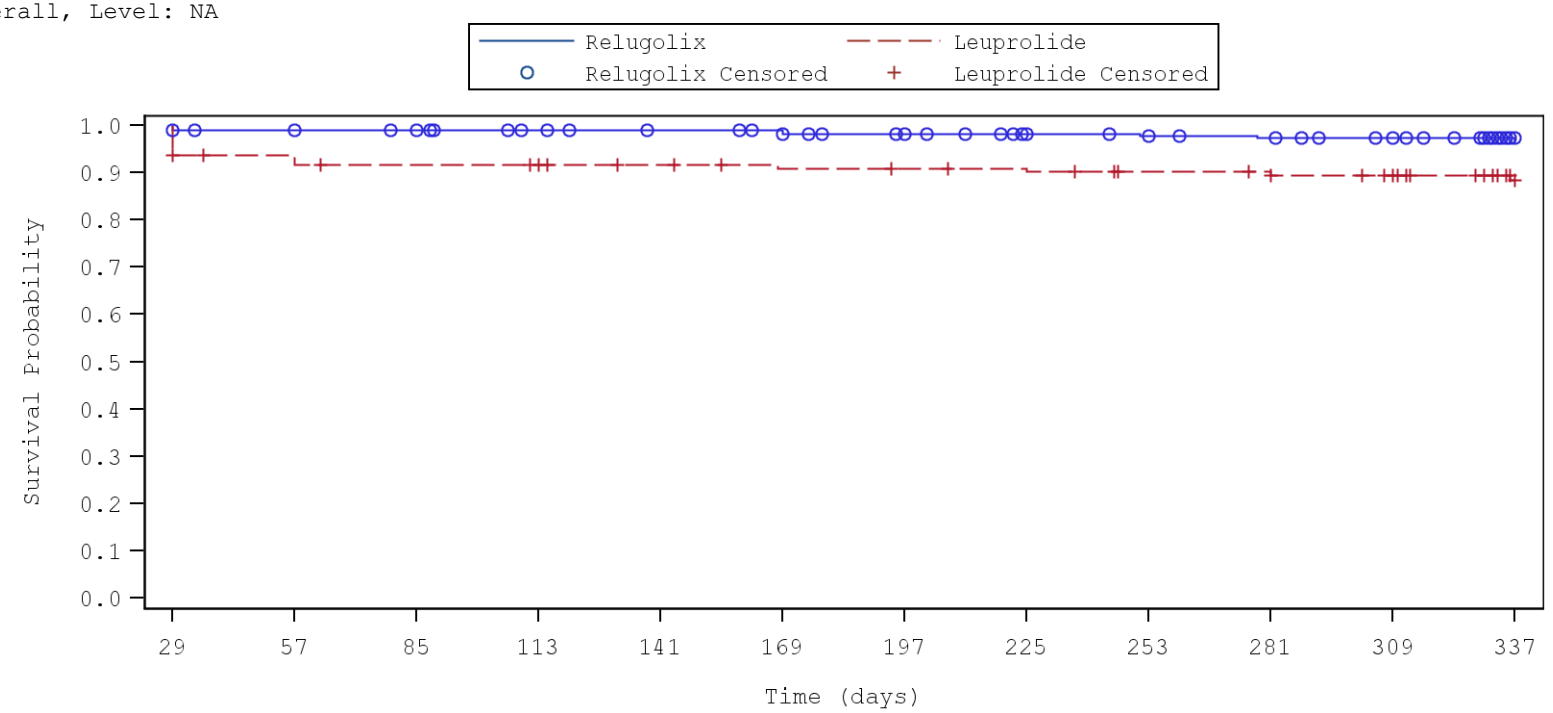
Myovant Sciences, Inc.: HERO AMNOG
Figure MOR.T2STCW5.KM.MITTM1: Kaplan-Meier Curves of Time to Sustained Castration Rate (Testosterone < 50 ng/dL) from Day 29 to Day 337 (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	278	276	271	268	266	258	250	247	242	238	177
Leuprolide	144	132	128	127	124	121	120	119	115	114	110	81

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 0.266 (0.117, 0.602)
P-value: 0.0015
Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (NE, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_MOR_KM.SAS
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6.1.4.1.4 Anhaltende profunde Kastration

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.T2SPCW5.KM.MITTM1: Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337 (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	36 (12.4)	254 (87.6)	NE [NE;NE]	NE	0.328 [0.211;0.510]	<.0001
Leuprolide	144	45 (31.3)	99 (68.8)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_KM.SAS

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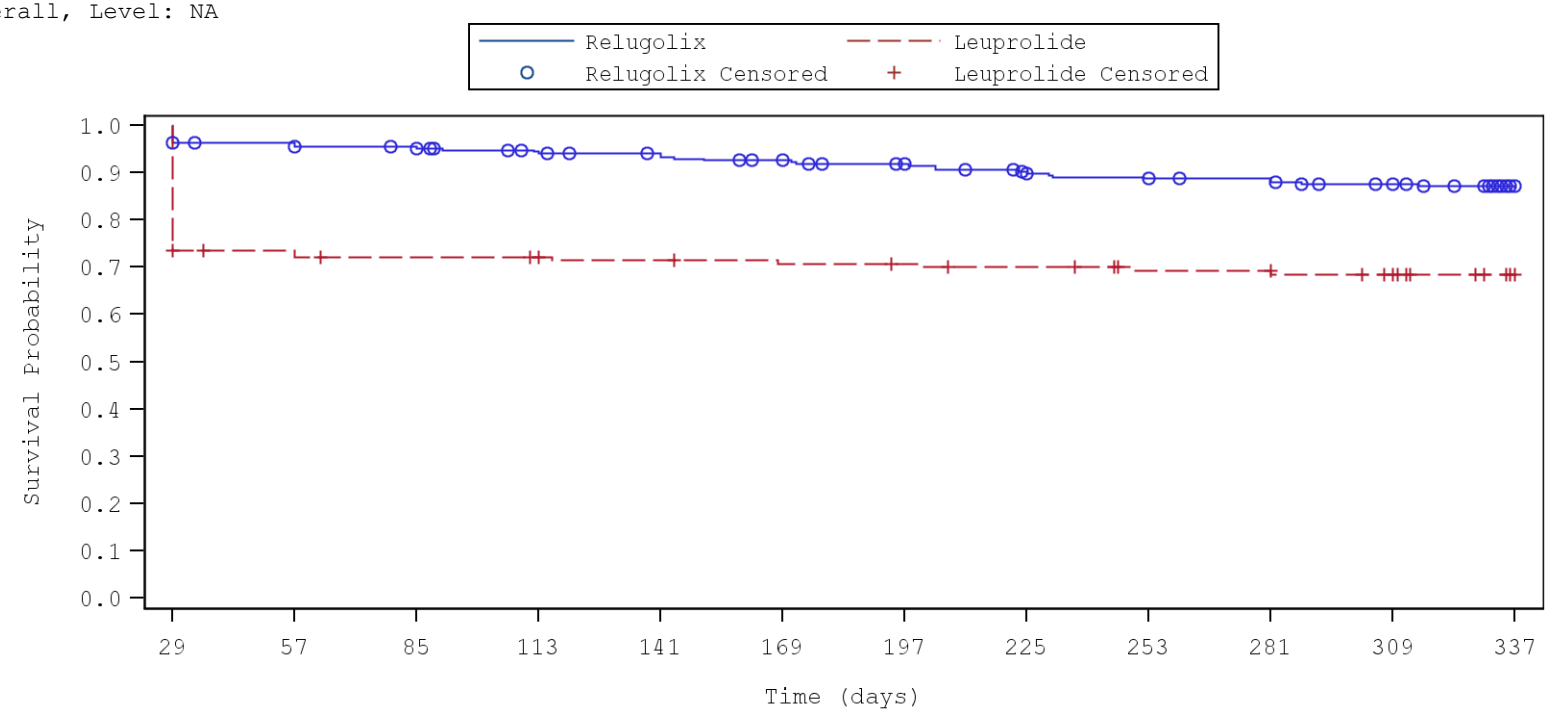
Myovant Sciences, Inc.: HERO AMNOG
Figure MOR.T2SPCW5.KM.MITTM1: Kaplan-Meier Curves of Time to Sustained Profound Castration Rate (Testosterone < 20 ng/dL) from Day 29 to Day 337 (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	270	266	258	254	248	240	230	225	221	214	158
Leuprolide	144	103	100	99	97	95	94	92	88	88	84	64

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 0.328 (0.211, 0.510)
P-value: <.0001
Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (NE, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_MOR_KM.SAS
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6.1.4.1.5 Wiederanstieg der Testosteronkonzentration

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.TG50SFU.BIN.MITTM1: Proportion of Patients with Recovery (Testosterone ≥ 50 ng/ml) at the 30-Day Safety Follow-Up Visit (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Relugolix	290	80 (27.6)	16.751	11.881	0.269	<.0001
Leuprolide	144	1 (0.7)	[5.611;50.011]	[4.139;34.104]	[0.216;0.322]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, region (per IWRS) and age group (per IWRS) as covariates.
[2] RR (95% CI) based on a Cochran-Mantel-Haenszel approach stratified by region (per IWRS) and age group (per IWRS).
[3] RD (95% CI) based on a Mantel-Haenszel approach stratified by region (per IWRS) and age group (per IWRS). 95% CIs based on the approximation to the normal distribution using the Sato estimator for the standard error.
[4] P-value based on a Cochran-Mantel-Haenszel test stratified by region (per IWRS) and age group (per IWRS). A continuity correction is applied in estimation of the OR, RR and p-value if zero events are observed in a given treatment group/stratum or if 100% of patients have an event in a given treatment group/stratum. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat.

