Clinical trial results:
Randomized phase III trial in elderly patients with previously untreated symptomatic Multiple Myeloma comparing MP-Thalidomide (MP-Thal) followed by thalidomide maintenance versus MP-Lenalidomide (MP-Len) followed by maintenance with lenalidomide

Summary

EudraCT number	2007-004007-34
Trial protocol	NL SE DK BE
Global end of trial date	07 October 2020

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	HOVON87MM/NMSG18

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	HOVON
Sponsor organisation address	De Boelelaan 1117, Amsterdam, Netherlands,
Public contact	HOVON Data Center, HOVON, hdc@erasmusmc.nl
Scientific contact	HOVON Data Center, HOVON, hdc@erasmusmc.nl

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 November 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 October 2014
Global end of trial reached?	Yes
Global end of trial date	07 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To compare progression free survival with Melphalan/Prednisone (MP)-Thalidomide followed by thalidomide maintenance versus MP-Lenalidomide followed by maintenance with lenalidomide

Protection of trial subjects:	
Monitoring and Insurance	
Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	26 January 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 511
Country: Number of subjects enrolled	Norway: 46
Country: Number of subjects enrolled	Sweden: 79
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Denmark: 29
Worldwide total number of subjects	668
EEA total number of subjects	668

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	22

From 65 to 84 years	635
85 years and over	11

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All subjects gave written informed consent and were screened according to the inclusion- and exclusion criteria.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

All patients will receive a fixed number of 9 cycles of melphalan 0.18 mg/kg per day for 4 days, prednisone 2 mg/kg per day for 4 days and thalidomide 200 mg from day 1 until 4 weeks after the last cycle of MPT. Therapy cycles will be given every 4 weeks.
Maintenance treatment with thalidomide 100 mg will start 4 weeks after start of the last cycle of MP-Thal.
Maintenance cycles will be repeated at 28-days intervals until relapse, progression or when a medical condition occurs that requires stopping the treatment.

Arm type	Active comparator
Investigational medicinal product name	Thalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Thalidomide during induction cycles together with MP (Melphalan; Prednisone) 200 mg daily.
Thalidomide maintenance: 100 mg daily until disease progression.

Investigational medicinal product name	Melphalan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Mephalan during induction cycles: 0.18 mg/kg day 1 - 4

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone during induction cycles: 2 mg/kg day 1 - 4

Arm title	Arm B

Arm description:

Patients will receive a fixed number of 9 cycles of melphalan 0.18 mg/kg per day for 4 days, prednisone

2 mg/kg per day for 4 days and lenalidomide 10 mg. Lenalidomide will be given on day 1-21 followed by a 1 week interval. Therapy cycles will be given every 4 weeks. Maintenance treatment with lenalidomide will be started 4 weeks after start of the last MP-Len cycle, at a dose of 10 mg days 1-21. Maintenance cycles will be repeated at 28-days intervals until relapse, progression or when a medical condition that requires stopping the treatment.

Arm type	Experimental
Investigational medicinal product name	Revlimid
Investigational medicinal product code	
Other name	Lenalidomide
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Revlimid (Lenalidomide) during induction cycles together with MP (Melphalan; Prednisone) 10 mg daily. Revlimid (Lenalidomide) maintenance: 10 mg daily until disease progression.

Investigational medicinal product name	Melphalan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Mephalan during induction cycles: 0.18 mg/kg day 1 - 4

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone during induction cycles: 2 mg/kg day 1 - 4

Number of subjects in period 1	Arm A	Arm B
Started	333	335
Completed	0	0
Not completed	333	335
Adverse reactions	187	113
Other	62	83
Lack of efficacy	84	139

Baseline characteristics

Reporting groups

Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	668	668	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	22	22	
From 65-84 years	635	635	
85 years and over	11	11	
Age continuous Units: years			
median	73		
full range (min-max)	49 to 91	-	
Gender categorical Units: Subjects			
Female	303	303	
Male	365	365	

End points

End points reporting groups

Reporting group title	Arm A

Reporting group description:

All patients will receive a fixed number of 9 cycles of melphalan 0.18 mg/kg per day for 4 days, prednisone 2 mg/kg per day for 4 days and thalidomide 200 mg from day 1 until 4 weeks after the last cycle of MPT. Therapy cycles will be given every 4 weeks.
Maintenance treatment with thalidomide 100 mg will start 4 weeks after start of the last cycle of MP-Thal.
Maintenance cycles will be repeated at 28-days intervals until relapse, progression or when a medical condition occurs that requires stopping the treatment.

