



## Clinical trial results:

### Mesothelioma Stratified Therapy (MiST):

**A stratified multi-arm phase IIa clinical trial to enable accelerated evaluation of targeted therapies for relapsed malignant mesothelioma.**

## Summary

EudraCT number	2017-003353-41
Trial protocol	GB
Global end of trial date	18 October 2024

## Results information

Result version number	v1 (current)
This version publication date	18 March 2026
First version publication date	18 March 2026

## Trial information

### Trial identification

Sponsor protocol code	0627
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### Additional study identifiers

ISRCTN number	ISRCTN39816629
ClinicalTrials.gov id (NCT number)	NCT03654833
WHO universal trial number (UTN)	-
Other trial identifiers	NIHR Portfolio Adoption number: 38247

Notes:

## Sponsors

Sponsor organisation name	University of Leicester
Sponsor organisation address	Research Governance Office, Research & Enterprise Office, University of Leicester, Leicester, United Kingdom,
Public contact	Professor Dean Fennell, University of Leicester, 0044 01162297249, df132@leicester.ac.uk
Scientific contact	Professor Dean Fennell, University of Leicester, 0044 01162297249, mistmailbox@leicester.ac.uk

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	19 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 April 2024
Global end of trial reached?	Yes
Global end of trial date	18 October 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To determine the disease control rate of stratified targeted therapies in relapsed mesothelioma at 12 weeks

MiST1 will evaluate the oral poly-ADP ribose polymerase (PARP) inhibitor rucaparib in patients with a specific molecular biomarker profile (loss of expression of BAP1 and/or BRCA1)

MiST2 will evaluate the oral small molecule inhibitor of CDK4 and CDK6 abemaciclib in patients with a specific molecular biomarker profile (loss of expression of p16INK4A)

MiST3 will evaluate the intravenously administered drug (pembrolizumab) in combination with the oral therapy (bemcentinib) in patients with no specific biomarker

MiST4 will evaluate the intravenously administered drug combination atezolizumab and bevacizumab in patients with a specific molecular biomarker profile (positive for PDL1 expression)

MiST5 will evaluate the intravenously administered drug (dostarlimab) in combination with the oral therapy (niraparib) in patients with Platinum Sensitive Relapsed Mesothelioma

Protection of trial subjects:

In order to confidently ensure the safety of participants and ensure the confidence of the collaborating pharmaceutical companies, patients can only be treated at sites that have been assessed to confirm that they have the required facilities and experience to administer treatment safely.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 January 2019
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	United Kingdom: 130
Worldwide total number of subjects	130
EEA total number of subjects	0

Notes:

### Subjects enrolled per age group

In utero	0
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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)	33
From 65 to 84 years	95
85 years and over	2

## Subject disposition

### Recruitment

Recruitment details:

186 patients were enrolled to MIST Master and 130 participants were recruited to arms. 26 participants were included in each MiST arm. An additional patient was recruited in MiST-5 and died before receiving treatment, they were therefore replaced with another participant and are not included in the figures reported here.

### Pre-assignment

Screening details:

MiST-1: 36 screened, 10 were found ineligible. 26 entered the trial  
MiST-2: 30 screened, 4 were found ineligible. 26 entered the trial  
MiST-3: 41 screened, 15 were found ineligible. 26 entered the trial  
MiST-4: 30 screened, 4 were found ineligible. 26 entered the trial  
MiST-5: 29 screened, 2 were found ineligible, 27 entered the trial

### Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	MiST 1

Arm description:

Trial Participants: Relapsed mesothelioma patients with prior treatment response to platinum doublet therapy.

Investigational Medicinal Product: Rucaparib supplied by Clovis Oncology, Inc.

Arm type	Experimental
Investigational medicinal product name	Rucaparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600mg twice daily (BID) every 28 days

<b>Arm title</b>	MiST 2
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Arm description:

Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy.

Investigational Medicinal Product: Abemaciclib supplied by Lilly.

Arm type	Experimental
Investigational medicinal product name	Abemaciclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

200mg twice daily (BID) for 28 days

<b>Arm title</b>	MiST 3
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Arm description:

Trial Participants: Patients with relapsed mesothelioma previously treated with platinum doublet therapy.

Investigational Medicinal Products: Bemcentinib will be supplied by BerGenBio. Pembrolizumab will be

supplied by MSD.

Arm type	Experimental
Investigational medicinal product name	Bemcentinib & Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Capsule
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Bemcentinib will be administered once daily. On the first 3 days of administration the dose will be a loading dose of 400mg. From Day 4 onwards, patients will receive a daily dose of 200mg. Each cycle will be 21 days duration.

Pembrolizumab will be given at a fixed dose of 200mg via IV infusion on Day 1 of each 21-day cycle.

Each drug will be administered for up to 35 cycles or until loss of clinical benefit, unacceptable toxicity or symptomatic deterioration attributed to disease progression.

<b>Arm title</b>	MiST 4
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Arm description:

Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy.

Investigational Medicinal Products: Atezolizumab and bevacizumab supplied by Roche/Genentech.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab and bevacizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab will be given as a fixed dose of 1200 milligrams (mg) via intravenous (IV) infusion on day 1 of a 21-day cycle.

Bevacizumab will be given as 15 milligrams per kilogram (mg/kg) via IV infusion on Days 1 of a 21-day cycle.

<b>Arm title</b>	MiST 5
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Arm description:

Trial Participants: Patients who have had Response or Stable disease, but not progression as their best response to first line or re challenge platinum doublet therapy.

Investigational Medicinal Products: Niraparib and dostarlimab supplied by GSK.

Arm type	Experimental
Investigational medicinal product name	Niraparib and dostarlimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Infusion
Routes of administration	Oral use, Intravenous use

Dosage and administration details:

Niraparib will be administered once daily depending on patient's weight and platelet count. A cycle consist of 21 days and there will be up to 35 cycles in total:

- $\geq 77$  kg and  $\geq 150,000$   $\mu$ L 300 mg (3 X 100 mg capsules)
- $< 77$  kg or  $< 150,000$   $\mu$ L 200 mg (2 X 100 mg capsules)

Dostarlimab will be given at a fixed dose of 500mg via IV infusion on Day 1 of each 21-day cycle for 4 cycles.

Followed by 1000mg via IV infusion on Day 1 of each 42-day cycle for up to 24 months.

• Each will be administered for up to 24 months or until loss of clinical benefit, unacceptable toxicity or symptomatic deterioration attributed to disease progression

Number of subjects in period 1	MiST 1	MiST 2	MiST 3
Started	26	26	26
Completed	26	26	26

Number of subjects in period 1	MiST 4	MiST 5
Started	26	26
Completed	26	26

## Period 2

Period 2 title	12 Weeks
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	MiST 1

### Arm description:

Trial Participants: Relapsed mesothelioma patients with prior treatment response to platinum doublet therapy.

Investigational Medicinal Products: Rucaparib supplied by Clovis Oncology, Inc.

Arm type	Experimental
Investigational medicinal product name	Rucaparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

### Dosage and administration details:

600mg twice daily (BID) every 28 days

<b>Arm title</b>	MiST 2
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### Arm description:

Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy.

Investigational Medicinal Products: Abemaciclib supplied by Lilly.

Arm type	Experimental
Investigational medicinal product name	Abemaciclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

### Dosage and administration details:

200mg twice daily (BID) for 28 days

<b>Arm title</b>	MiST 3
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### Arm description:

Trial Participants: Patients with relapsed mesothelioma previously treated with platinum doublet

therapy.

Investigational Medicinal Products: Bemcentinib will be supplied by BerGenBio. Pembrolizumab will be supplied by MSD.

Arm type	Experimental
Investigational medicinal product name	Bemcentinib & Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Injection
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Bemcentinib will be administered once daily. On the first 3 days of administration the dose will be a loading dose of 400mg. From Day 4 onwards, patients will receive a daily dose of 200mg. Each cycle will be 21 days duration.

Pembrolizumab will be given at a fixed dose of 200mg via IV infusion on Day 1 of each 21-day cycle.

Each drug will be administered for up to 35 cycles or until loss of clinical benefit, unacceptable toxicity or symptomatic deterioration attributed to disease progression.

<b>Arm title</b>	MiST 4
------------------	--------

Arm description:

Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy.

Investigational Medicinal Products: Atezolizumab and bevacizumab supplied by Roche/Genentech.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab and bevacizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab will be given as a fixed dose of 1200 milligrams (mg) via intravenous (IV) infusion on day 1 of a 21-day cycle.

Bevacizumab will be given as 15 milligrams per kilogram (mg/kg) via IV infusion on Days 1 of a 21-day cycle.

<b>Arm title</b>	MiST 5
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Arm description:

Trial Participants: Patients who have had Response or Stable disease, but not progression as their best response to first line or re challenge platinum doublet therapy.

Investigational Medicinal Product: Niraparib and dostarlimab supplied by GSK.

Arm type	Experimental
Investigational medicinal product name	Niraparib and dostarlimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Infusion
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Niraparib will be administered once daily depending on patient's weight and platelet count. A cycle consist of 21 days and there will be up to 35 cycles in total:

- $\geq 77$  kg and  $\geq 150,000$   $\mu$ L 300 mg (3 X 100 mg capsules)
- $< 77$  kg or  $< 150,000$   $\mu$ L 200 mg (2 X 100 mg capsules)

Dostarlimab will be given at a fixed dose of 500mg via IV infusion on Day 1 of each 21-day cycle for 4 cycles.

Followed by 1000mg via IV infusion on Day 1 of each 42-day cycle for up to 24 months.

- Each will be administered for up to 24 months or until loss of clinical benefit, unacceptable toxicity or symptomatic deterioration attributed to disease progression

Number of subjects in period 2	MiST 1	MiST 2	MiST 3
Started	26	26	26
Completed	18	14	18
Not completed	8	12	8
Physician decision	1	2	-
Toxicity	1	1	-
Death	-	2	3
Patient Choice	-	1	-
Did not attend 12 week CT scan	-	-	1
Lack of efficacy	6	6	4

Number of subjects in period 2	MiST 4	MiST 5
Started	26	26
Completed	18	21
Not completed	8	5
Physician decision	-	-
Toxicity	-	-
Death	3	-
Patient Choice	-	-
Did not attend 12 week CT scan	-	-
Lack of efficacy	5	5

### Period 3

Period 3 title	24 Weeks
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	MiST 1

Arm description:

Trial Participants: Relapsed mesothelioma patients with prior treatment response to platinum doublet therapy.

Investigational Medicinal Products: Rucaparib supplied by Clovis Oncology, Inc.

Arm type	Experimental
Investigational medicinal product name	Rucaparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use



Dosage and administration details:  
600mg twice daily (BID) every 28 days

<b>Arm title</b>	MiST 2
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Arm description:

Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy.  
Investigational Medicinal Products: Abemaciclib supplied by Lilly.

Arm type	Experimental
Investigational medicinal product name	Abemaciclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:  
200mg twice daily (BID) for 28 days

<b>Arm title</b>	MiST 3
------------------	--------

Arm description:

Trial Participants: Patients with relapsed mesothelioma previously treated with platinum doublet therapy.  
Investigational Medicinal Products: Bemcentinib will be supplied by BerGenBio. Pembrolizumab will be supplied by MSD.

Arm type	Experimental
Investigational medicinal product name	Bemcentinib & Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Injection
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Bemcentinib will be administered once daily. On the first 3 days of administration the dose will be a loading dose of 400mg. From Day 4 onwards, patients will receive a daily dose of 200mg. Each cycle will be 21 days duration.

Pembrolizumab will be given at a fixed dose of 200mg via IV infusion on Day 1 of each 21-day cycle. Each drug will be administered for up to 35 cycles or until loss of clinical benefit, unacceptable toxicity or symptomatic deterioration attributed to disease progression.

<b>Arm title</b>	MiST 4
------------------	--------

Arm description:

Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy.  
Investigational Medicinal Products: Atezolizumab and bevacizumab supplied by Roche/Genentech.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab and bevacizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab will be given as a fixed dose of 1200 milligrams (mg) via intravenous (IV) infusion on day 1 of a 21-day cycle.

Bevacizumab will be given as 15 milligrams per kilogram (mg/kg) via IV infusion on Days 1 of a 21-day cycle.

<b>Arm title</b>	MiST 5
------------------	--------

Arm description:

Trial Participants: Patients who have had Response or Stable disease, but not progression as their best

response to first line or re challenge platinum doublet therapy.

Investigational Medicinal Products: Niraparib and dostarlimab supplied by GSK.

Arm type	Experimental
Investigational medicinal product name	Niraparib and dostarlimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Infusion
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Niraparib will be administered once daily depending on patient's weight and platelet count. A cycle consist of 21 days and there will be up to 35 cycles in total:

- $\geq 77$  kg and  $\geq 150,000$   $\mu\text{L}$  300 mg (3 X 100 mg capsules)
- $< 77$  kg or  $< 150,000$   $\mu\text{L}$  200 mg (2 X 100 mg capsules)

Dostarlimab will be given at a fixed dose of 500mg via IV infusion on Day 1 of each 21-day cycle for 4 cycles.

Followed by 1000mg via IV infusion on Day 1 of each 42-day cycle for up to 24 months.

- Each will be administered for up to 24 months or until loss of clinical benefit, unacceptable toxicity or symptomatic deterioration attributed to disease progression

<b>Number of subjects in period 3</b>	MiST 1	MiST 2	MiST 3
Started	18	14	18
Completed	10	7	10
Not completed	8	7	8
Physician decision	-	-	-
Missed 24 week visit	-	1	-
Death	-	1	4
Patient Choice	-	1	-
Lack of efficacy	8	4	4

<b>Number of subjects in period 3</b>	MiST 4	MiST 5
Started	18	21
Completed	9	11
Not completed	9	10
Physician decision	-	1
Missed 24 week visit	-	-
Death	1	3
Patient Choice	-	-
Lack of efficacy	8	6

## Baseline characteristics

### Reporting groups

Reporting group title	MiST 1
Reporting group description:	
Trial Participants: Relapsed mesothelioma patients with prior treatment response to platinum doublet therapy.	
Investigational Medicinal Product: Rucaparib supplied by Clovis Oncology, Inc.	
Reporting group title	MiST 2
Reporting group description:	
Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy.	
Investigational Medicinal Product: Abemaciclib supplied by Lilly.	
Reporting group title	MiST 3
Reporting group description:	
Trial Participants: Patients with relapsed mesothelioma previously treated with platinum doublet therapy.	
Investigational Medicinal Products: Bemcentinib will be supplied by BerGenBio. Pembrolizumab will be supplied by MSD.	
Reporting group title	MiST 4
Reporting group description:	
Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy.	
Investigational Medicinal Products: Atezolizumab and bevacizumab supplied by Roche/Genentech.	
Reporting group title	MiST 5
Reporting group description:	
Trial Participants: Patients who have had Response or Stable disease, but not progression as their best response to first line or re challenge platinum doublet therapy.	
Investigational Medicinal Products: Niraparib and dostarlimab supplied by GSK.	

Reporting group values	MiST 1	MiST 2	MiST 3
Number of subjects	26	26	26
Age categorical			
Age categorical			
Units: Subjects			
Adults (18-64 years)	12	8	3
From 65-84 years	14	18	22
85 years and over	0	0	1
Age continuous			
Age continuous			
Units: years			
median	66.5	67.5	72.5
inter-quartile range (Q1-Q3)	60.0 to 71.0	64.0 to 74.0	69.0 to 75.0
Gender categorical			
Gender			
Units: Subjects			
Female	4	3	3
Male	22	23	23
Smoking status			
Smoking status			
Units: Subjects			
Smoker	2	2	1
Non smoker	15	14	12
Ex smoker	9	10	13

Mesothelioma subtype			
Mesothelioma subtype			
Units: Subjects			
Epithelioid	21	21	23
Biphasic	5	4	2
Sarcomatoid	0	0	1
NOS	0	1	0
History of asbestos			
History of asbestos			
Units: Subjects			
Yes	15	20	20
No	2	2	0
Unknown	9	4	6
ECOG status			
ECOG status			
Units: Subjects			
zero	4	4	6
one	22	22	20
Primary Tumour Site			
Primary Tumour Site			
Units: Subjects			
Thoracic	25	26	25
Abdominal	1	0	0
Pelvis	0	0	0
Missing	0	0	1
T-stage			
T-stage			
Units: Subjects			
T1	3	4	5
T2	3	9	2
T3	10	5	9
T4	9	8	6
TX	0	0	2
Unobtainable	0	0	2
Missing	1	0	0
N-stage			
N-stage			
Units: Subjects			
N0	9	10	16
N1	6	8	6
N2	7	8	2
N3	3	0	0
Unobtainable	0	0	2
Missing	1	0	0
M-stage			
M-stage			
Units: Subjects			
M0	21	21	19
M1	4	5	5
Unobtainable	0	0	2
Missing	1	0	0

P16 negative			
P16 negative			
Units: Subjects			
Positive	6	0	0
Negative	20	26	0
Not applicable	0	0	26
Number of prior courses of systemic anticancer therapy			
Number of prior courses of systemic anticancer therapy			
Units: Subjects			
One	12	10	17
Two	6	7	7
Three	6	5	2
Four	1	3	0
Five	1	1	0
First line therapy			
First line therapy			
Units: Subjects			
Bevacizumab and Pemetrexed and/or Carboplatin	0	0	5
Bevacizumab alone	0	0	0
Pemetrexed alone	0	0	0
Pemetrexed and/or Carboplatin	0	17	11
Pemetrexed and/or Cisplatin	0	8	8
Radiotherapy	0	1	1
Pemetrexed and Cisplatin/Carboplatin	0	0	1
Pemetrexed/Carboplatin	7	0	0
Pemetrexed/Cisplatin	3	0	0
Pemetrexed & Carboplatin	9	0	0
Pemetrexed & Cisplatin	3	0	0
Pemetrexed & Cisplatin & Bevacizumab	1	0	0
Other	3	0	0
Missing	0	0	0
Second line therapy			
Second line therapy			
Units: Subjects			
Pemetrexed and/or Carboplatin	4	5	3
Bevacizumab	2	0	2
ADI-Peg 20/placebo	0	0	0
RSO-1	0	0	0
Carboplatin and taxel	0	0	0
Pemetrexed and/or Cisplatin	0	1	0
Vinorelbine	0	2	0
Gemcitabine & AZD6738	0	0	1
Pemetrexed/Carboplatin and Bevacizumab	0	0	1
Vinorelbine & carboplatin	0	0	1
Radiotherapy	0	0	1
Rucaparib	0	2	0
Nivolumab/Placebo	0	4	0
Other	6	2	0

Pembrolizumab + Defactinib	1	0	0
Missing	13	10	17

Body Mass Index			
Body Mass Index			
Units: kg/m <sup>2</sup>			
median	26.0	25.5	26.6
inter-quartile range (Q1-Q3)	23.7 to 29.3	24.0 to 28.5	23.4 to 28.9

Reporting group values	MiST 4	MiST 5	Total
Number of subjects	26	26	130
Age categorical			
Age categorical			
Units: Subjects			
Adults (18-64 years)	6	4	33
From 65-84 years	20	21	95
85 years and over	0	1	2
Age continuous			
Age continuous			
Units: years			
median	68	69.5	
inter-quartile range (Q1-Q3)	67.0 to 74.0	68.0 to 74.0	-
Gender categorical			
Gender			
Units: Subjects			
Female	8	5	23
Male	18	21	107
Smoking status			
Smoking status			
Units: Subjects			
Smoker	2	4	11
Non smoker	13	12	66
Ex smoker	11	10	53
Mesothelioma subtype			
Mesothelioma subtype			
Units: Subjects			
Epithelioid	20	21	106
Biphasic	2	1	14
Sarcomatoid	3	2	6
NOS	1	2	4
History of asbestos			
History of asbestos			
Units: Subjects			
Yes	16	18	89
No	2	0	6
Unknown	8	8	35
ECOG status			
ECOG status			
Units: Subjects			
zero	4	2	20
one	22	24	110

Primary Tumour Site			
Primary Tumour Site			
Units: Subjects			
Thoracic	24	24	124
Abdominal	1	2	4
Pelvis	1	0	1
Missing	0	0	1
T-stage			
T-stage			
Units: Subjects			
T1	2	6	20
T2	3	4	21
T3	7	6	37
T4	13	8	44
TX	1	0	3
Unobtainable	0	1	3
Missing	0	1	2
N-stage			
N-stage			
Units: Subjects			
N0	11	13	59
N1	6	7	33
N2	8	2	27
N3	1	2	6
Unobtainable	0	1	3
Missing	0	1	2
M-stage			
M-stage			
Units: Subjects			
M0	20	16	97
M1	6	6	26
Unobtainable	0	3	5
Missing	0	1	2
P16 negative			
P16 negative			
Units: Subjects			
Positive	7	0	13
Negative	10	0	56
Not applicable	9	26	61
Number of prior courses of systemic anticancer therapy			
Number of prior courses of systemic anticancer therapy			
Units: Subjects			
One	12	20	71
Two	8	6	34
Three	4	0	17
Four	1	0	5
Five	1	0	3
First line therapy			
First line therapy			
Units: Subjects			

Bevacizumab and Pemetrexed and/or Carboplatin	0	1	6
Bevacizumab alone	0	1	1
Pemetrexed alone	0	1	1
Pemetrexed and/or Carboplatin	16	17	61
Pemetrexed and/or Cisplatin	5	3	24
Radiotherapy	0	0	2
Pemetrexed and Cisplatin/Carboplatin	0	0	1
Pemetrexed/Carboplatin	0	0	7
Pemetrexed/Cisplatin	0	0	3
Pemetrexed & Carboplatin	0	0	9
Pemetrexed & Cisplatin	0	0	3
Pemetrexed & Cisplatin & Bevacizumab	0	0	1
Other	5	0	8
Missing	0	3	3
Second line therapy			
Second line therapy			
Units: Subjects			
Pemetrexed and/or Carboplatin	3	2	17
Bevacizumab	0	1	5
ADI-Peg 20/placebo	0	1	1
RSO-1	0	1	1
Carboplatin and taxel	0	1	1
Pemetrexed and/or Cisplatin	3	0	4
Vinorelbine	4	0	6
Gemcitabine & AZD6738	0	0	1
Pemetrexed/Carboplatin and Bevacizumab	0	0	1
Vinorelbine & carboplatin	0	0	1
Radiotherapy	0	0	1
Rucaparib	0	0	2
Nivolumab/Placebo	0	0	4
Other	0	0	8
Pembrolizumab + Defactinib	0	0	1
Missing	16	20	76
Body Mass Index			
Body Mass Index			
Units: kg/m^2			
median	25.7	25.5	
inter-quartile range (Q1-Q3)	21.9 to 28.8	24.1 to 28.0	-



## End points

### End points reporting groups

Reporting group title	MiST 1
Reporting group description: Trial Participants: Relapsed mesothelioma patients with prior treatment response to platinum doublet therapy. Investigational Medicinal Product: Rucaparib supplied by Clovis Oncology, Inc.	
Reporting group title	MiST 2
Reporting group description: Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy. Investigational Medicinal Product: Abemaciclib supplied by Lilly.	
Reporting group title	MiST 3
Reporting group description: Trial Participants: Patients with relapsed mesothelioma previously treated with platinum doublet therapy. Investigational Medicinal Products: Bemcentinib will be supplied by BerGenBio. Pembrolizumab will be supplied by MSD.	
Reporting group title	MiST 4
Reporting group description: Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy. Investigational Medicinal Products: Atezolizumab and bevacizumab supplied by Roche/Genentech.	
Reporting group title	MiST 5
Reporting group description: Trial Participants: Patients who have had Response or Stable disease, but not progression as their best response to first line or re challenge platinum doublet therapy. Investigational Medicinal Products: Niraparib and dostarlimab supplied by GSK.	
Reporting group title	MiST 1
Reporting group description: Trial Participants: Relapsed mesothelioma patients with prior treatment response to platinum doublet therapy. Investigational Medicinal Products: Rucaparib supplied by Clovis Oncology, Inc.	
Reporting group title	MiST 2
Reporting group description: Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy. Investigational Medicinal Products: Abemaciclib supplied by Lilly.	
Reporting group title	MiST 3
Reporting group description: Trial Participants: Patients with relapsed mesothelioma previously treated with platinum doublet therapy. Investigational Medicinal Products: Bemcentinib will be supplied by BerGenBio. Pembrolizumab will be supplied by MSD.	
Reporting group title	MiST 4
Reporting group description: Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy. Investigational Medicinal Products: Atezolizumab and bevacizumab supplied by Roche/Genentech.	
Reporting group title	MiST 5
Reporting group description: Trial Participants: Patients who have had Response or Stable disease, but not progression as their best response to first line or re challenge platinum doublet therapy. Investigational Medicinal Product: Niraparib and dostarlimab supplied by GSK.	
Reporting group title	MiST 1
Reporting group description: Trial Participants: Relapsed mesothelioma patients with prior treatment response to platinum doublet therapy. Investigational Medicinal Products: Rucaparib supplied by Clovis Oncology, Inc.	

Reporting group title	MiST 2
Reporting group description:	
Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy.	
Investigational Medicinal Products: Abemaciclib supplied by Lilly.	
Reporting group title	MiST 3
Reporting group description:	
Trial Participants: Patients with relapsed mesothelioma previously treated with platinum doublet therapy.	
Investigational Medicinal Products: Bemcentinib will be supplied by BerGenBio. Pembrolizumab will be supplied by MSD.	
Reporting group title	MiST 4
Reporting group description:	
Trial Participants: Relapsed mesothelioma patients previously treated with platinum doublet therapy.	
Investigational Medicinal Products: Atezolizumab and bevacizumab supplied by Roche/Genentech.	
Reporting group title	MiST 5
Reporting group description:	
Trial Participants: Patients who have had Response or Stable disease, but not progression as their best response to first line or re challenge platinum doublet therapy.	
Investigational Medicinal Products: Niraparib and dostarlimab supplied by GSK.	
Subject analysis set title	Dummy analysis
Subject analysis set type	Full analysis
Subject analysis set description:	
A placeholder value of 1 was entered for [Dummy Arm Name] to satisfy system validation requirements for a single-arm sub-study. This arm does not exist in the clinical protocol, and no data from this 'subject' was used in the actual analysis.	

### Primary: Disease Control Rate at 12 weeks

End point title	Disease Control Rate at 12 weeks
End point description:	
End point type	Primary
End point timeframe:	
12 week	

End point values	MiST 1	MiST 2	MiST 3	MiST 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	26	26	26
Units: Number of patients				
Complete Response	0	0	0	0
Partial Response	2	3	4	1
Stable Disease	13	11	8	12
Progressive Disease	10	2	11	8
Not Evaluable	1	10	3	5

End point values	MiST 5	Dummy analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	26	1 <sup>[1]</sup>		

Units: Number of patients				
Complete Response	0	0		
Partial Response	3	0		
Stable Disease	14	0		
Progressive Disease	8	0		
Not Evaluable	1	1		

Notes:

[1] - Placeholder value of 1 was entered for Dummy Arm to satisfy system validation requirements

## Statistical analyses

<b>Statistical analysis title</b>	MiST 1 Disease Control Rate at 12 weeks
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Statistical analysis description:

The primary analysis of the primary outcome, DCR12w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with DCR will be presented with exact 95% confidence intervals.

Comparison groups	MiST 1 v Dummy analysis
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other <sup>[2]</sup>
Parameter estimate	Proportion
Point estimate	57.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	36.9
upper limit	76.7

Notes:

[2] - Comparison of a proportion to a reference value. Disease control in at least 11/26 patients, will result in the rejecting of the null hypothesis and concluding that the true response rate is greater than 25%. In this case the null hypothesis was rejected.

<b>Statistical analysis title</b>	MiST 2 Disease Control Rate at 12 weeks
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Statistical analysis description:

The primary analysis of the primary outcome, DCR12w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with DCR will be presented with exact 90% confidence intervals.

Comparison groups	MiST 2 v Dummy analysis
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other <sup>[3]</sup>
Parameter estimate	Proportion
Point estimate	53.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	36.2
upper limit	70.8

Notes:

[3] - Comparison of a proportion to a reference value. Disease control in at least 11/26 patients, will result in the rejecting of the null hypothesis and concluding that the true response rate is greater than 25%. In this case the null hypothesis was rejected.

<b>Statistical analysis title</b>	MiST 3 Disease Control Rate at 12 weeks
Statistical analysis description:	
The primary analysis of the primary outcome, DCR12w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with DCR will be presented with exact 90% confidence intervals.	
Comparison groups	MiST 3 v Dummy analysis
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other <sup>[4]</sup>
Parameter estimate	Proportion
Point estimate	46.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	29.2
upper limit	63.8

Notes:

[4] - Comparison of a proportion to a reference value. Disease control in at least 11/26 patients, will result in the rejecting of the null hypothesis and concluding that the true response rate is greater than 25%. In this case the null hypothesis was rejected.

<b>Statistical analysis title</b>	MiST 4 Disease Control Rate at 12 weeks
Statistical analysis description:	
The primary analysis of the primary outcome, DCR12w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with DCR will be presented with exact 90% confidence intervals.	
Comparison groups	MiST 4 v Dummy analysis
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other <sup>[5]</sup>
Parameter estimate	Proportion
Point estimate	50
Confidence interval	
level	90 %
sides	2-sided
lower limit	32.7
upper limit	67.3

Notes:

[5] - Comparison of a proportion to a reference value. Disease control in at least 11/26 patients, will result in the rejecting of the null hypothesis and concluding that the true response rate is greater than 25%. In this case the null hypothesis was rejected.

<b>Statistical analysis title</b>	MiST 5 Disease Control Rate at 12 weeks
Statistical analysis description:	
The primary analysis of the primary outcome, DCR12w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with DCR will be presented with exact 90% confidence intervals.	
Comparison groups	MiST 5 v Dummy analysis

Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other <sup>[6]</sup>
Parameter estimate	Proportion
Point estimate	65.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	47.4
upper limit	80.6

Notes:

[6] - Comparison of a proportion to a reference value. Disease control in at least 11/26 patients, will result in the rejecting of the null hypothesis and concluding that the true response rate is greater than 25%. In this case the null hypothesis was rejected.

### Secondary: Objective Response Rate at 24 weeks

End point title	Objective Response Rate at 24 weeks
End point description:	
End point type	Secondary
End point timeframe:	
24 weeks	

End point values	MiST 1	MiST 2	MiST 3	MiST 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	26	26	26
Units: Number of patients				
Complete Response	0	0	0	0
Partial Response	3	4	4	1
Stable Disease	16	14	15	18
Progressive Disease	4	2	5	4
Not Evaluable	3	6	2	3

End point values	MiST 5	Dummy analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	26	1 <sup>[7]</sup>		
Units: Number of patients				
Complete Response	0	0		
Partial Response	4	0		
Stable Disease	17	0		
Progressive Disease	4	0		
Not Evaluable	1	1		

Notes:

[7] - Placeholder value of 1 was entered for Dummy Arm to satisfy system validation requirements

## Statistical analyses

<b>Statistical analysis title</b>	MiST 1 Objective Response Rate at 24 weeks
Statistical analysis description: The secondary analysis of the secondary outcome, ORR24w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with ORR will be presented with exact 95% confidence intervals.	
Comparison groups	MiST 1 v Dummy analysis
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Proportion
Point estimate	11.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	30.2

<b>Statistical analysis title</b>	MiST 2 Objective Response Rate at 24 weeks
Statistical analysis description: The secondary analysis of the secondary outcome, ORR24w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with ORR will be presented with exact 95% confidence intervals.	
Comparison groups	MiST 2 v Dummy analysis
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Proportion
Point estimate	15.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.4
upper limit	34.9

<b>Statistical analysis title</b>	MiST 3 Objective Response Rate at 24 weeks
Statistical analysis description: The secondary analysis of the secondary outcome, ORR24w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with ORR will be presented with exact 95% confidence intervals.	
Comparison groups	MiST 3 v Dummy analysis

Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Proportion
Point estimate	15.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.4
upper limit	34.9

<b>Statistical analysis title</b>	MiST 4 Objective Response Rate at 24 weeks
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Statistical analysis description:

The secondary analysis of the secondary outcome, ORR24w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with ORR will be presented with exact 95% confidence intervals.

Comparison groups	MiST 4 v Dummy analysis
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Proportion
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	19.6

<b>Statistical analysis title</b>	MiST 5 Objective Response Rate at 24 weeks
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Statistical analysis description:

The secondary analysis of the secondary outcome, ORR24w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with ORR will be presented with exact 95% confidence intervals.

Comparison groups	MiST 5 v Dummy analysis
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Proportion
Point estimate	15.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.4
upper limit	34.9

**Secondary: Disease Control Rate at 24 weeks**

End point title	Disease Control Rate at 24 weeks
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End point description:

End point type	Secondary
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End point timeframe:

24 weeks

End point values	MiST 1	MiST 2	MiST 3	MiST 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	26	26	26
Units: Number of patients				
Complete Response	0	0	0	0
Partial Response	1	3	4	0
Stable Disease	5	3	6	7
Progressive Disease	19	7	12	14
Not Evaluable	1	13	4	5

End point values	MiST 5	Dummy analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	26	1 <sup>[8]</sup>		
Units: Number of patients				
Complete Response	0	0		
Partial Response	3	0		
Stable Disease	5	0		
Progressive Disease	17	0		
Not Evaluable	1	1		

Notes:

[8] - Placeholder value of 1 was entered for Dummy Arm to satisfy system validation requirements

**Statistical analyses**

<b>Statistical analysis title</b>	MiST 1 Disease Control Rate at 24 weeks
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Statistical analysis description:

The primary analysis of the primary outcome, DCR24w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with DCR will be presented with exact 95% confidence intervals.

Comparison groups	MiST 1 v Dummy analysis
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Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Proportion
Point estimate	23.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	9
upper limit	43.7

<b>Statistical analysis title</b>	MiST 2 Disease Control Rate at 24 weeks
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Statistical analysis description:

The primary analysis of the primary outcome, DCR24w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with DCR will be presented with exact 95% confidence intervals.

Comparison groups	MiST 2 v Dummy analysis
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Proportion
Point estimate	23.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	9
upper limit	43.6

<b>Statistical analysis title</b>	MiST 3 Disease Control Rate at 24 weeks
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Statistical analysis description:

The primary analysis of the primary outcome, DCR24w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with DCR will be presented with exact 95% confidence intervals.

Comparison groups	MiST 3 v Dummy analysis
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Proportion
Point estimate	38.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.2
upper limit	59.4

<b>Statistical analysis title</b>	MiST 4 Disease Control Rate at 24 weeks
Statistical analysis description:	
The primary analysis of the primary outcome, DCR24w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with DCR will be presented with exact 95% confidence intervals.	
Comparison groups	MiST 4 v Dummy analysis
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Proportion
Point estimate	26.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.6
upper limit	47.8

<b>Statistical analysis title</b>	MiST 5 Disease Control Rate at 24 weeks
Statistical analysis description:	
The primary analysis of the primary outcome, DCR24w, will be analysed in the efficacy population. Patients will be included in the analysis if they have received at least one dose of study treatment. A total of 26 evaluable patients will be analysed for this arm. Proportion of patients with DCR will be presented with exact 95% confidence intervals.	
Comparison groups	MiST 5 v Dummy analysis
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Proportion
Point estimate	30.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.3
upper limit	51.8

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All adverse events in the database at time of data lock for primary outcome analysis.

Adverse event reporting additional description:

In addition to the SAEs reported for MiST 1-5 participants, one individual that was pre screening for MiST-2 but did not go into the MiST-2 trial had a SAE. The SAE term: Dyspnea in SOC: Respiratory, thoracic and mediastinal disorders.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	28.1
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### Reporting groups

Reporting group title	MiST 1
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Reporting group description: -

Reporting group title	MiST 2
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Reporting group description: -

Reporting group title	MiST 3
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Reporting group description: -

Reporting group title	MiST 4
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Reporting group description: -

Reporting group title	MiST 5
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Reporting group description: -

Serious adverse events	MiST 1	MiST 2	MiST 3
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 26 (34.62%)	6 / 26 (23.08%)	10 / 26 (38.46%)
number of deaths (all causes)	12	12	16
number of deaths resulting from adverse events	0	1	0
Vascular disorders			
Superior vena cava occlusion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Joint dislocation			

subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovesical fistula			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hepatitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 26 (3.85%)	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			

subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	MiST 4	MiST 5	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 26 (42.31%)	9 / 26 (34.62%)	
number of deaths (all causes)	7	15	
number of deaths resulting from adverse events	1	1	
Vascular disorders			
Superior vena cava occlusion			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	



General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			

subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovesical fistula			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Autoimmune hepatitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
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			
Arthralgia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 26 (3.85%)	2 / 26 (7.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary tract infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	MiST 1	MiST 2	MiST 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 26 (92.31%)	22 / 26 (84.62%)	24 / 26 (92.31%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	14 / 26 (53.85%)	16 / 26 (61.54%)	12 / 26 (46.15%)
occurrences (all)	14	17	16
Dry mouth			
subjects affected / exposed	3 / 26 (11.54%)	1 / 26 (3.85%)	2 / 26 (7.69%)
occurrences (all)	3	1	2
Mouth ulceration			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	2	0	0
Non cardiac chest pain			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	1 / 26 (3.85%)
occurrences (all)	0	2	1
Weight decreased			
subjects affected / exposed	1 / 26 (3.85%)	6 / 26 (23.08%)	2 / 26 (7.69%)
occurrences (all)	1	6	3
Sore mouth or throat			
subjects affected / exposed	1 / 26 (3.85%)	3 / 26 (11.54%)	0 / 26 (0.00%)
occurrences (all)	1	3	0
Cold symptoms			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Fever			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	2 / 26 (7.69%)
occurrences (all)	1	1	2
General pain			

subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	2 / 26 (7.69%)
occurrences (all)	0	1	2
Swollen legs and feet			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	0	3
Abdominal pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Joint pain (Shoulder, hip and/or general)			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Neck or shoulder ache			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Chest infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0

Increased sweating subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0
Breathlessness subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0
COVID-19 subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Constipation subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0
Epistaxis subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea subjects affected / exposed occurrences (all)	8 / 26 (30.77%) 9	6 / 26 (23.08%) 7	3 / 26 (11.54%) 3
Shortness of breath subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	3 / 26 (11.54%) 3
Cough subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1
Investigations			
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	3 / 26 (11.54%) 3	0 / 26 (0.00%) 0



Raised creatinine subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	4 / 26 (15.38%) 5	4 / 26 (15.38%) 4
Weight loss subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1	2 / 26 (7.69%) 4
Increased ALT subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1	2 / 26 (7.69%) 4
Increased AST subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1	1 / 26 (3.85%) 1
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	3 / 26 (11.54%) 3	1 / 26 (3.85%) 1	0 / 26 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	1 / 26 (3.85%) 1	1 / 26 (3.85%) 1
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	6 / 26 (23.08%) 9	8 / 26 (30.77%) 14	5 / 26 (19.23%) 12
Platelet count decreased subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	4 / 26 (15.38%) 8	1 / 26 (3.85%) 1
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	2 / 26 (7.69%) 2	0 / 26 (0.00%) 0
Ascites subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	2 / 26 (7.69%) 2	0 / 26 (0.00%) 0
Leg and/or ankle oedema			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Hypomagnesaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	2	0	0
Constipation			
subjects affected / exposed	6 / 26 (23.08%)	6 / 26 (23.08%)	7 / 26 (26.92%)
occurrences (all)	6	6	9
Diarrhoea			
subjects affected / exposed	7 / 26 (26.92%)	13 / 26 (50.00%)	7 / 26 (26.92%)
occurrences (all)	9	19	12
Nausea			
subjects affected / exposed	18 / 26 (69.23%)	9 / 26 (34.62%)	11 / 26 (42.31%)
occurrences (all)	21	11	12
Vomiting			
subjects affected / exposed	4 / 26 (15.38%)	5 / 26 (19.23%)	2 / 26 (7.69%)
occurrences (all)	4	7	2
Acid reflux			
subjects affected / exposed	2 / 26 (7.69%)	2 / 26 (7.69%)	2 / 26 (7.69%)
occurrences (all)	2	2	2
Abdominal pain			
subjects affected / exposed	1 / 26 (3.85%)	2 / 26 (7.69%)	2 / 26 (7.69%)
occurrences (all)	1	3	2
Dysphagia			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	2 / 26 (7.69%)
occurrences (all)	1	1	3
Oral candidiasis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Mucositis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1

Hepatobiliary disorders			
	Increased ALT		
	subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)
	occurrences (all)	0	2
	Increased AST		
	subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)
	occurrences (all)	0	3
Skin and subcutaneous tissue disorders	Rash		
	subjects affected / exposed	3 / 26 (11.54%)	3 / 26 (11.54%)
	occurrences (all)	3	7
	Pruritus		
	subjects affected / exposed	3 / 26 (11.54%)	3 / 26 (11.54%)
	occurrences (all)	4	0
	Dry skin		
	subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)
	occurrences (all)	1	2
	Itchy skin		
	subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)
	occurrences (all)	0	5
Renal and urinary disorders	Proteinuria		
	subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)
	occurrences (all)	0	3
	Raised creatinine		
	subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)
	occurrences (all)	0	2
Musculoskeletal and connective tissue disorders	Non cardiac chest pain		
	subjects affected / exposed	4 / 26 (15.38%)	3 / 26 (11.54%)
	occurrences (all)	4	1
	Leg pain		
	subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)
	occurrences (all)	2	1
	Back pain		

subjects affected / exposed	1 / 26 (3.85%)	2 / 26 (7.69%)	4 / 26 (15.38%)
occurrences (all)	1	2	4
Joint pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	0	4
Parasthesia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	3
Osteoarthritis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	4
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	6 / 26 (23.08%)	1 / 26 (3.85%)	1 / 26 (3.85%)
occurrences (all)	8	1	1
Urinary tract infection			
subjects affected / exposed	1 / 26 (3.85%)	3 / 26 (11.54%)	1 / 26 (3.85%)
occurrences (all)	1	3	1
COVID-19			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Chest infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	2	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 26 (38.46%)	8 / 26 (30.77%)	3 / 26 (11.54%)
occurrences (all)	11	9	3
Hypophosphataemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	3
Weight loss			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	0	4
Anorexia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1

<b>Non-serious adverse events</b>	MiST 4	MiST 5	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 26 (96.15%)	26 / 26 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 26 (3.85%)	2 / 26 (7.69%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 26 (30.77%)	12 / 26 (46.15%)	
occurrences (all)	10	12	
Dry mouth			
subjects affected / exposed	1 / 26 (3.85%)	2 / 26 (7.69%)	
occurrences (all)	1	2	
Mouth ulceration			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Non cardiac chest pain			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences (all)	2	1	
Weight decreased			
subjects affected / exposed	3 / 26 (11.54%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Sore mouth or throat			
subjects affected / exposed	0 / 26 (0.00%)	3 / 26 (11.54%)	
occurrences (all)	0	4	
Cold symptoms			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Fever			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0
General pain		
subjects affected / exposed	1 / 26 (3.85%)	4 / 26 (15.38%)
occurrences (all)	1	4
Swollen legs and feet		
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0
Abdominal pain		
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences (all)	2	0
Joint pain (Shoulder, hip and/or general)		
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)
occurrences (all)	3	0
Nausea		
subjects affected / exposed	1 / 26 (3.85%)	2 / 26 (7.69%)
occurrences (all)	1	2
Decreased appetite		
subjects affected / exposed	1 / 26 (3.85%)	5 / 26 (19.23%)
occurrences (all)	1	5
Dizziness		
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	2
Cough		
subjects affected / exposed	0 / 26 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	3
Neck or shoulder ache		
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	3
Chest infection		
subjects affected / exposed	0 / 26 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	3
Lethargy		
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	2

Restless legs syndrome subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	2 / 26 (7.69%) 2	
Increased sweating subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	2 / 26 (7.69%) 2	
Breathlessness subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	4 / 26 (15.38%) 4	
COVID-19 subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	2 / 26 (7.69%) 2	
Chills subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	2 / 26 (7.69%) 2	
Constipation subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 3	0 / 26 (0.00%) 0	
Epistaxis subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 3	1 / 26 (3.85%) 1	
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	5 / 26 (19.23%) 5	
Shortness of breath subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	1 / 26 (3.85%) 1	
Cough subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	2 / 26 (7.69%) 2	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	2 / 26 (7.69%) 2	
Investigations			

Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	
Raised creatinine subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 3	0 / 26 (0.00%) 0	
Weight loss subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 26 (0.00%) 0	
Increased ALT subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	0 / 26 (0.00%) 0	
Increased AST subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 26 (0.00%) 0	
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 3	0 / 26 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	4 / 26 (15.38%) 4	0 / 26 (0.00%) 0	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	5 / 26 (19.23%) 6	
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 26 (3.85%) 2	
Neutropenia subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 26 (3.85%) 2	
Ascites			



subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Leg and/or ankle oedema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Hypomagnesaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	4 / 26 (15.38%)	7 / 26 (26.92%)	
occurrences (all)	4	7	
Diarrhoea			
subjects affected / exposed	2 / 26 (7.69%)	1 / 26 (3.85%)	
occurrences (all)	3	2	
Nausea			
subjects affected / exposed	1 / 26 (3.85%)	9 / 26 (34.62%)	
occurrences (all)	1	10	
Vomiting			
subjects affected / exposed	3 / 26 (11.54%)	3 / 26 (11.54%)	
occurrences (all)	3	3	
Acid reflux			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	1 / 26 (3.85%)	4 / 26 (15.38%)	
occurrences (all)	1	4	
Dysphagia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	

Mucositis subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	2 / 26 (7.69%) 2	
Hepatobiliary disorders Increased ALT subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	
Increased AST subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	4 / 26 (15.38%) 4	2 / 26 (7.69%) 4	
Pruritus subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	4 / 26 (15.38%) 4	
Dry skin subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	
Itchy skin subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	
Raised creatinine subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	0 / 26 (0.00%) 0	
Musculoskeletal and connective tissue disorders Non cardiac chest pain subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	3 / 26 (11.54%) 3	
Leg pain			

subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Joint pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Parasthesia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Osteoarthritis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 26 (3.85%)	3 / 26 (11.54%)	
occurrences (all)	1	3	
Urinary tract infection			
subjects affected / exposed	1 / 26 (3.85%)	3 / 26 (11.54%)	
occurrences (all)	1	4	
COVID-19			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Chest infection			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Infection			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 26 (7.69%)	2 / 26 (7.69%)	
occurrences (all)	2	2	
Hypophosphataemia			

subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences (all)	1	2	
Weight loss			
subjects affected / exposed	0 / 26 (0.00%)	0 / 26 (0.00%)	
occurrences (all)	0	0	
Anorexia			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 August 2018	MiST-1, SA01: Updated to version 3.0 following an amendment to the statistical design of the study.
12 December 2018	MiST-1, SA02: Change CI & Protocol V4
25 March 2019	MiST-2, SA03: Addition of MiST 2
01 May 2019	MiST-2, SA05: Resubmission of MiST 2 addition after GNA
07 May 2019	MiST-1, SA04: Master & MiST 1 protocols v5.0 & uploaded IB
14 June 2019	MiST-4, SA06: Addition of MiST 4
24 July 2019	MiST-3, SA07: Addition of MiST 3
01 September 2019	MiST-1, SA08: MiST 1 Protocol V6.0
01 December 2019	MiST-1, SA09: Changes to stats section, Protocol v7.0
01 January 2020	MiST-2, SA10: Changes to stats section, Protocol v3.0
01 February 2020	MiST-4, SA11: Changes to stats section, Protocol v2.0
01 May 2020	MiST-2, SA12: COVID-19 adjustments, Patient safety letter Protocol v4.0
01 July 2020	MiST-4, SA13: Removal of PD-L1 requirement Protocol v3.0
09 September 2020	Master MiST, SA14: Add text re: MiST 5 and update re: MiST 4 being an all comers arm Protocol v6.0
23 September 2020	MiST-2, SA15: Patient safety letter (Protocol v4.0 unchanged)
09 November 2020	MiST-3, SA16: Update to MSD QP details in preparation for Brexit
30 November 2020	MiST-5, SA17: Addition of the MiST 5 arm
07 December 2020	MiST-3, SA18: Updated lbs, stats analysis change, update to PIS
28 January 2021	MiST-5, SA19: Addition of the MiST 5 arm (re-submission following MHRA GNA of SA17)
12 March 2021	Mist-5, SA20: COVID Adaptations and change to MHRA products form

12 March 2021	MiST-3, SA22: MHRA Products Form updated with new MIA number
18 March 2021	MiST-4, SA21: Update IB and PIS
01 June 2021	MiST-3, SA23: Update RSI, Protocol changes and updated PIS
08 February 2022	MiST-5, SA24: Updated Niraparib IB and RSI, updated protocol and PIS, new patient diary and end date extension
11 May 2022	MiST-3, SA25: Update RSI for both IMPs
06 July 2022	MiST-5, SA26: Updated CTA with new MA number and QP release addresses
16 November 2022	MiST-5, SA27: IB update for Dostarlimab and Niraparib, updated PIS side effects and pregnancy
16 February 2023	Master & MiST-3 & MiST-5, SA28: Mater MiST, M3 and M5
22 July 2024	MiST-5, SA29: IB update for Dostarlimab and Niraparib, updated PIS side effects and pregnancy

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
19 March 2020	In light of the situation with COVID-19 research capacity was reduce significantly in the coming weeks, therefore this action was taken to prioritise treatment and maximise patient safety for those patients already on the study.	-

Notes:

## Limitations and caveats

None reported