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6.1.4.2 Prostataspezifisches-Antigen-Ansprechrate

Myovant Sciences, Inc.: HERO AMNOG

Table MOR.PSAR50W3.BIN.MITTM1: Proportion of Patients with > 50 % PSA Reduction from Baseline at Week 3 Day 1 and Confirmed at Week 5 Day 1 (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Relugolix	290	241 (83.1)	9.629	2.388	0.483	<.0001
Leuprolide	144	50 (34.7)	[6.027;15.385]	[1.900;3.002]	[0.394;0.571]	

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group. Patients with missing assessments are considered as non-responders.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group, region (per IWRS) and age group (per IWRS) as covariates.
[2] RR (95% CI) based on a Cochran-Mantel-Haenszel approach stratified by region (per IWRS) and age group (per IWRS).
[3] RD (95% CI) based on a Mantel-Haenszel approach stratified by region (per IWRS) and age group (per IWRS). 95% CIs based on the approximation to the normal distribution using the Sato estimator for the standard error.
[4] P-value based on a Cochran-Mantel-Haenszel test stratified by region (per IWRS) and age group (per IWRS). A continuity correction is applied in estimation of the OR, RR and p-value if zero events are observed in a given treatment group/stratum or if 100% of patients have an event in a given treatment group/stratum. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; mITT: Modified intent-to-treat; PSA: Prostate-specific antigen.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_MOR_BIN.SAS

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6.1.5 Gesundheitsbezogene Lebensqualität

6.1.5.1 Gesundheitsbezogene Lebensqualität (European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire C30)

6.1.5.1.1 Skala: Globaler Gesundheitszustand

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2GLBH15.KM.MITTM1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	131 (45.2)	159 (54.8)	340.0 [337.0;NE]	80.0	0.844 [0.633;1.126]	0.2500
Leuprolide	144	73 (50.7)	71 (49.3)	260.0 [171.0;344.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.GLBHCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Global Health Status Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	73.12 (20.410)			
	Week 5 Day 1	275 (94.8)	75.00 (16.923)	270 (93.1) 1.05 (0.917)	1.54 [-1.41; 4.49] 0.3058	0.11 [-0.10; 0.31]
Leuprolide (N=144)	Baseline	143 (99.3)	72.67 (19.765)			
	Week 5 Day 1	143 (99.3)	73.14 (20.326)	142 (98.6) -0.49 (1.245)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	74.82 (17.098)	273 (94.1) 0.29 (0.993)	0.54 [-2.70; 3.78] 0.7440	0.03 [-0.17; 0.24]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	73.74 (20.262)	138 (95.8) -0.25 (1.373)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	72.16 (19.392)	266 (91.7) -2.17 (1.021)	-1.15 [-4.51; 2.21] 0.5023	-0.07 [-0.28; 0.14]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	73.54 (17.311)	131 (91.0) -1.02 (1.426)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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Table QS.GLBHCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Global Health Status Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	73.22 (17.647)	244 (84.1) -1.63 (1.028)	0.29 [-3.10; 3.68] 0.8661	0.02 [-0.20; 0.24]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	73.40 (15.629)	120 (83.3) -1.92 (1.436)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	71.29 (18.833)	232 (80.0) -3.61 (1.087)	-1.56 [-5.18; 2.07] 0.3987	-0.10 [-0.32; 0.13]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	72.73 (15.920)	110 (76.4) -2.05 (1.537)		
Relugolix (N=290)	Overall	284 (97.9)	73.07 (14.900)	279 (96.2) -1.21 (0.747)	-0.07 [-2.44; 2.30] 0.9552	0.00 [-0.21; 0.20]
Leuprolide (N=144)	Overall	143 (99.3)	72.23 (15.817)	142 (98.6) -1.15 (1.022)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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6.1.5.1.2 Skala: Körperliche Funktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2PHYS15.KM.MITTM1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	80 (27.6)	210 (72.4)	352.0 [352.0;NE]	8.0	0.813 [0.567;1.166]	0.2604
Leuprolide	144	48 (33.3)	96 (66.7)	344.0 [339.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.PHYSCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Physical Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	85.09 (17.728)			
	Week 5 Day 1	275 (94.8)	86.76 (16.566)	270 (93.1) 0.60 (0.726)	2.33 [0.02; 4.63] 0.0478	0.21 [0.00; 0.41]
Leuprolide (N=144)	Baseline	143 (99.3)	86.43 (14.999)			
	Week 5 Day 1	143 (99.3)	85.03 (16.180)	142 (98.6) -1.72 (0.979)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	84.86 (15.720)	273 (94.1) -1.77 (0.789)	0.73 [-1.82; 3.28] 0.5730	0.06 [-0.15; 0.26]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	84.36 (17.560)	138 (95.8) -2.50 (1.084)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	83.46 (17.593)	266 (91.7) -3.46 (0.879)	0.43 [-2.45; 3.31] 0.7707	0.03 [-0.18; 0.24]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	83.87 (17.443)	131 (91.0) -3.89 (1.222)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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Table QS.PHYSCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Physical Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	84.27 (16.467)	244 (84.1) -3.50 (0.945)	2.01 [-1.11; 5.13] 0.2060	0.14 [-0.08; 0.36]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	82.50 (17.047)	120 (83.3) -5.51 (1.319)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	82.32 (18.314)	232 (80.0) -5.44 (0.991)	-0.19 [-3.49; 3.11] 0.9100	-0.01 [-0.24; 0.21]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	83.03 (16.813)	110 (76.4) -5.25 (1.398)		
Relugolix (N=290)	Overall	284 (97.9)	83.54 (16.164)	279 (96.2) -2.71 (0.692)	1.06 [-1.14; 3.27] 0.3447	0.08 [-0.12; 0.28]
Leuprolide (N=144)	Overall	143 (99.3)	83.26 (15.322)	142 (98.6) -3.77 (0.946)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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6.1.5.1.4 Skala: Rollenfunktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2ROLE15.KM.MITTM1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Role Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	151 (52.1)	139 (47.9)	260.0 [252.0;339.0]	4.0	0.855 [0.652;1.120]	0.2551
Leuprolide	144	82 (56.9)	62 (43.1)	256.0 [169.0;337.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.ROLECHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Role Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	85.21 (22.687)			
	Week 5 Day 1	275 (94.8)	86.55 (20.006)	270 (93.1) -0.28 (1.068)	3.83 [0.41; 7.25] 0.0282	0.23 [0.03; 0.43]
Leuprolide (N=144)	Baseline	143 (99.3)	88.58 (17.957)			
	Week 5 Day 1	143 (99.3)	84.15 (23.597)	142 (98.6) -4.11 (1.445)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	84.00 (21.295)	273 (94.1) -3.14 (1.183)	-0.54 [-4.40; 3.32] 0.7829	-0.03 [-0.23; 0.18]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	85.85 (22.154)	138 (95.8) -2.60 (1.635)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	83.27 (21.291)	266 (91.7) -4.31 (1.208)	0.89 [-3.07; 4.86] 0.6589	0.05 [-0.16; 0.26]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	84.35 (21.459)	131 (91.0) -5.20 (1.682)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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Table QS.ROLECHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Role Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	82.86 (21.806)	244 (84.1) -5.86 (1.292)	0.12 [-4.15; 4.39] 0.9559	0.01 [-0.21; 0.22]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	83.61 (21.605)	120 (83.3) -5.98 (1.805)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	81.92 (21.644)	232 (80.0) -6.81 (1.328)	0.71 [-3.72; 5.14] 0.7526	0.04 [-0.19; 0.26]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	82.58 (20.983)	110 (76.4) -7.52 (1.876)		
Relugolix (N=290)	Overall	284 (97.9)	82.97 (18.073)	279 (96.2) -4.08 (0.943)	1.00 [-2.01; 4.01] 0.5133	0.05 [-0.15; 0.26]
Leuprolide (N=144)	Overall	143 (99.3)	83.56 (19.347)	142 (98.6) -5.08 (1.292)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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6.1.5.1.5 Skala: Kognitive Funktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2COGN15.KM.MITTM1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	153 (52.8)	137 (47.2)	253.0 [171.0;337.0]	1.0	1.015 [0.772;1.334]	0.9173
Leuprolide	144	79 (54.9)	65 (45.1)	252.0 [169.0;344.0]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat.

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Table QS.COGNCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Cognitive Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	87.15 (17.391)			
	Week 5 Day 1	275 (94.8)	86.91 (15.867)	270 (93.1) -0.82 (0.801)	-0.46 [-3.03; 2.10] 0.7240	-0.04 [-0.24; 0.17]
Leuprolide (N=144)	Baseline	143 (99.3)	85.66 (16.142)			
	Week 5 Day 1	143 (99.3)	86.48 (14.393)	142 (98.6) -0.36 (1.087)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	84.90 (16.714)	273 (94.1) -2.94 (0.884)	-0.01 [-2.89; 2.87] 0.9941	0.00 [-0.21; 0.20]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	84.05 (17.245)	138 (95.8) -2.93 (1.222)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	82.59 (18.557)	266 (91.7) -5.35 (0.991)	-1.79 [-5.06; 1.49] 0.2844	-0.11 [-0.32; 0.10]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	83.46 (16.857)	131 (91.0) -3.56 (1.387)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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Table QS.COGNCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Cognitive Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	84.61 (17.346)	244 (84.1) -4.10 (0.964)	0.27 [-2.92; 3.45] 0.8690	0.02 [-0.20; 0.24]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	83.19 (16.806)	120 (83.3) -4.37 (1.348)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	83.69 (16.592)	232 (80.0) -5.17 (0.975)	-0.58 [-3.83; 2.67] 0.7253	-0.04 [-0.27; 0.19]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	82.27 (17.235)	110 (76.4) -4.59 (1.380)		
Relugolix (N=290)	Overall	284 (97.9)	84.34 (14.449)	279 (96.2) -3.68 (0.703)	-0.51 [-2.75; 1.73] 0.6518	-0.04 [-0.24; 0.17]
Leuprolide (N=144)	Overall	143 (99.3)	83.89 (13.419)	142 (98.6) -3.16 (0.964)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

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6.1.5.1.6 Skala: Emotionale Funktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2EMOT15.KM.MITTM1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	98 (33.8)	192 (66.2)	NE [344.0;NE]	NE	1.120 [0.785;1.598]	0.5309
Leuprolide	144	45 (31.3)	99 (68.8)	NE [344.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