Reporting group title	Arm B

Reporting group description:

Patients will receive a fixed number of 9 cycles of melphalan 0.18 mg/kg per day for 4 days, prednisone 2 mg/kg per day for 4 days and lenalidomide 10 mg. Lenalidomide will be given on day 1-21 followed by a 1 week interval. Therapy cycles will be given every 4 weeks. Maintenance treatment with lenalidomide will be started 4 weeks after start of the last MP-Len cycle, at a dose of 10 mg days 1-21.
Maintenance cycles will be repeated at 28-days intervals until relapse, progression or when a medical condition that requires stopping the treatment.

Primary: Primary endpoint

End point title	Primary endpoint[1]

End point description:

End point type	Primary

End point timeframe:

See publication.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis has been uploaded in the chart section.

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	318	319		
Units: Whole	318	319		

Attachments (see zip file)	Statistical data section from publication/HO87_Statistical data List of reported SAE's/saedata87-21Nov2022.pdf List of reported non-SAE's/nonsaedata87-21Nov2022.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events of Grade 2 or higher, and polyneuropathy grade ≥ 1 have to be reported. Progression of disease should not be reported as adverse event. Adverse events occurring after 30 days should also be reported if considered related to study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	3.0

Reporting groups

Reporting group title	Arm A
Reporting group description: -	
Reporting group title	Arm B

Reporting group description: -

Serious adverse events	Arm A	Arm B	
Total subjects affected by serious adverse events			
subjects affected / exposed	215 / 324 (66.36%)	229 / 332 (68.98%)	
number of deaths (all causes)	247	233	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm benign, malignant and unspecif.	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	43 / 324 (13.27%)	59 / 332 (17.77%)	
occurrences causally related to treatment / all	24 / 52	43 / 73	
deaths causally related to treatment / all	7 / 14	11 / 14	
Vascular disorders			
Vascular disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	21 / 324 (6.48%)	21 / 332 (6.33%)	
occurrences causally related to treatment / all	17 / 21	21 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Surgical and medical procedures	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	0 / 324 (0.00%)	2 / 332 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

General disorders and administration site conditions	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	40 / 324 (12.35%)	36 / 332 (10.84%)	
occurrences causally related to treatment / all	23 / 50	32 / 44	
deaths causally related to treatment / all	1 / 6	0 / 0	
Immune system disorders			
Immune system disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	0 / 324 (0.00%)	3 / 332 (0.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Reproductive system and breast disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 324 (0.31%)	1 / 332 (0.30%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	32 / 324 (9.88%)	26 / 332 (7.83%)	
occurrences causally related to treatment / all	19 / 36	20 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychiatric disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	6 / 324 (1.85%)	0 / 332 (0.00%)	
occurrences causally related to treatment / all	4 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Investigations	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	3 / 324 (0.93%)	1 / 332 (0.30%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All combined, see SAE chart for details		