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Table QS.EMOTCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Emotional Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	83.92 (17.906)			
	Week 5 Day 1	275 (94.8)	86.58 (17.274)	270 (93.1) 2.33 (0.761)	0.54 [-1.89; 2.98] 0.6616	0.05 [-0.16; 0.25]
Leuprolide (N=144)	Baseline	143 (99.3)	83.68 (16.896)			
	Week 5 Day 1	143 (99.3)	86.01 (15.404)	142 (98.6) 1.79 (1.030)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	86.01 (15.818)	273 (94.1) 1.54 (0.833)	1.45 [-1.26; 4.17] 0.2936	0.11 [-0.09; 0.31]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	84.53 (18.730)	138 (95.8) 0.09 (1.151)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	84.23 (19.010)	266 (91.7) -0.51 (0.953)	-1.19 [-4.34; 1.97] 0.4602	-0.08 [-0.29; 0.13]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	85.81 (17.410)	131 (91.0) 0.68 (1.332)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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Table QS.EMOTCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Emotional Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	85.79 (16.114)	244 (84.1) 0.13 (0.864)	0.18 [-2.66; 3.02] 0.9005	0.01 [-0.20; 0.23]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	85.56 (15.420)	120 (83.3) -0.05 (1.204)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	85.98 (15.878)	232 (80.0) -0.17 (0.923)	-0.56 [-3.63; 2.51] 0.7195	-0.04 [-0.27; 0.19]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	85.76 (16.449)	110 (76.4) 0.39 (1.303)		
Relugolix (N=290)	Overall	284 (97.9)	84.99 (14.813)	279 (96.2) 0.66 (0.670)	0.09 [-2.05; 2.22] 0.9373	0.01 [-0.20; 0.21]
Leuprolide (N=144)	Overall	143 (99.3)	84.86 (14.979)	142 (98.6) 0.58 (0.917)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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6.1.5.1.7 Skala: Soziale Funktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2SOC15.KM.MITTM1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	143 (49.3)	147 (50.7)	330.0 [253.0;341.0]	-7.0	0.977 [0.733;1.303]	0.8750
Leuprolide	144	70 (48.6)	74 (51.4)	337.0 [169.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.SOCCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Social Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	284 (97.9)	87.38 (19.268)			
	Week 5 Day 1	275 (94.8)	88.55 (17.530)	270 (93.1) 0.93 (0.957)	-0.06 [-3.10; 2.99] 0.9711	0.00 [-0.21; 0.20]
Leuprolide (N=144)	Baseline	143 (99.3)	87.30 (18.338)			
	Week 5 Day 1	143 (99.3)	88.58 (16.948)	142 (98.6) 0.99 (1.295)		
Relugolix (N=290)	Week 13 Day 1	277 (95.5)	88.63 (16.848)	273 (94.1) 0.86 (1.061)	2.55 [-0.90; 5.99] 0.1468	0.15 [-0.05; 0.36]
Leuprolide (N=144)	Week 13 Day 1	139 (96.5)	86.09 (21.665)	138 (95.8) -1.69 (1.463)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	86.36 (19.230)	266 (91.7) -1.84 (1.115)	-1.04 [-4.69; 2.61] 0.5762	-0.06 [-0.27; 0.15]
Leuprolide (N=144)	Week 25 Day 1	131 (91.0)	87.28 (19.593)	131 (91.0) -0.80 (1.551)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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Table QS.SOCCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-C30 Social Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	86.76 (18.747)	244 (84.1) -1.99 (1.205)	1.30 [-2.67; 5.28] 0.5190	0.07 [-0.15; 0.29]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	84.86 (20.611)	120 (83.3) -3.30 (1.682)		
Relugolix (N=290)	Week 49 Day 1	236 (81.4)	86.86 (18.303)	232 (80.0) -2.43 (1.232)	1.15 [-2.94; 5.24] 0.5812	0.06 [-0.16; 0.29]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	84.70 (19.307)	110 (76.4) -3.58 (1.735)		
Relugolix (N=290)	Overall	284 (97.9)	86.99 (15.239)	279 (96.2) -0.90 (0.894)	0.78 [-2.07; 3.63] 0.5905	0.05 [-0.16; 0.25]
Leuprolide (N=144)	Overall	143 (99.3)	86.22 (17.259)	142 (98.6) -1.68 (1.224)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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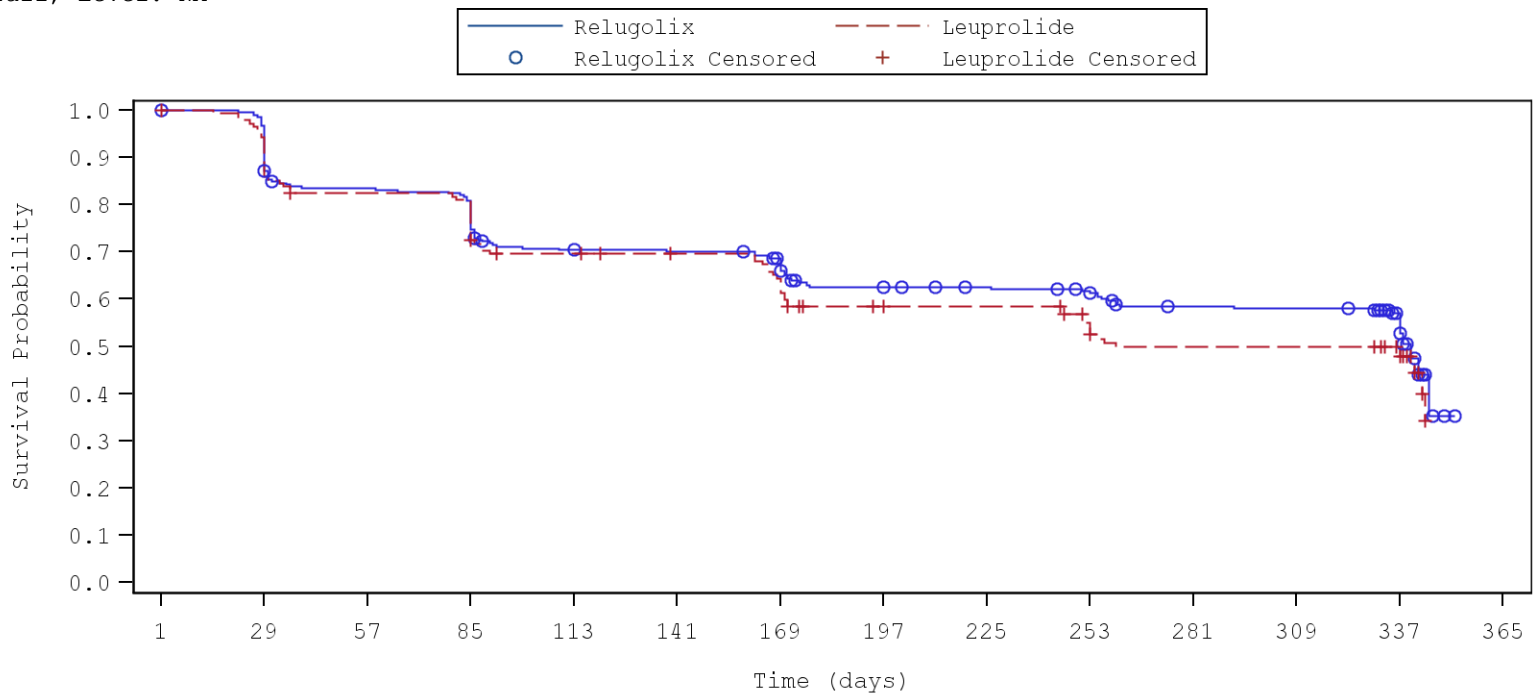
6.1.5.1.8 Kaplan-Meier-Kurven zu Time-to-Event-Analysen des EORTC-QLQ-C30 (QoL)

Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2GLBH15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Global Health Status Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



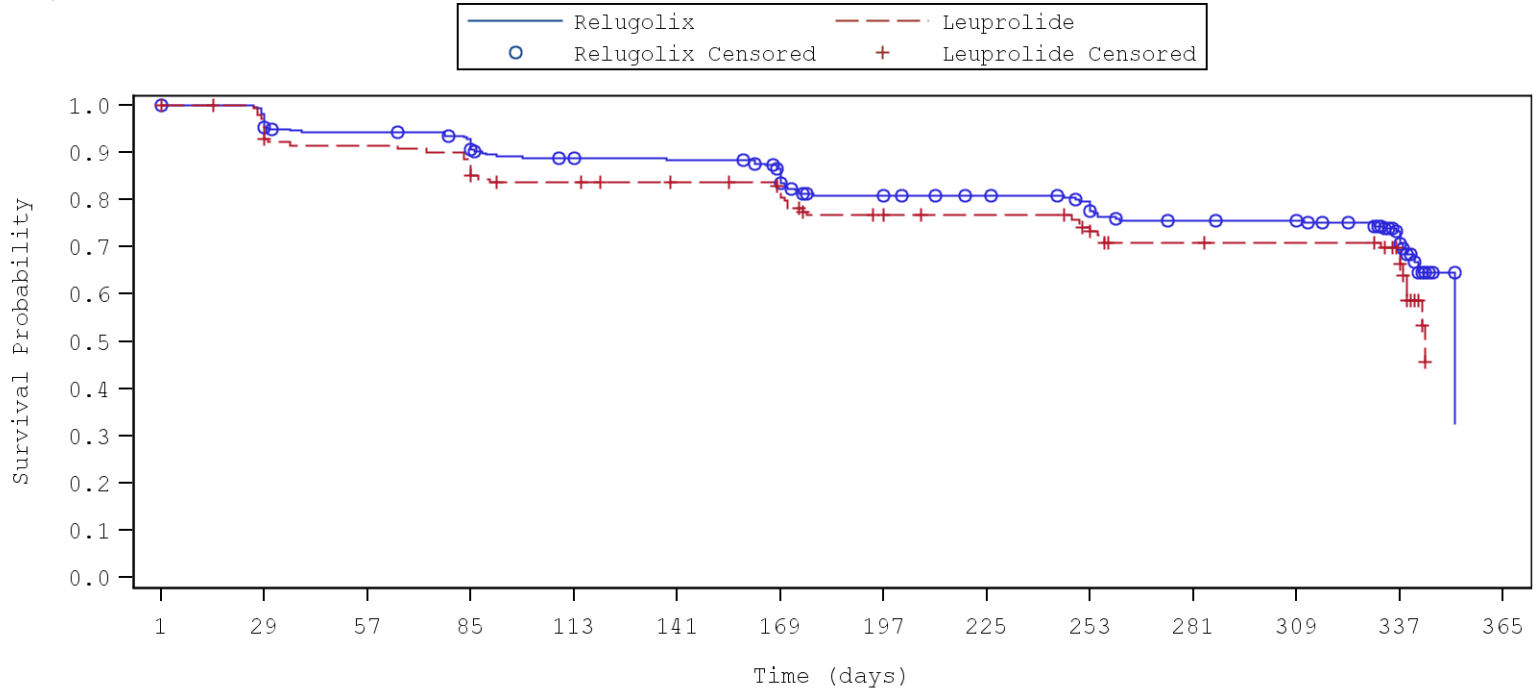
No. of Patients at Risk

Relugolix	290	270	230	223	192	190	183	162	158	154	141	140	104	0
Leuprolide	144	134	116	114	96	93	86	74	73	65	57	57	48	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 0.844 (0.633, 1.126)
P-value: 0.2500