subjects affected / exposed	18 / 324 (5.56%)	20 / 332 (6.02%)	
occurrences causally related to treatment / all	2 / 19	1 / 21	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cardiac disorders			
Cardiac disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	20 / 324 (6.17%)	23 / 332 (6.93%)	
occurrences causally related to treatment / all	14 / 28	10 / 24	
deaths causally related to treatment / all	0 / 3	0 / 4	
Nervous system disorders			
Nervous system disorder	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	25 / 324 (7.72%)	20 / 332 (6.02%)	
occurrences causally related to treatment / all	20 / 27	10 / 22	
deaths causally related to treatment / all	1 / 1	1 / 1	
Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	15 / 324 (4.63%)	27 / 332 (8.13%)	
occurrences causally related to treatment / all	13 / 15	26 / 29	
deaths causally related to treatment / all	0 / 0	1 / 2	
Ear and labyrinth disorders			
Ear and labyrinth disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	2 / 324 (0.62%)	2 / 332 (0.60%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eye disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	0 / 324 (0.00%)	2 / 332 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	25 / 324 (7.72%)	24 / 332 (7.23%)	
occurrences causally related to treatment / all	18 / 25	13 / 26	
deaths causally related to treatment / all	1 / 1	0 / 0	
Hepatobiliary disorders			
Hepatobiliary disorders	Additional description: All combined, see SAE chart for details		

subjects affected / exposed	1 / 324 (0.31%)	5 / 332 (1.51%)	
occurrences causally related to treatment / all	0 / 2	4 / 6	
deaths causally related to treatment / all	0 / 0	1 / 1	
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	3 / 324 (0.93%)	4 / 332 (1.20%)	
occurrences causally related to treatment / all	3 / 3	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal and urinary disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	7 / 324 (2.16%)	11 / 332 (3.31%)	
occurrences causally related to treatment / all	3 / 7	6 / 11	
deaths causally related to treatment / all	0 / 0	0 / 1	
Endocrine disorders			
Endocrine disorders	Additional description: All combined, see SAE chart for detail		
subjects affected / exposed	0 / 324 (0.00%)	1 / 332 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	12 / 324 (3.70%)	13 / 332 (3.92%)	
occurrences causally related to treatment / all	1 / 12	6 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infections and infestations	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	75 / 324 (23.15%)	83 / 332 (25.00%)	
occurrences causally related to treatment / all	55 / 96	72 / 114	
deaths causally related to treatment / all	7 / 9	3 / 6	
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	8 / 324 (2.47%)	7 / 332 (2.11%)	
occurrences causally related to treatment / all	4 / 8	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Arm A	Arm B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	307 / 324 (94.75%)	318 / 332 (95.78%)	
Vascular disorders			
Vascular	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	13 / 324 (4.01%)	9 / 332 (2.71%)	
occurrences (all)	15	11	
Surgical and medical procedures			
Surgery/intra-operative injury	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	3 / 324 (0.93%)	2 / 332 (0.60%)	
occurrences (all)	4	3	
General disorders and administration site conditions			
Constitutional symptoms	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	118 / 324 (36.42%)	127 / 332 (38.25%)	
occurrences (all)	154	184	
Death	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 324 (0.62%)	1 / 332 (0.30%)	
occurrences (all)	2	1	
Secondary malignancy	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	3 / 324 (0.93%)	3 / 332 (0.90%)	
occurrences (all)	3	3	
Syndromes	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	5 / 324 (1.54%)	7 / 332 (2.11%)	
occurrences (all)	5	8	
Immune system disorders			
Allergy/immunology	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	5 / 324 (1.54%)	3 / 332 (0.90%)	
occurrences (all)	5	3	
Reproductive system and breast disorders			
Sexual/reproductive function	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	0 / 324 (0.00%)	2 / 332 (0.60%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			