Relugolix Median (95% CI): 340.0 (337.0, NE)
Leuprolide Median (95% CI): 260.0 (171.0, 344.0)

Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2PHYS15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Physical Functioning Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	274	260	254	240	238	229	208	204	198	184	183	137	0
Leuprolide	144	137	128	124	114	111	108	97	95	88	80	79	61	0

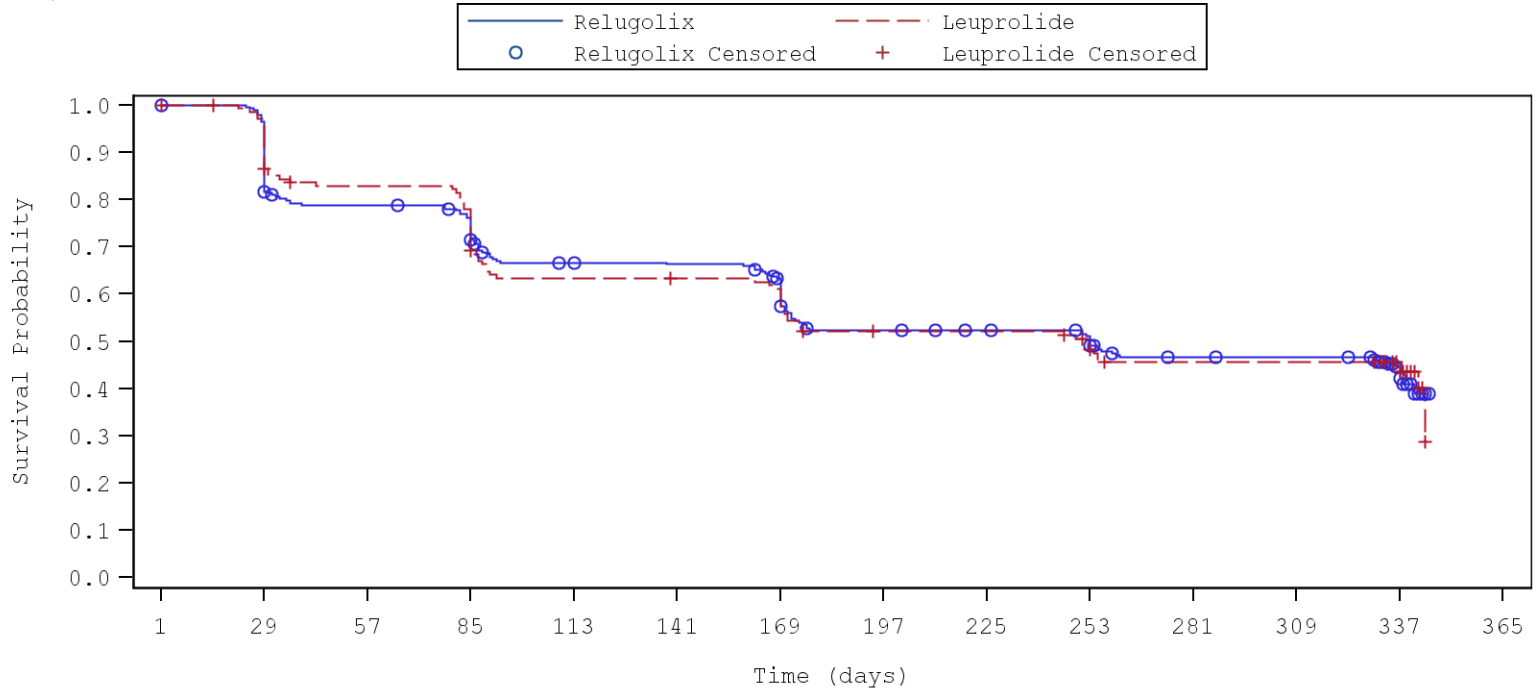
Relugolix vs Leuprolide

Hazard Ratio (95% CI): 0.813 (0.567, 1.166)
P-value: 0.2604

Relugolix Median (95% CI): 352.0 (352.0, NE)
Leuprolide Median (95% CI): 344.0 (339.0, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_QS_KM.SAS

Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2COGN15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Cognitive Functioning Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	269	217	208	178	176	165	132	129	124	109	108	74	0
Leuprolide	144	137	115	108	86	85	82	68	68	62	54	54	43	0

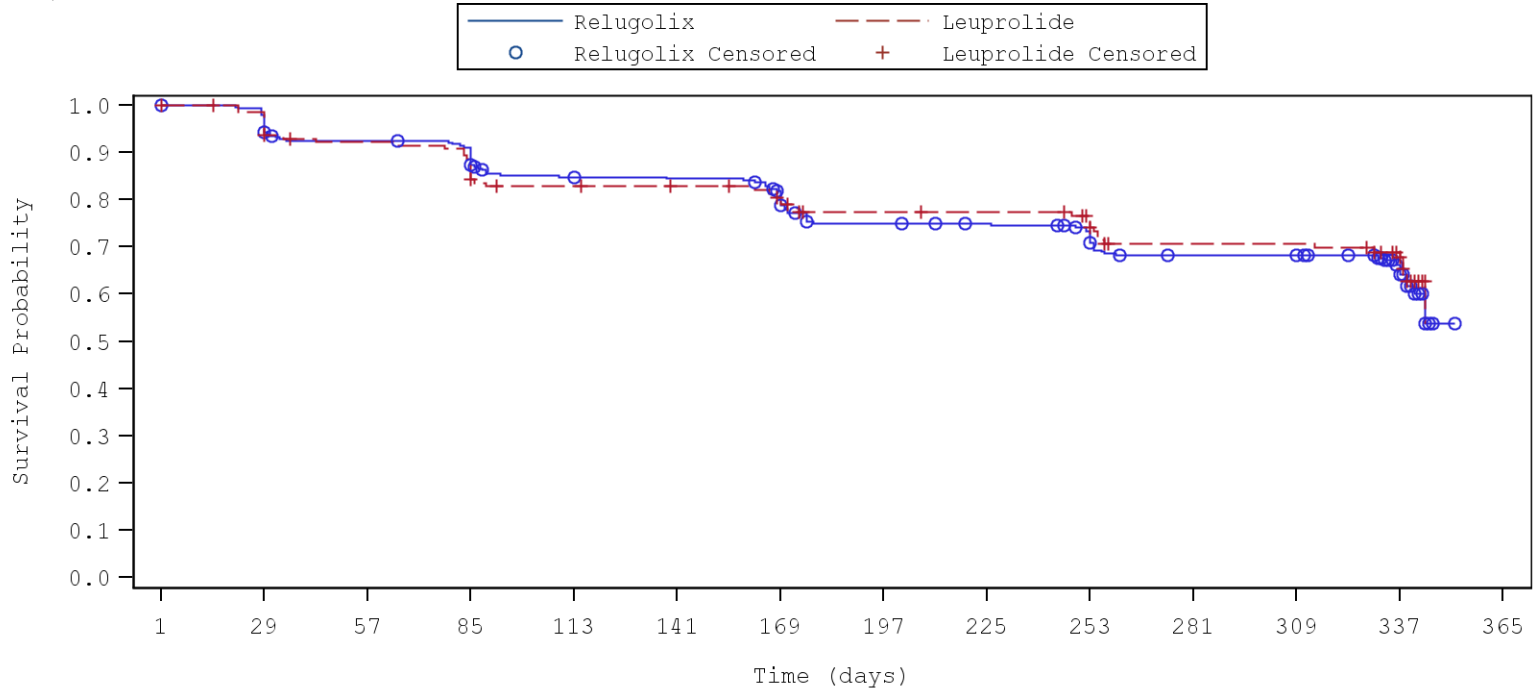
Relugolix vs Leuprolide

Hazard Ratio (95% CI): 1.015 (0.772, 1.334)
P-value: 0.9173

Relugolix Median (95% CI): 253.0 (171.0, 337.0)
Leuprolide Median (95% CI): 252.0 (169.0, 344.0)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_QS_KM.SAS

Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2EMOT15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Emotional Functioning Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	273	255	250	229	227	217	194	191	184	166	166	121	0
Leuprolide	144	139	128	123	112	110	105	98	97	91	80	80	65	0

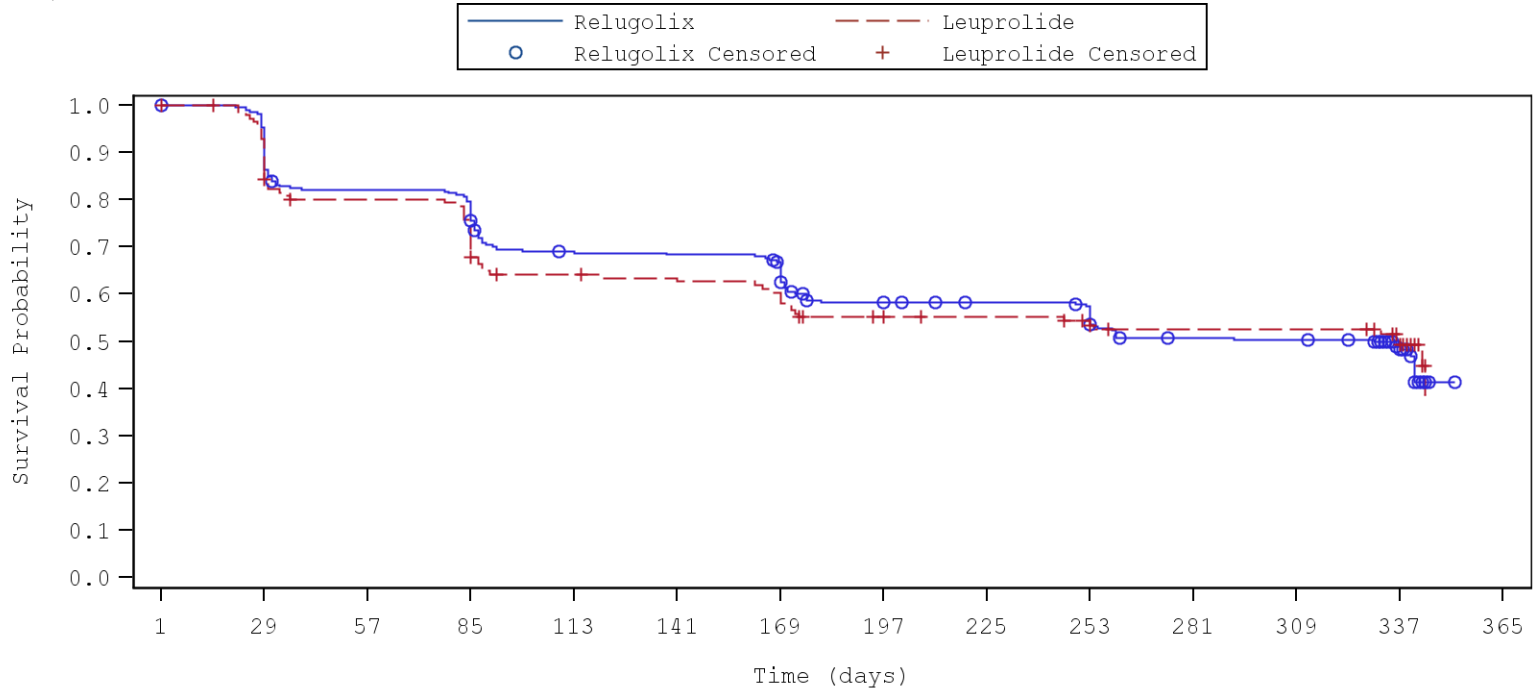
Relugolix vs Leuprolide

Hazard Ratio (95% CI): 1.120 (0.785, 1.598)
P-value: 0.5309

Relugolix Median (95% CI): NE (344.0, NE)
Leuprolide Median (95% CI): NE (344.0, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_QS_KM.SAS

Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2SOC15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Decrease in EORTC-QLQ-C30 Social Functioning Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	266	228	221	189	187	181	152	148	145	125	124	88	0
Leuprolide	144	131	111	105	86	84	80	70	68	63	58	58	47	0

Relugolix vs Leuprolide

Hazard Ratio (95% CI): 0.977 (0.733, 1.303)
P-value: 0.8750

Relugolix Median (95% CI): 330.0 (253.0, 341.0)
Leuprolide Median (95% CI): 337.0 (169.0, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_QS_KM.SAS

6.1.5.2 Gesundheitsbezogene Lebensqualität (European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire PR25)

6.1.5.2.1 Skala: Sexuelle Aktivität

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2SEXA15.KM.MITTM1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	79 (27.2)	211 (72.8)	NE [NE;NE]	NE	1.142 [0.767;1.701]	0.5137
Leuprolide	144	36 (25.0)	108 (75.0)	NE [NE;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

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Table QS.SEXACHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-PR25 Sexual Activity Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	283 (97.6)	76.33 (25.048)			
	Week 5 Day 1	272 (93.8)	83.70 (20.942)	266 (91.7) 7.30 (1.110)	1.06 [-2.49; 4.61] 0.5585	0.06 [-0.14; 0.26]
Leuprolide (N=144)	Baseline	143 (99.3)	79.14 (24.978)			
	Week 5 Day 1	143 (99.3)	83.45 (22.158)	142 (98.6) 6.24 (1.500)		
Relugolix (N=290)	Week 13 Day 1	275 (94.8)	85.58 (21.121)	270 (93.1) 9.23 (1.123)	-1.72 [-5.36; 1.93] 0.3549	-0.10 [-0.30; 0.11]
Leuprolide (N=144)	Week 13 Day 1	138 (95.8)	88.04 (17.784)	138 (95.8) 10.94 (1.549)		
Relugolix (N=290)	Week 25 Day 1	270 (93.1)	83.89 (24.062)	265 (91.4) 7.89 (1.400)	-2.06 [-6.72; 2.60] 0.3850	-0.09 [-0.30; 0.12]
Leuprolide (N=144)	Week 25 Day 1	130 (90.3)	87.44 (20.340)	130 (90.3) 9.95 (1.967)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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Table QS.SEXACHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-PR25 Sexual Activity Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	248 (85.5)	86.29 (23.670)	243 (83.8) 9.96 (1.399)	0.23 [-4.42; 4.87] 0.9234	0.01 [-0.21; 0.23]
Leuprolide (N=144)	Week 37 Day 1	120 (83.3)	86.94 (22.577)	120 (83.3) 9.73 (1.962)		
Relugolix (N=290)	Week 49 Day 1	235 (81.0)	88.30 (21.047)	230 (79.3) 11.27 (1.380)	4.12 [-0.50; 8.74] 0.0801	0.20 [-0.03; 0.43]
Leuprolide (N=144)	Week 49 Day 1	110 (76.4)	84.39 (24.239)	110 (76.4) 7.15 (1.955)		
Relugolix (N=290)	Overall	284 (97.9)	85.12 (17.815)	278 (95.9) 9.13 (0.938)	0.33 [-2.67; 3.32] 0.8309	0.02 [-0.19; 0.22]
Leuprolide (N=144)	Overall	143 (99.3)	86.00 (16.473)	142 (98.6) 8.80 (1.290)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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6.1.5.2.2 Skala: Sexualfunktion

Myovant Sciences, Inc.: HERO AMNOG

Table QS.T2SEXF15.KM.MITTM1: Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**Censored patients n (%)**	**Median time to 1st event [95% CI][1]**	**Median difference**	**HR [95% CI][2]**	**p-value[3]**
Relugolix	290	35 (12.1)	255 (87.9)	253.0 [91.0;338.0]	0.0	1.234 [0.690;2.207]	0.4791
Leuprolide	144	22 (15.3)	122 (84.7)	253.0 [120.0;NE]			

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
Patients with no baseline assessment and/or with no non-missing post-baseline assessments during the Treatment Period for the given parameter (endpoint) are censored at Baseline (Day 1). All other patients without an event are censored at the earliest date of ('Last non-missing assessment in the Treatment Period for the given parameter (endpoint)' and 'Death').
[1] Based on Kaplan-Meier estimates. 95% CIs are calculated by log-log transformation of the survivor function in each treatment group.
[2] HRs (and 95% CIs) are based on a Cox proportional hazards model stratified by region (per IWRS) and age group (per IWRS) with treatment group as a covariate. 95% CIs are based on the approximation to the normal distribution. The reference group is Leuprolide.
[3] Treatment p-value is based on a Wald test from the Cox proportional hazards model defined above.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with an event; HR: Hazard ratio; CI: Confidence interval; mITT: Modified intent-to-treat; NE: Non-estimable.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_KM.SAS

Date/time of run: 29JUL2022 11:52 Data Cut Date: 23SEP2020

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Table QS.SEXFCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-PR25 Sexual Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Baseline	102 (35.2)	61.79 (23.252)			
	Week 5 Day 1	68 (23.4)	59.60 (20.051)	50 (17.2) -4.59 (2.514)	-5.88 [-12.66; 0.90] 0.0883	-0.41 [-0.87; 0.05]
Leuprolide (N=144)	Baseline	48 (33.3)	57.70 (20.382)			
	Week 5 Day 1	38 (26.4)	58.48 (21.360)	29 (20.1) 1.29 (3.036)		
Relugolix (N=290)	Week 13 Day 1	55 (19.0)	50.56 (24.634)	37 (12.8) -9.11 (3.618)	-3.81 [-13.90; 6.28] 0.4562	-0.18 [-0.66; 0.30]
Leuprolide (N=144)	Week 13 Day 1	35 (24.3)	54.44 (22.255)	30 (20.8) -5.30 (3.997)		
Relugolix (N=290)	Week 25 Day 1	63 (21.7)	53.04 (24.470)	35 (12.1) -2.67 (3.325)	0.37 [-8.71; 9.45] 0.9362	0.02 [-0.50; 0.54]
Leuprolide (N=144)	Week 25 Day 1	28 (19.4)	56.85 (24.747)	23 (16.0) -3.04 (3.707)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

Date/time of run: 10AUG2022 12:29 Data Cut Date: 23SEP2020

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Table QS.SEXFCHG.MM.MITTM1: Summary of Change from Baseline in EORTC-QLQ-PR25 Sexual Functioning Scale Score (mITT Metastatic Population)

Study: HERO

Treatment	Study visit	n (%)[1]	Mean (SD)[1]	Change from baseline n (%)[2] LS-mean change (SE)[3]	Difference LS-mean change [95% CI] p-value[3]	Standard Mean Difference Hedges' g [95% CI][3]
Relugolix (N=290)	Week 37 Day 1	41 (14.1)	42.89 (24.049)	25 (8.6) -16.98 (3.882)	-7.39 [-18.33; 3.54] 0.1831	-0.34 [-0.94; 0.25]
Leuprolide (N=144)	Week 37 Day 1	22 (15.3)	55.43 (21.729)	19 (13.2) -9.59 (4.281)		
Relugolix (N=290)	Week 49 Day 1	40 (13.8)	54.79 (23.712)	31 (10.7) -10.63 (4.012)	3.31 [-8.43; 15.06] 0.5770	0.16 [-0.42; 0.73]
Leuprolide (N=144)	Week 49 Day 1	26 (18.1)	50.96 (27.419)	18 (12.5) -13.94 (4.703)		
Relugolix (N=290)	Overall	115 (39.7)	52.27 (21.781)	67 (23.1) -8.80 (2.540)	-2.68 [-9.04; 3.69] 0.4058	-0.14 [-0.52; 0.24]
Leuprolide (N=144)	Overall	63 (43.8)	54.01 (23.353)	43 (29.9) -6.12 (2.694)		

Post hoc analysis. The denominator for percentages is the number of patients in the mITT Metastatic Population for each treatment group.
[1] Summary statistics are based on observed data. For the Overall visit, summary statistics are calculated based on the mean observed value across all post-baseline visits within each patient.
[2] Number of patients with non-missing change from baseline.
[3] LS means, LS mean differences (and 95% CIs), p-value and Hedges' g (95% CIs) are based on a mixed model with repeated measures (MMRM) with treatment, visit, baseline value, region (per IWRS) and age group (per IWRS) and treatment-by-visit interaction as fixed effects using an unstructured covariance matrix. Hedges' g is calculated using a small sample bias correction.
The reference group for the LS mean difference and Hedges' g is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: number of patients with data; SD: standard deviation; SE: Standard error; LS: least squares; CI: confidence interval; mITT: Modified intent-to-treat.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\Tab_QS_MM.SAS

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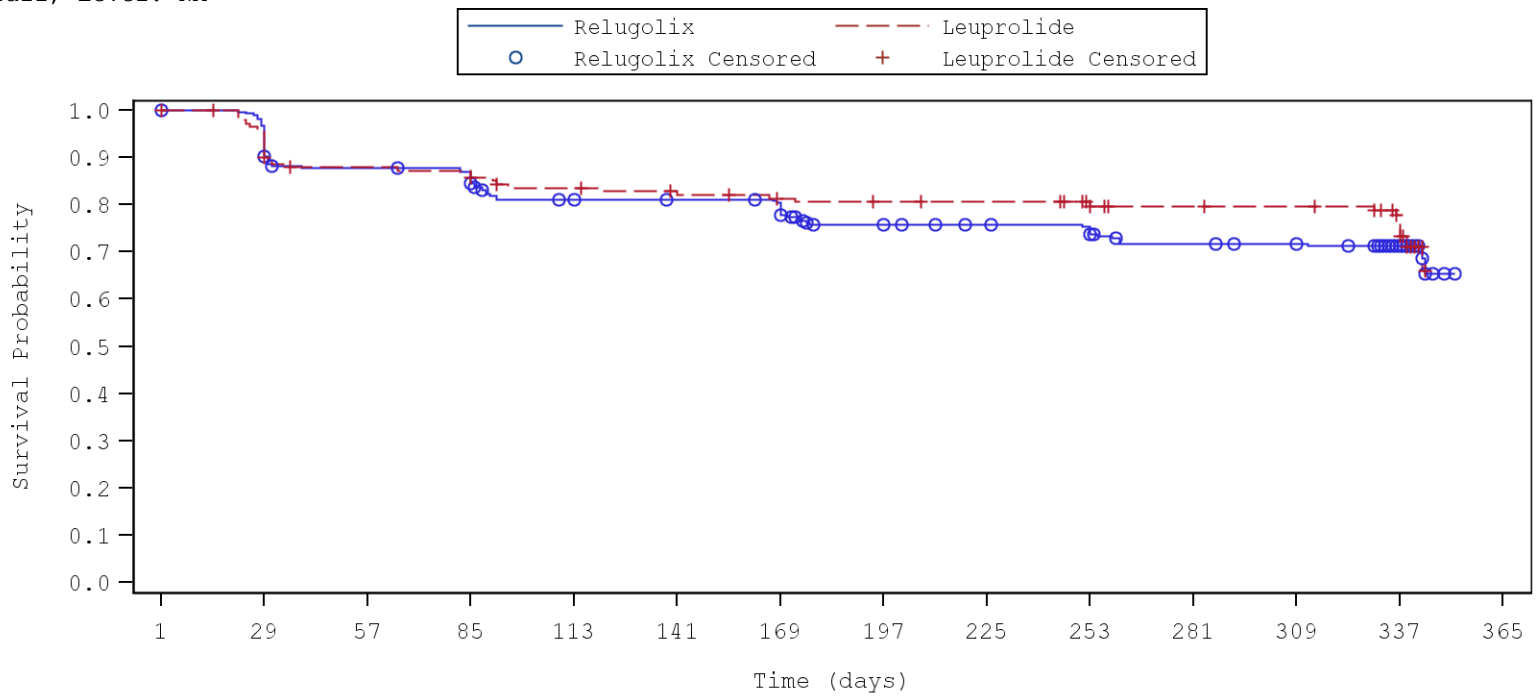
6.1.5.2.3 Kaplan-Meier-Kurven zu Time-to-Event-Analysen des EORTC-QLQ-PR25 (QoL)

Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2SEXA15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Activity Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

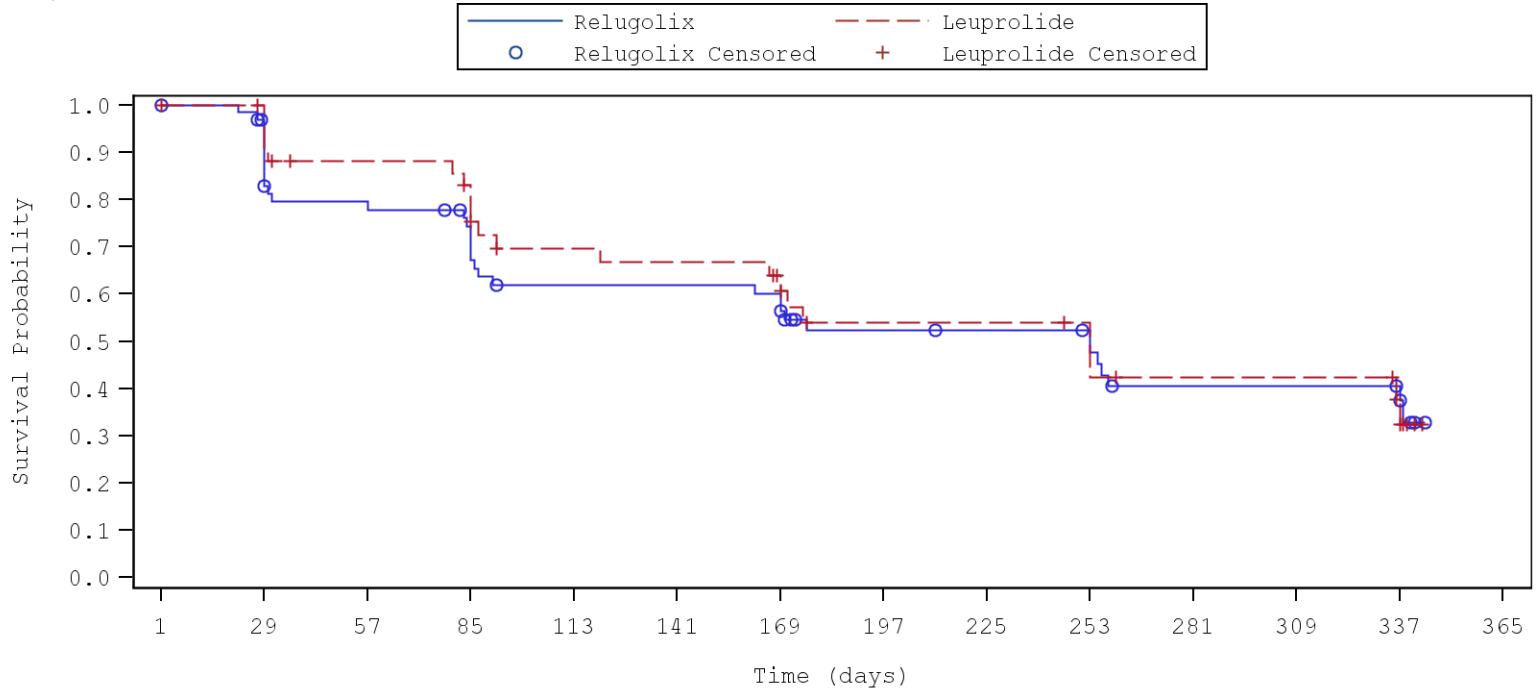
Relugolix	290	269	241	238	218	216	213	194	189	187	174	172	127	0
Leuprolide	144	135	122	121	113	110	106	104	103	95	90	89	70	0

Relugolix vs Leuprolide

Hazard Ratio (95% CI): 1.142 (0.767, 1.701)
P-value: 0.5137

Relugolix Median (95% CI): NE (NE, NE)
Leuprolide Median (95% CI): NE (NE, NE)

Myovant Sciences, Inc.: HERO AMNOG
Figure QS.T2SEXF15.KM.MITTM1: Kaplan-Meier Curves of Time to at least 15 % (15 points) Decrease in EORTC-QLQ-PR25 Sexual Functioning Scale Score (mITT Metastatic Population)
Study: HERO
Subgroup: Overall, Level: NA



No. of Patients at Risk

Relugolix	290	62	47	42	34	34	33	24	23	22	16	16	14	0
Leuprolide	144	42	35	32	24	23	20	15	15	14	10	10	7	0

Relugolix vs Leuprolide
Hazard Ratio (95% CI): 1.234 (0.690, 2.207)
P-value: 0.4791
Relugolix Median (95% CI): 253.0 (91.0, 338.0)
Leuprolide Median (95% CI): 253.0 (120.0, NE)

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\Fig_QS_KM.SAS

6.1.6 Sicherheit

6.1.6.1 Gesamtrate jeglicher UE

Myovant Sciences, Inc.: HERO AMNOG

Table AE.TEAE.ANY.BIN.SAFM1: Proportion of Patients with at Least One Treatment Emergent Adverse Event (Safety Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Relugolix	290	268 (92.4)	1.416	1.032	0.028	0.3621
Leuprolide	144	129 (89.6)	[0.711;2.821]	[0.967;1.101]	[-0.030;0.087]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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6.1.6.2 Häufige jegliche UE nach SOC und PT

Table AE.TEAE.SPT.BIN.SAFM1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Any event						
Relugolix	290	268 (92.4)	1.416	1.032	0.028	0.3621
Leuprolide	144	129 (89.6)	[0.711;2.821]	[0.967;1.101]	[-0.030;0.087]	
Blood and lymphatic system disorders						
Any preferred term						
Relugolix	290	22 (7.6)	0.706	0.728	-0.028	0.3621
Leuprolide	144	15 (10.4)	[0.354;1.406]	[0.390;1.361]	[-0.087;0.030]	
Anaemia						
Relugolix	290	13 (4.5)	0.567	0.587	-0.032	0.1859
Leuprolide	144	11 (7.6)	[0.248;1.300]	[0.270;1.277]	[-0.081;0.018]	
Cardiac disorders						
Any preferred term						
Relugolix	290	24 (8.3)	0.594	0.627	-0.049	0.1247
Leuprolide	144	19 (13.2)	[0.314;1.124]	[0.356;1.107]	[-0.113;0.015]	
Eye disorders						
Any preferred term						
Relugolix	290	34 (11.7)	1.606	1.535	0.041	0.2417
Leuprolide	144	11 (7.6)	[0.788;3.271]	[0.801;2.939]	[-0.016;0.098]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

Table AE.TEAE.SPT.BIN.SAFM1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Gastrointestinal disorders						
Any preferred term						
Relugolix	290	114 (39.3)	1.425	1.258	0.081	0.1128
Leuprolide	144	45 (31.3)	[0.933;2.177]	[0.949;1.667]	[-0.014;0.175]	
Constipation						
Relugolix	290	45 (15.5)	1.019	1.016	0.002	1.0000
Leuprolide	144	22 (15.3)	[0.585;1.773]	[0.635;1.624]	[-0.070;0.074]	
Nausea						
Relugolix	290	32 (11.0)	1.662	1.589	0.041	0.2272
Leuprolide	144	10 (6.9)	[0.793;3.484]	[0.804;3.141]	[-0.014;0.096]	
Diarrhoea						
Relugolix	290	29 (10.0)	2.175	2.057	0.051	0.0947
Leuprolide	144	7 (4.9)	[0.929;5.092]	[0.924;4.582]	[0.002;0.101]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

Date/time of run: 04AUG2022 10:40 Data Cut Date: 23SEP2020

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Table AE.TEAE.SPT.BIN.SAFM1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
General disorders and administration site conditions						
Any preferred term						
Relugolix	290	119 (41.0)	0.920	0.953	-0.020	0.7565
Leuprolide	144	62 (43.1)	[0.614;1.379]	[0.755;1.203]	[-0.119;0.079]	
Fatigue						
Relugolix	290	67 (23.1)	1.191	1.147	0.030	0.5399
Leuprolide	144	29 (20.1)	[0.730;1.945]	[0.779;1.690]	[-0.052;0.111]	
Oedema peripheral						
Relugolix	290	23 (7.9)	0.868	0.879	-0.011	0.7137
Leuprolide	144	13 (9.0)	[0.426;1.768]	[0.459;1.683]	[-0.067;0.045]	
Asthenia						
Relugolix	290	21 (7.2)	1.046	1.043	0.003	1.0000
Leuprolide	144	10 (6.9)	[0.479;2.284]	[0.505;2.155]	[-0.048;0.054]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

Date/time of run: 04AUG2022 10:40 Data Cut Date: 23SEP2020

Table AE.TEAE.SPT.BIN.SAFM1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
General disorders and administration site conditions						
Pyrexia						
Relugolix	290	10 (3.4)	2.536	2.483	0.021	0.3519
Leuprolide	144	2 (1.4)	[0.548;11.729]	[0.551;11.182]	[-0.008;0.049]	
Infections and infestations						
Any preferred term						
Relugolix	290	105 (36.2)	1.909	1.580	0.133	0.0061
Leuprolide	144	33 (22.9)	[1.209;3.013]	[1.129;2.211]	[0.045;0.221]	
Nasopharyngitis						
Relugolix	290	24 (8.3)	2.508	2.383	0.048	0.0670
Leuprolide	144	5 (3.5)	[0.937;6.717]	[0.929;6.117]	[0.004;0.092]	
Urinary tract infection						
Relugolix	290	20 (6.9)	1.704	1.655	0.027	0.2916
Leuprolide	144	6 (4.2)	[0.669;4.340]	[0.680;4.031]	[-0.016;0.071]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

Date/time of run: 04AUG2022 10:40 Data Cut Date: 23SEP2020

Table AE.TEAE.SPT.BIN.SAFM1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Infections and infestations						
Upper respiratory tract infection						
Relugolix	290	12 (4.1)	1.511	1.490	0.014	0.5951
Leuprolide	144	4 (2.8)	[0.479;4.770]	[0.489;4.537]	[-0.022;0.049]	
Injury, poisoning and procedural complications						
Any preferred term						
Relugolix	290	36 (12.4)	1.559	1.490	0.041	0.2553
Leuprolide	144	12 (8.3)	[0.785;3.097]	[0.800;2.775]	[-0.018;0.100]	
Fall						
Relugolix	290	11 (3.8)	0.907	0.910	-0.004	0.7995
Leuprolide	144	6 (4.2)	[0.328;2.503]	[0.344;2.412]	[-0.043;0.036]	
Investigations						
Any preferred term						
Relugolix	290	66 (22.8)	1.074	1.057	0.012	0.8077
Leuprolide	144	31 (21.5)	[0.663;1.741]	[0.725;1.541]	[-0.070;0.095]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

Date/time of run: 04AUG2022 10:40 Data Cut Date: 23SEP2020

Table AE.TEAE.SPT.BIN.SAFM1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Investigations						
Weight increased						
Relugolix	290	26 (9.0)	0.992	0.993	-0.001	1.0000
Leuprolide	144	13 (9.0)	[0.494;1.994]	[0.526;1.874]	[-0.058;0.057]	
Alanine aminotransferase increased						
Relugolix	290	18 (6.2)	2.316	2.234	0.034	0.1640
Leuprolide	144	4 (2.8)	[0.769;6.975]	[0.770;6.481]	[-0.004;0.073]	
Aspartate aminotransferase increased						
Relugolix	290	13 (4.5)	3.332	3.228	0.031	0.1599
Leuprolide	144	2 (1.4)	[0.742;14.969]	[0.738;14.111]	[0.000;0.061]	
Metabolism and nutrition disorders						
Any preferred term						
Relugolix	290	52 (17.9)	0.992	0.993	-0.001	1.0000
Leuprolide	144	26 (18.1)	[0.590;1.668]	[0.648;1.521]	[-0.078;0.076]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

Date/time of run: 04AUG2022 10:40 Data Cut Date: 23SEP2020

Table AE.TEAE.SPT.BIN.SAFM1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Metabolism and nutrition disorders						
Decreased appetite						
Relugolix	290	17 (5.9)	0.934	0.938	-0.004	0.8336
Leuprolide	144	9 (6.3)	[0.406;2.150]	[0.429;2.052]	[-0.052;0.044]	
Musculoskeletal and connective tissue disorders						
Any preferred term						
Relugolix	290	129 (44.5)	1.154	1.086	0.035	0.5373
Leuprolide	144	59 (41.0)	[0.770;1.731]	[0.859;1.373]	[-0.064;0.134]	
Arthralgia						
Relugolix	290	47 (16.2)	1.949	1.795	0.072	0.0540
Leuprolide	144	13 (9.0)	[1.018;3.733]	[1.004;3.209]	[0.009;0.135]	
Back pain						
Relugolix	290	28 (9.7)	0.593	0.632	-0.056	0.1094
Leuprolide	144	22 (15.3)	[0.326;1.078]	[0.375;1.065]	[-0.124;0.012]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

Date/time of run: 04AUG2022 10:40 Data Cut Date: 23SEP2020

Table AE.TEAE.SPT.BIN.SAFM1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Musculoskeletal and connective tissue disorders						
Musculoskeletal pain						
Relugolix	290	21 (7.2)	1.327	1.303	0.017	0.6834
Leuprolide	144	8 (5.6)	[0.573;3.074]	[0.592;2.870]	[-0.031;0.065]	
Pain in extremity						
Relugolix	290	19 (6.6)	0.939	0.943	-0.004	0.8414
Leuprolide	144	10 (6.9)	[0.425;2.077]	[0.450;1.976]	[-0.054;0.046]	
Muscular weakness						
Relugolix	290	15 (5.2)	3.873	3.724	0.038	0.0664
Leuprolide	144	2 (1.4)	[0.873;17.171]	[0.863;16.065]	[0.006;0.070]	
Bone pain						
Relugolix	290	13 (4.5)	0.919	0.922	-0.004	0.8133
Leuprolide	144	7 (4.9)	[0.358;2.355]	[0.376;2.261]	[-0.046;0.039]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

Date/time of run: 04AUG2022 10:40 Data Cut Date: 23SEP2020

Table AE.TEAE.SPT.BIN.SAFM1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Musculoskeletal and connective tissue disorders						
Myalgia						
Relugolix	290	13 (4.5)	0.798	0.807	-0.011	0.6391
Leuprolide	144	8 (5.6)	[0.323;1.971]	[0.342;1.903]	[-0.055;0.034]	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Any preferred term						
Relugolix	290	23 (7.9)	1.464	1.428	0.024	0.4324
Leuprolide	144	8 (5.6)	[0.638;3.360]	[0.655;3.112]	[-0.025;0.072]	
Nervous system disorders						
Any preferred term						
Relugolix	290	70 (24.1)	0.991	0.993	-0.002	1.0000
Leuprolide	144	35 (24.3)	[0.622;1.579]	[0.698;1.414]	[-0.087;0.084]	
Headache						
Relugolix	290	16 (5.5)	2.044	1.986	0.027	0.2333
Leuprolide	144	4 (2.8)	[0.671;6.229]	[0.676;5.833]	[-0.010;0.065]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

Date/time of run: 04AUG2022 10:40 Data Cut Date: 23SEP2020

Table AE.TEAE.SPT.BIN.SAFM1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Nervous system disorders						
Dizziness						
Relugolix	290	13 (4.5)	0.567	0.587	-0.032	0.1859
Leuprolide	144	11 (7.6)	[0.248;1.300]	[0.270;1.277]	[-0.081;0.018]	
Psychiatric disorders						
Any preferred term						
Relugolix	290	52 (17.9)	1.280	1.230	0.033	0.4159
Leuprolide	144	21 (14.6)	[0.737;2.221]	[0.772;1.959]	[-0.039;0.106]	
Insomnia						
Relugolix	290	20 (6.9)	0.896	0.903	-0.007	0.8436
Leuprolide	144	11 (7.6)	[0.417;1.924]	[0.445;1.833]	[-0.060;0.045]	
Renal and urinary disorders						
Any preferred term						
Relugolix	290	75 (25.9)	1.009	1.007	0.002	1.0000
Leuprolide	144	37 (25.7)	[0.639;1.593]	[0.717;1.413]	[-0.086;0.089]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.TEAE.SPT.BIN.SAFM1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Renal and urinary disorders						
Urinary incontinence						
Relugolix	290	18 (6.2)	1.125	1.117	0.007	1.0000
Leuprolide	144	8 (5.6)	[0.477;2.653]	[0.498;2.508]	[-0.040;0.053]	
Nocturia						
Relugolix	290	17 (5.9)	0.934	0.938	-0.004	0.8336
Leuprolide	144	9 (6.3)	[0.406;2.150]	[0.429;2.052]	[-0.052;0.044]	
Pollakiuria						
Relugolix	290	14 (4.8)	1.410	1.390	0.014	0.6237
Leuprolide	144	5 (3.5)	[0.498;3.995]	[0.511;3.785]	[-0.025;0.052]	
Dysuria						
Relugolix	290	12 (4.1)	0.845	0.851	-0.007	0.8042
Leuprolide	144	7 (4.9)	[0.325;2.194]	[0.342;2.116]	[-0.049;0.035]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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Table AE.TEAE.SPT.BIN.SAFM1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Reproductive system and breast disorders						
Any preferred term						
Relugolix	290	30 (10.3)	0.923	0.931	-0.008	0.8687
Leuprolide	144	16 (11.1)	[0.485;1.755]	[0.525;1.651]	[-0.070;0.054]	
Respiratory, thoracic and mediastinal disorders						
Any preferred term						
Relugolix	290	45 (15.5)	1.469	1.397	0.044	0.2424
Leuprolide	144	16 (11.1)	[0.799;2.702]	[0.818;2.383]	[-0.022;0.110]	
Skin and subcutaneous tissue disorders						
Any preferred term						
Relugolix	290	54 (18.6)	0.907	0.925	-0.015	0.6994
Leuprolide	144	29 (20.1)	[0.549;1.501]	[0.617;1.386]	[-0.095;0.064]	
Hyperhidrosis						
Relugolix	290	13 (4.5)	0.516	0.538	-0.039	0.1258
Leuprolide	144	12 (8.3)	[0.229;1.162]	[0.252;1.149]	[-0.090;0.013]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

Date/time of run: 04AUG2022 10:40 Data Cut Date: 23SEP2020

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Table AE.TEAE.SPT.BIN.SAFM1: Frequent Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Skin and subcutaneous tissue disorders						
Rash						
Relugolix	290	11 (3.8)	1.096	1.092	0.003	1.0000
Leuprolide	144	5 (3.5)	[0.374;3.216]	[0.387;3.085]	[-0.034;0.040]	
Vascular disorders						
Any preferred term						
Relugolix	290	163 (56.2)	1.214	1.094	0.048	0.3581
Leuprolide	144	74 (51.4)	[0.813;1.813]	[0.906;1.321]	[-0.051;0.148]	
Hot flush						
Relugolix	290	146 (50.3)	1.198	1.098	0.045	0.4149
Leuprolide	144	66 (45.8)	[0.803;1.789]	[0.889;1.357]	[-0.055;0.145]	
Hypertension						
Relugolix	290	34 (11.7)	1.233	1.206	0.020	0.6267
Leuprolide	144	14 (9.7)	[0.639;2.379]	[0.669;2.174]	[-0.041;0.081]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 10% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_SPT_BIN.SAS

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6.1.6.3 Gesamtrate der schweren UE (CTCAE-Grad ≥ 3)

Myovant Sciences, Inc.: HERO AMNOG

Table AE.G35TEAE.ANY.BIN.SAFM1: Proportion of Patients with at Least One Grade 3 or Above Treatment Emergent Adverse Event (Safety Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Relugolix	290	72 (24.8)	1.029	1.021	0.005	1.0000
Leuprolide	144	35 (24.3)	[0.646;1.637]	[0.719;1.451]	[-0.081;0.091]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

SOURCE: \Studies\MYV\MYV104\Analysis\Prod\Progs\TFLs\TAB_AE_ANY_BIN.SAS

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6.1.6.4 Häufige schwere UE (CTCAE-Grad ≥ 3) nach SOC und PT

Table AE.G35TEAE.SPT.BIN.SAFM1: Frequent Grade 3 or Above Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT **Treatment**	**N**	**n (%)**	**OR[1]** **[95% CI]**	**RR[2]** **[95% CI]**	**RD[3]** **[95% CI]**	**p-value[4]**
Any event						
Relugolix	290	72 (24.8)	1.029	1.021	0.005	1.0000
Leuprolide	144	35 (24.3)	[0.646;1.637]	[0.719;1.451]	[-0.081;0.091]	
Cardiac disorders						
Any preferred term						
Relugolix	290	11 (3.8)	0.670	0.683	-0.018	0.4565
Leuprolide	144	8 (5.6)	[0.264;1.705]	[0.281;1.660]	[-0.061;0.026]	
Infections and infestations						
Any preferred term						
Relugolix	290	13 (4.5)	2.206	2.152	0.024	0.2837
Leuprolide	144	3 (2.1)	[0.618;7.867]	[0.623;7.431]	[-0.009;0.057]	
Investigations						
Any preferred term						
Relugolix	290	14 (4.8)	1.410	1.390	0.014	0.6237
Leuprolide	144	5 (3.5)	[0.498;3.995]	[0.511;3.785]	[-0.025;0.052]	
Musculoskeletal and connective tissue disorders						
Any preferred term						
Relugolix	290	10 (3.4)	0.993	0.993	0.000	1.0000
Leuprolide	144	5 (3.5)	[0.333;2.961]	[0.346;2.851]	[-0.037;0.036]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03. MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

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Table AE.G35TEAE.SPT.BIN.SAFM1: Frequent Grade 3 or Above Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Renal and urinary disorders						
Any preferred term						
Relugolix	290	10 (3.4)	0.821	0.828	-0.007	0.7880
Leuprolide	144	6 (4.2)	[0.293;2.307]	[0.307;2.232]	[-0.046;0.032]	
Vascular disorders						
Any preferred term						
Relugolix	290	11 (3.8)	5.638	5.462	0.031	0.1150
Leuprolide	144	1 (0.7)	[0.721;44.104]	[0.712;41.895]	[0.005;0.057]	
Hypertension						
Relugolix	290	10 (3.4)	5.107	4.966	0.028	0.1098
Leuprolide	144	1 (0.7)	[0.647;40.290]	[0.642;38.414]	[0.003;0.053]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03. MedDRA Version 22.0.

[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.

[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.

[4] P-value based on a Fisher's exact test.

A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.

The reference group for the OR, RR and RD is Leuprolide.

Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

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6.1.6.5 Gesamtrate der SUE

Myovant Sciences, Inc.: HERO AMNOG

Table AE.STEAE.ANY.BIN.SAFM1: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event (Safety Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Relugolix	290	49 (16.9)	1.017	1.014	0.002	1.0000
Leuprolide	144	24 (16.7)	[0.595;1.736]	[0.649;1.583]	[-0.072;0.077]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

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6.1.6.6 Gesamtrate der SUE ohne MACE-Events

Myovant Sciences, Inc.: HERO AMNOG

Table AE.STEAES1.ANY.BIN.SAFM1: Proportion of Patients with at Least One Serious Treatment Emergent Adverse Event Excluding Pre-defined MACE (Safety Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Relugolix	290	40 (13.8)	0.992	0.993	-0.001	1.0000
Leuprolide	144	20 (13.9)	[0.556;1.769]	[0.603;1.634]	[-0.070;0.068]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events are counted only once.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; MACE: Major cardiovascular adverse events.

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6.1.6.7 Häufige SUE nach SOC und PT

Myovant Sciences, Inc.: HERO AMNOG

Table AE.STEAE.SPT.BIN.SAFM1: Frequent Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Safety Metastatic Population)

Study: HERO

SOC/PT Treatment	N	n (%)	OR[1] [95% CI]	RR[2] [95% CI]	RD[3] [95% CI]	p-value[4]
Any event						
Relugolix	290	49 (16.9)	1.017	1.014	0.002	1.0000
Leuprolide	144	24 (16.7)	[0.595;1.736]	[0.649;1.583]	[-0.072;0.077]	
Cardiac disorders						
Any preferred term						
Relugolix	290	10 (3.4)	0.607	0.621	-0.021	0.3138
Leuprolide	144	8 (5.6)	[0.234;1.573]	[0.250;1.539]	[-0.064;0.022]	
Infections and infestations						
Any preferred term						
Relugolix	290	12 (4.1)	2.029	1.986	0.021	0.4038
Leuprolide	144	3 (2.1)	[0.563;7.306]	[0.569;6.928]	[-0.012;0.053]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events for a given SOC or PT are counted only once for each SOC and PT. Only SOCs or PTs for which there are at least 5% of patients with an event in at least one treatment group OR at least 10 patients with an event in at least one treatment group AND at least 1% of patients with an event in at least one treatment group are presented. Events are sorted by SOC alphabetically and then by decreasing frequency of PT in the Relugolix group. MedDRA Version 22.0.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval; SOC: System organ class; PT: Preferred Term.

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6.1.6.8 Absetzen der Studienmedikation aufgrund von UE

Myovant Sciences, Inc.: HERO AMNOG

Table AE.TEAED.ANY.BIN.SAFM1: Proportion of Patients with at Least One Treatment Emergent Adverse Event with Action Taken of Study Treatment Discontinuation (Safety Metastatic Population)

Study: HERO

Treatment	**N**	**n (%)**	**OR[1] [95% CI]**	**RR[2] [95% CI]**	**RD[3] [95% CI]**	**p-value[4]**
Relugolix	290	14 (4.8)	15.156	14.450	0.048	0.0066
Leuprolide	144	0	[0.898;255.885]	[0.868;240.531]	[0.024;0.073]	

Post hoc analysis. The denominator for percentages is the number of patients in the Safety Metastatic Population for each treatment group. Patients with multiple events are counted only once.
Adverse events with action taken of study treatment discontinuation are taken from the adverse events case report form.
[1] OR (95% CI) based on a logistic regression model adjusting for treatment group as a covariate.
[2] RR (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[3] RD (95% CI) based on an unstratified approach. 95% CIs based on the approximation to the normal distribution.
[4] P-value based on a Fisher's exact test.
A continuity correction is applied in estimation of the OR and RR if zero events are observed in a given treatment group or if 100% of patients have an event in a given treatment group. No continuity correction is applied in estimation of the RD.
The reference group for the OR, RR and RD is Leuprolide.
Abbreviations: N: Number of patients in treatment group; n: Number of patients with ≥ 1 event; OR: Odds ratio; RR: Risk ratio; RD: Risk difference; CI: Confidence interval.

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