Pulmonary/upper respiratory	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	43 / 324 (13.27%)	41 / 332 (12.35%)	
occurrences (all)	49	46	
Cardiac disorders			
Cardiac arrythmia	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	26 / 324 (8.02%)	24 / 332 (7.23%)	
occurrences (all)	30	30	
Cardiac general	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	20 / 324 (6.17%)	21 / 332 (6.33%)	
occurrences (all)	26	24	
Nervous system disorders			
Neurology	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	244 / 324 (75.31%)	127 / 332 (38.25%)	
occurrences (all)	562	219	
Pain	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	68 / 324 (20.99%)	81 / 332 (24.40%)	
occurrences (all)	82	125	
Blood and lymphatic system disorders			
Blood/bone marrow	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	178 / 324 (54.94%)	273 / 332 (82.23%)	
occurrences (all)	589	1580	
Coagulation	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 324 (0.62%)	3 / 332 (0.90%)	
occurrences (all)	2	3	
Hemorrhage/bleeding	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	5 / 324 (1.54%)	14 / 332 (4.22%)	
occurrences (all)	6	17	
Lymphatics	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	38 / 324 (11.73%)	16 / 332 (4.82%)	
occurrences (all)	39	16	
Ear and labyrinth disorders			
Auditory/ear	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	11 / 324 (3.40%)	12 / 332 (3.61%)	
occurrences (all)	11	13	
Eye disorders			
Ocular/visual	Additional description: All combined, see non-SAE chart for details		

subjects affected / exposed	16 / 324 (4.94%)	15 / 332 (4.52%)	
occurrences (all)	19	16	
Gastrointestinal disorders			
Gastrointestinal	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	104 / 324 (32.10%)	114 / 332 (34.34%)	
occurrences (all)	153	180	
Hepatobiliary disorders			
Hepatobiliary/pancreas	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	0 / 324 (0.00%)	3 / 332 (0.90%)	
occurrences (all)	0	3	
Skin and subcutaneous tissue disorders			
Dermatology/skin	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	48 / 324 (14.81%)	50 / 332 (15.06%)	
occurrences (all)	63	63	
Renal and urinary disorders			
Renal/genitourinary	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	14 / 324 (4.32%)	19 / 332 (5.72%)	
occurrences (all)	14	19	
Endocrine disorders			
Endocrine	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	5 / 324 (1.54%)	1 / 332 (0.30%)	
occurrences (all)	6	1	
Musculoskeletal and connective tissue disorders			
Musculoskeletal/soft tissue	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	27 / 324 (8.33%)	38 / 332 (11.45%)	
occurrences (all)	34	54	
Infections and infestations			
Infection	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	88 / 324 (27.16%)	101 / 332 (30.42%)	
occurrences (all)	128	185	
Metabolism and nutrition disorders			
Metabolic/laboratory	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	42 / 324 (12.96%)	52 / 332 (15.66%)	
occurrences (all)	90	113	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 April 2009	Addition of plasmacytoma §8.1.1; pregnancy §8.1.2; clarification of thrombosis prophylaxis §9.1.1. & 9.2.1; polyneuropathy §13.2; rephrasing response rate §14.1 & 14.2; adjustment appendix A; C; G; H; J; adjustment in QoL logistics §11.4; adjustment in the required investigations.
15 September 2010	Clarification of the dose reduction instructions and addition of diagrams in appendix G and H; adjustments in section §9.1.1; §9.2.1; §11.1; §11.2; §11.4; §13.3; §15.2; addition of proton pump inhibitors in appendix I and gene expression profiling information in appendix J.
26 October 2011	Number of patients has been expanded form 452 --> 668 §3 and §17.1 (statistical paragraph) ; adjustment in §9.3 (bottles --> wallets); addition of Second primary malignancy report §16.1; clarification of anemia (appendix A).
22 February 2012	Adjustment in §9.3 (drug supply); §11.2; SPM reporting as SAE (§13.1 & §16.1)
04 June 2019	Adjustment in § 3 'Synopsis': All patients will be followed until October 1, 2018 or, for patients who are still on maintenance therapy at that moment, until completion of maintenance therapy; § 4 is updated; § 16.1 is clarified.
01 May 2020	With protocol amendment 6, the study will be stopped and all patients still on maintenance treatment will continue their current maintenance treatment outside the scope of this study; The continued supply of lenalidomide and thalidomide for the patients still on maintenance treatment after study stop is aligned between the sponsor, the principal investigator and Celgene/BMS. These processes may depend on local regulations or commercial availability of the drugs; § 3; § 9.1.1; § 9.2.1; § 9.3 are updated with this information.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported