Clinical trial results:
A Phase 2, International, Multicenter, Randomized, Open-label, Parallel Group Study to Evaluate the Efficacy and Safety of CC-486 (oral azacitidine) Alone and in Combination With Durvalumab (MEDI4736) in Subjects With Myelodysplastic Syndromes Who Fail to Achieve an Objective Response to Treatment With Azacitidine for Injection or Decitabine

Summary

EudraCT number	2014-002675-29
Trial protocol	FR GB BE ES DE PL IT
Global end of trial date	14 September 2023

Results information

Result version number	v1 (current)
This version publication date	25 September 2024
First version publication date	25 September 2024

Trial information

Trial identification

Sponsor protocol code	CC-486-MDS-006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02281084
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium,
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

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	14 September 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the safety and efficacy of oral azacitidne (CC-486) twice daily (BID) in subjects with myelodysplastic syndromes who failed to achieve an objective response post injectable hypomethylating agent (iHMA) treatment

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 July 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 31
Worldwide total number of subjects	65
EEA total number of subjects	26

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)	6
From 65 to 84 years	56
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Participants were randomized at 33 sites globally. The sites were located in: Australia (3), Europe (18) and the United States (12).

Pre-assignment

Screening details:

Participants were eligible who did not respond to an adequate course of therapy with an injectable hypomethylating agent (iHMA - azacitidine or decitabine) or were unable to tolerate an iHMA following at least 3 months of attempted treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Stable Disease (SD) Cohort: Oral Azacitidine

Arm description:

Participants were given oral azacitidine (AZA) 100 mg, 150 mg, or 200 mg tablets twice daily (BID) on days 1 to 21 of each 28-day treatment cycle. Participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	CC-486
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral azacitidine (AZA) 100 mg, 150 mg, or 200 mg tablets twice daily (BID) on days 1 to 21 of each 28-day treatment cycle. Participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.

Arm title	Progressive Disease (PD) Cohort: Oral Azacitidine

Arm description:

Participants were given oral azacitidine 100 mg, 150mg, or 200mg tablets BID on days 1 to 21 of each 28-day treatment cycle. Participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	CC-486
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral azacitidine (AZA) 100 mg, 150 mg, or 200 mg tablets twice daily (BID) on days 1 to 21 of each 28-day treatment cycle. Participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.

Arm title	Stable Disease Cohort: Oral Azacitidine and Durvalumab

Arm description:

Participants received 100 mg oral azacitidine (AZA) tablets BID on days 1 to 14 or days 1 to 21 of each

28-day treatment cycle and durvalumab (Durva) 1500 mg by intravenous infusion on day 1 of each 28-day treatment cycle; participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.

Arm type	Experimental
Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	Imfinzi, MEDI4736
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Durvalumab 1500 mg by IV infusion on Day 1 of each 28 day treatment cycle.

Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	CC-486
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral azacitidine (AZA) 100 mg, 150 mg, or 200 mg tablets twice daily (BID) on days 1 to 21 of each 28-day treatment cycle. Participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.

Arm title	Progressive Disease Cohort: Oral Azacitidine and Durvalumab

Arm description:

Participants received 100 mg oral azacitidine tablets BID on days 1 to 14 or days 1 to 21 of each 28-day treatment cycle and durvalumab 1500 mg by intravenous infusion on day 1 of each 28-day treatment cycle; participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.

Arm type	Experimental
Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	Imfinzi, MEDI4736
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Durvalumab 1500 mg by IV infusion on Day 1 of each 28 day treatment cycle.

Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	CC-486
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral azacitidine (AZA) 100 mg, 150 mg, or 200 mg tablets twice daily (BID) on days 1 to 21 of each 28-day treatment cycle. Participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.

Number of subjects in period 1	Stable Disease (SD) Cohort: Oral Azacitidine	Progressive Disease (PD) Cohort: Oral Azacitidine	Stable Disease Cohort: Oral Azacitidine and Durvalumab
Started	32	22	6
Completed	3	1	1
Not completed	29	21	5

Adverse event, serious fatal	21	18	3
Consent withdrawn by subject	2	2	-
Adverse event, non-fatal	1	-	-
Site Closure by Sponsor	5	1	2

Number of subjects in period 1	Progressive Disease Cohort: Oral Azacitidine and Durvalumab
Started	5
Completed	0
Not completed	5
Adverse event, serious fatal	5
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Site Closure by Sponsor	-

Baseline characteristics

Reporting groups	
Reporting group title	Stable Disease (SD) Cohort: Oral Azacitidine
Reporting group description:	
Participants were given oral azacitidine (AZA) 100 mg, 150 mg, or 200 mg tablets twice daily (BID) on days 1 to 21 of each 28-day treatment cycle. Participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.	
Reporting group title	Progressive Disease (PD) Cohort: Oral Azacitidine
Reporting group description:	
Participants were given oral azacitidine 100 mg, 150mg, or 200mg tablets BID on days 1 to 21 of each 28-day treatment cycle. Participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.	
Reporting group title	Stable Disease Cohort: Oral Azacitidine and Durvalumab
Reporting group description:	
Participants received 100 mg oral azacitidine (AZA) tablets BID on days 1 to 14 or days 1 to 21 of each 28-day treatment cycle and durvalumab (Durva) 1500 mg by intravenous infusion on day 1 of each 28-day treatment cycle; participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.	
Reporting group title	Progressive Disease Cohort: Oral Azacitidine and Durvalumab
Reporting group description:	
Participants received 100 mg oral azacitidine tablets BID on days 1 to 14 or days 1 to 21 of each 28-day treatment cycle and durvalumab 1500 mg by intravenous infusion on day 1 of each 28-day treatment cycle; participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.	

Reporting group values	Stable Disease (SD) Cohort: Oral Azacitidine	Progressive Disease (PD) Cohort: Oral Azacitidine	Stable Disease Cohort: Oral Azacitidine and Durvalumab
Number of subjects	32	22	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	2	3
From 65-84 years	29	18	3
85 years and over	1	2	0
Age Continuous Units: Years			
arithmetic mean	73.9	75.1	70.0
standard deviation	± 7.62	± 7.56	± 7.21
Sex: Female, Male Units: Participants			
Female	12	7	0
Male	20	15	6

Race/Ethnicity, Customized Units: Subjects			
White	28	18	6
Black	0	1	0
Asian	1	1	0
Native Hawaiian or Other Pacific Islander	0	1	0
American Indian or Alaska Native	0	0	0
Other	1	1	0
Not Collected or Reported	2	0	0
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	1	1	0
Not Hispanic or Latino	30	21	6
Unknown	1	0	0
Myelodysplastic Syndrome (MDS) World Health Organization Classification 2008			
The World Health Organization (WHO) 2008 classification recognizes eight subtypes of MDS that are distinguished by the percentage of myeloblasts, presence or absence of ringed sideroblasts (i.e., erythroid precursors with iron deposits surrounding the nucleus), presence of a monocytosis or a deletion 5q.			
Units: Subjects			
Refractory Anemia (RA) with Ringed Sideroblasts	1	0	0
Refractory Cytopenia with Multilineage Dysplasia	11	2	1
RA With Excess Blasts-1 (RAEB-1)	10	6	1
RA With Excess Blasts-2 (RAEB-2)	8	11	4
MDS Unclassified (MDS-U)	1	3	0
MDS Associated with Isolated del (5q)	0	0	0
Missing	1	0	0
International Prognostic Scoring System Risk Classification			
The international prognostic scoring system (IPSS) is a standard for risk assessment in primary myelodysplastic syndromes (MDS) that categorizes prognoses taking into account cytogenetics, cytopenias, blasts and blood counts. The IPSS prognostic subgroups consist of low-, intermediate-1-, intermediate-2-, and high-risk groups. The scale is 0-3.5 at 0.5 increments. Scores of 0=Low; 0.5-1.0=Int-1; 1.5-2.0=Int-2; 2.5-3.5=High risk which corresponds to poorer prognosis.			
Units: Subjects			
Low (0)	4	2	0
Intermediate 1 (0.5-1.0)	12	5	1
Intermediate (2) (1.0-2.0)	7	7	4
High (2) (≥ 2.5)	8	8	1
Unknown	1	0	0
French-American-British (FAB) Classification			
FAB is a classification system for five (5) subtypes of myelodysplastic syndrome that are distinguished by the percentage of myeloblasts, presence or absence of ringed sideroblasts or a monocytosis.			
Units: Subjects			
Refractory Anemia (RA)	6	2	0
Refractory Anemia with Ringed Sideroblasts (RARS)	6	1	1
Refractory Anemia with Excess Blasts (RAEB)	17	16	5
RAEB in Transformation	2	3	0

Chronic Myelomonocytic Leukemia (CMML)	0	0	0
Missing	1	0	0
Eastern Cooperative Oncology Group (ECOG) Performance Status (PS)			
ECOG performance status is used by doctors and researchers to assess how a subject's disease is progressing, assess how the disease affects the daily living activities of the subject and determine appropriate treatment and prognosis. 0 = Fully Active (Most Favorable Activity); 1 = Restricted activity but ambulatory; 2 = Ambulatory but unable to carry out work activities; 3 = Limited Self-Care; 4 = Completely Disabled, No self-care (Least Favorable Activity)			
Units: Subjects			
0 (Fully active)	5	6	3
1 (Restricted but Ambulatory)	22	13	3
2 (Ambulatory But Unable to Work)	5	3	0
3 (Limited Self-Care)	0	0	0
4 (Completely Disabled)	0	0	0
5 (Death)	0	0	0
Baseline Platelet Transfusion Status			
Baseline Platelet transfusion dependence is defined as ≥ 2 transfusions (in units) during the 56 days prior to treatment. Platelet transfusion independence is defined as 0 transfusions (in units) during the 56 days prior to treatment.			
Units: Subjects			
Dependent	4	5	0
Independent	25	13	6
Other	3	4	0
Baseline Red Blood Cell (RBC) Transfusion Status			
Baseline RBC Transfusion Dependence is defined as ≥ 4 transfusions (in units) during the 56 days prior to treatment. RBC transfusion independence is defined as 0 transfusions (in units) during the 56 days prior to treatment.			
Units: Subjects			
Dependent	8	7	0
Independent	8	6	3
Other	16	9	3
Average Red Blood Cell (RBC) Transfusion Requirement			
Documentation of all red blood cell transfusions received by the participant within 8 weeks (56 days) prior to the first dose of study drug.			
Units: units per 56 days			
median	4.00	3.50	3.00
full range (min-max)	0.00 to 10.0	0.0 to 7.0	0.0 to 7.0

Reporting group values	Progressive Disease Cohort: Oral Azacitidine and Durvalumab	Total	
Number of subjects	5	65	
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)	0	7	
From 65-84 years	5	55	
85 years and over	0	3	
Age Continuous			
Units: Years			
arithmetic mean	72.4		
standard deviation	± 5.55	-	
Sex: Female, Male			
Units: Participants			
Female	0	19	
Male	5	46	
Race/Ethnicity, Customized			
Units: Subjects			
White	5	57	
Black	0	1	
Asian	0	2	
Native Hawaiian or Other Pacific Islander	0	1	
American Indian or Alaska Native	0	0	
Other	0	2	
Not Collected or Reported	0	2	
Race/Ethnicity, Customized			
Units: Subjects			
Hispanic or Latino	2	4	
Not Hispanic or Latino	3	60	
Unknown	0	1	
Myelodysplastic Syndrome (MDS) World Health Organization Classification 2008			
The World Health Organization (WHO) 2008 classification recognizes eight subtypes of MDS that are distinguished by the percentage of myeloblasts, presence or absence of ringed sideroblasts (i.e., erythroid precursors with iron deposits surrounding the nucleus), presence of a monocytosis or a deletion 5q.			
Units: Subjects			
Refractory Anemia (RA) with Ringed Sideroblasts	0	1	
Refractory Cytopenia with Multilineage Dysplasia	0	14	
RA With Excess Blasts-1 (RAEB-1)	2	19	
RA With Excess Blasts-2 (RAEB-2)	3	26	
MDS Unclassified (MDS-U)	0	4	
MDS Associated with Isolated del (5q)	0	0	
Missing	0	1	
International Prognostic Scoring System Risk Classification			
The international prognostic scoring system (IPSS) is a standard for risk assessment in primary myelodysplastic syndromes (MDS) that categorizes prognoses taking into account cytogenetics, cytopenias, blasts and blood counts. The IPSS prognostic subgroups consist of low-, intermediate-1-, intermediate-2-, and high-risk groups. The scale is 0-3.5 at 0.5 increments. Scores of 0=Low; 0.5-1.0=Int-1; 1.5-2.0=Int-2; 2.5-3.5=High risk which corresponds to poorer prognosis.			
Units: Subjects			
Low (0)	0	6	
Intermediate 1 (0.5-1.0)	2	20	
Intermediate (2) (1.0-2.0)	2	20	
High (2) (≥ 2.5)	1	18	

Unknown	0	1	
French-American-British (FAB) Classification			
FAB is a classification system for five (5) subtypes of myelodysplastic syndrome that are distinguished by the percentage of myeloblasts, presence or absence of ringed sideroblasts or a monocytosis.			
Units: Subjects			
Refractory Anemia (RA)	0	8	
Refractory Anemia with Ringed Sideroblasts (RARS)	0	8	
Refractory Anemia with Excess Blasts (RAEB)	4	42	
RAEB in Transformation	1	6	
Chronic Myelomonocytic Leukemia (CMML)	0	0	
Missing	0	1	
Eastern Cooperative Oncology Group (ECOG) Performance Status (PS)			
ECOG performance status is used by doctors and researchers to assess how a subject's disease is progressing, assess how the disease affects the daily living activities of the subject and determine appropriate treatment and prognosis. 0 = Fully Active (Most Favorable Activity); 1 = Restricted activity but ambulatory; 2 = Ambulatory but unable to carry out work activities; 3 = Limited Self-Care; 4 = Completely Disabled, No self-care (Least Favorable Activity)			
Units: Subjects			
0 (Fully active)	2	16	
1 (Restricted but Ambulatory)	3	41	
2 (Ambulatory But Unable to Work)	0	8	
3 (Limited Self-Care)	0	0	
4 (Completely Disabled)	0	0	
5 (Death)	0	0	
Baseline Platelet Transfusion Status			
Baseline Platelet transfusion dependence is defined as ≥ 2 transfusions (in units) during the 56 days prior to treatment. Platelet transfusion independence is defined as 0 transfusions (in units) during the 56 days prior to treatment.			
Units: Subjects			
Dependent	1	10	
Independent	4	48	
Other	0	7	
Baseline Red Blood Cell (RBC) Transfusion Status			
Baseline RBC Transfusion Dependence is defined as ≥ 4 transfusions (in units) during the 56 days prior to treatment. RBC transfusion independence is defined as 0 transfusions (in units) during the 56 days prior to treatment.			
Units: Subjects			
Dependent	2	17	
Independent	2	19	
Other	1	29	
Average Red Blood Cell (RBC) Transfusion Requirement			
Documentation of all red blood cell transfusions received by the participant within 8 weeks (56 days) prior to the first dose of study drug.			
Units: units per 56 days			
median	4.00		
full range (min-max)	0.0 to 15.0	-	

End points

End points reporting groups

Reporting group title	Stable Disease (SD) Cohort: Oral Azacitidine

Reporting group description:

Participants were given oral azacitidine (AZA) 100 mg, 150 mg, or 200 mg tablets twice daily (BID) on days 1 to 21 of each 28-day treatment cycle. Participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.

Reporting group title	Progressive Disease (PD) Cohort: Oral Azacitidine

Reporting group description:

Participants were given oral azacitidine 100 mg, 150mg, or 200mg tablets BID on days 1 to 21 of each 28-day treatment cycle. Participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.

Reporting group title	Stable Disease Cohort: Oral Azacitidine and Durvalumab

Reporting group description:

Participants received 100 mg oral azacitidine (AZA) tablets BID on days 1 to 14 or days 1 to 21 of each 28-day treatment cycle and durvalumab (Durva) 1500 mg by intravenous infusion on day 1 of each 28-day treatment cycle; participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.

Reporting group title	Progressive Disease Cohort: Oral Azacitidine and Durvalumab

Reporting group description:

Participants received 100 mg oral azacitidine tablets BID on days 1 to 14 or days 1 to 21 of each 28-day treatment cycle and durvalumab 1500 mg by intravenous infusion on day 1 of each 28-day treatment cycle; participants continued to receive their assigned study treatment unless disease progression, unacceptable toxicity, lost to follow-up or withdrawal by participant occurred.

Primary: Overall Response Rate Based on the Modified International Working Group (IWG) 2006 Response Criteria for Myelodysplastic Syndrome (MDS)

End point title	Overall Response Rate Based on the Modified International Working Group (IWG) 2006 Response Criteria for Myelodysplastic Syndrome (MDS)[1]

End point description:

The overall response rate (ORR) was defined as the percentage of participants who achieved an objective response including: hematologic improvement (HI), partial remission (PR), complete remission (CR), or marrow complete remission (mCR). Hematologic response was defined as: • CR: ≤ 5% myeloblasts with normal maturation of all cell lines; peripheral blood (PB) shows: hemoglobin ≥11 g/dL, neutrophils ≥1.0x10^9/L, platelets ≥100x10^9/dL, blasts (0%) • PR: same as CR bone marrow (BM) shows blasts decreased by ≥ 50% over pre-treatment but still > 5%; cellularity and morphology not relevant • mCR: BM: ≤ 5% myeloblasts and decrease by ≥ 50% over pre-treatment PB, PB: if HI responses, noted in addition to mCR • HI: HI erythroid response (HI-E); HI neutrophil response (HI-N) ; HI platelet response (HI-P)

End point type	Primary

End point timeframe:

Response was assessed every 2 cycles following treatment during the first 6 cycles, then every 3 cycles thereafter; median duration of treatment = 5.26 and 3.81 months for SD/PD for oral AZA arms respectively, and 1.84 months for AZA and Durva SD/PD arms

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 was not planned as per study plan.

End point values	Stable Disease (SD) Cohort: Oral Azacitidine	Progressive Disease (PD) Cohort: Oral Azacitidine	Stable Disease Cohort: Oral Azacitidine and Durvalumab	Progressive Disease Cohort: Oral Azacitidine and Durvalumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	22	6	5
Units: Percentage of Participants				
number (confidence interval 95%)	6.3 (0.8 to 20.8)	4.5 (0.1 to 22.8)	16.7 (0.4 to 64.1)	99999 (99999 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Overall Survival

End point title	Kaplan-Meier Estimate of Overall Survival

End point description:

Overall survival (OS) was defined as the time from randomization to death from any cause, and was calculated using date of first dose and date of death, or date of last follow-up for censored subjects.

End point type	Secondary

End point timeframe:

From first dose till death due to any cause (Up to 91 months)

End point values	Stable Disease (SD) Cohort: Oral Azacitidine	Progressive Disease (PD) Cohort: Oral Azacitidine	Stable Disease Cohort: Oral Azacitidine and Durvalumab	Progressive Disease Cohort: Oral Azacitidine and Durvalumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	22	6	5
Units: Months				
median (confidence interval 95%)	17.00 (10.03 to 24.99)	6.28 (4.50 to 15.19)	14.70 (1.58 to 99999)	14.56 (9.73 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan Meier Estimate of Time to Onset of First and Best Response

End point title	Kaplan Meier Estimate of Time to Onset of First and Best Response

End point description:

Time to onset of first response was defined as the time between the date of first investigational product (IP) dose and the earliest date any response (CR, PR, mCR, or HI) was first observed. Participants who did not achieve any defined response during the treatment period were censored at the date of treatment discontinuation, disease progression, or death, whichever occurred first. Best response is the best recorded response or treatment outcome from the start of the study treatment until the end of the study treatment taking into account the requirements for confirmation of response.

End point type	Secondary

End point timeframe:

Response was assessed every 2 cycles following treatment during the first 6 cycles, then every 3 cycles thereafter; median duration of treatment = 5.26 and 3.81 months for SD/PD for oral AZA arms respectively, and 1.84 months for AZA and Durva SD/PD arms

End point values	Stable Disease (SD) Cohort: Oral Azacitidine	Progressive Disease (PD) Cohort: Oral Azacitidine	Stable Disease Cohort: Oral Azacitidine and Durvalumab	Progressive Disease Cohort: Oral Azacitidine and Durvalumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	22	6	5
Units: Months				
median (confidence interval 95%)				
Onset of First Response	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)
Onset of Best Response	3.68 (2.10 to 99999)	4.41 (1.68 to 99999)	3.29 (1.64 to 99999)	2.17 (1.64 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan Meier Estimate of Duration of First Response

End point title	Kaplan Meier Estimate of Duration of First Response[2]

End point description:

Duration of hematologic response and/or improvement was defined as the time from the date response or improvement was first observed to the date of documented relapse or disease progression as defined by the modified IWG 2006 criteria. Particpants who maintained hematologic response and/or improvement through the end of the treatment period were censored as the date of treatment discontinuation or death, whichever occurred first.

End point type	Secondary

End point timeframe:

Response was assessed every 2 cycles following treatment during the first 6 cycles, then every 3 cycles thereafter; median duration of treatment = 5.26 and 3.81 months for SD/PD for oral AZA arms respectively, and 1.84 months for AZA and Durva SD/PD arms

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis was not planned as per study plan.

End point values	Stable Disease (SD) Cohort: Oral Azacitidine	Progressive Disease (PD) Cohort: Oral Azacitidine	Stable Disease Cohort: Oral Azacitidine and Durvalumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	2	1	
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan Meier Estimate of Duration of Best Response

End point title	Kaplan Meier Estimate of Duration of Best Response

End point description:

Duration of hematologic response and/or improvement was defined as the time from the date response or improvement was first observed to the date of documented relapse or disease progression as defined by the modified IWG 2006 criteria. Particpants who maintained hematologic response and/or improvement through the end of the treatment period were censored as the date of treatment discontinuation or death, whichever occurred first.

End point type	Secondary

End point timeframe:

Response was assessed every 2 cycles following treatment during the first 6 cycles, then every 3 cycles thereafter; median duration of treatment = 5.26 and 3.81 months for SD/PD for oral AZA arms respectively, and 1.84 months for AZA and Durva SD/PD arms

End point values	Stable Disease (SD) Cohort: Oral Azacitidine	Progressive Disease (PD) Cohort: Oral Azacitidine	Stable Disease Cohort: Oral Azacitidine and Durvalumab	Progressive Disease Cohort: Oral Azacitidine and Durvalumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	22	6	5
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Progression Free Survival (PFS)

End point title	Kaplan-Meier Estimate of Progression Free Survival (PFS)

End point description:

Progression-free survival is defined as the time from first dose to the first documented progressive disease (PD), relapse, or death due to any cause during or after the treatment period, whichever occurred first, according to IWG 2006 response criteria for MDS. Participants who were still alive and progression-free were censored at the date of their last response assessment. Progressive disease is defined as follows: - an increase in BM blasts relative to nadir: •If nadir less than 5% blasts: ≥ 50% increase in blasts to > 5% blasts •If nadir 5% - 10% blasts: ≥ 50% increase in blasts to > 10% blasts •If nadir 10% - 20% blasts: ≥ 50% increase in blasts to > 20% blasts •If nadir 20% - 30% blasts: ≥ 50% increase in blasts to > 30% blasts And any of the following: •At least 50% decrement from maximum remission/response levels in granulocytes or platelets •Reduction in Hgb concentration by ≥ 2

g/dL •Transfusion dependence

End point type	Secondary

End point timeframe:

From first dose to the first documented progressive disease (PD), relapse, or death due to any cause (Up to 91 months)

End point values	Stable Disease (SD) Cohort: Oral Azacitidine	Progressive Disease (PD) Cohort: Oral Azacitidine	Stable Disease Cohort: Oral Azacitidine and Durvalumab	Progressive Disease Cohort: Oral Azacitidine and Durvalumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	22	6	5
Units: Months				
median (confidence interval 95%)	14.86 (9.27 to 24.99)	6.28 (4.50 to 15.19)	14.70 (1.58 to 99999)	12.10 (2.17 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Onset to Achieve Stable Disease

End point title	Kaplan-Meier Estimate of Onset to Achieve Stable Disease[3]

End point description:

A participant was considered as having a stable disease if the disease neither responded nor progressed during or after study treatment.

End point type	Secondary

End point timeframe:

Response was assessed every 2 cycles following treatment during the first 6 cycles, then every 3 cycles thereafter; median duration of treatment = 5.26 and 3.81 months for SD/PD for oral AZA arms respectively, and 1.84 months for AZA and Durva SD/PD arms

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis was not planned as per study plan.

End point values	Progressive Disease (PD) Cohort: Oral Azacitidine	Progressive Disease Cohort: Oral Azacitidine and Durvalumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	5		
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Progressive Disease at Baseline who Achieved Stable Disease

End point title	Percentage of Participants with Progressive Disease at Baseline who Achieved Stable Disease[4]

End point description:

A participant was considered as having a stable disease if the disease neither responded nor progressed during or after study treatment.

End point type	Secondary

End point timeframe:

Response was assessed every 2 cycles following treatment during the first 6 cycles, then every 3 cycles thereafter; median duration of treatment = 5.26 and 3.81 months for SD/PD for oral AZA arms respectively, and 1.84 months for AZA and Durva SD/PD arms

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis was not planned as per study plan.

End point values	Progressive Disease (PD) Cohort: Oral Azacitidine	Progressive Disease Cohort: Oral Azacitidine and Durvalumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	5		
Units: Percentage of Participants				
number (not applicable)	36.4	20.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Duration of Stable Disease

End point title	Kaplan-Meier Estimate of Duration of Stable Disease[5]

End point description:

The duration of stable disease was defined as the time between any two observations of objective disease progression (modified IWG criteria), starting from the first day of dosing with IP. Participants who maintained stable disease through the end of the treatment period were censored at the date of study termination.

End point type	Secondary

End point timeframe:

Response was assessed every 2 cycles following treatment during the first 6 cycles, then every 3 cycles thereafter; median duration of treatment = 5.26 and 3.81 months for SD/PD for oral AZA arms respectively, and 1.84 months for AZA and Durva SD/PD arms

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis was not planned as per study plan.

End point values	Stable Disease (SD) Cohort: Oral Azacitidine	Progressive Disease (PD) Cohort: Oral Azacitidine	Progressive Disease Cohort: Oral Azacitidine and Durvalumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	22	5	
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Progressed to Acute Myelogenous Leukemia (AML)

End point title	Percentage of Participants who Progressed to Acute Myelogenous Leukemia (AML)

End point description:

For all participants who received at least one dose of study drug, continuous monitoring for progression to AML occurred in the post treatment follow up period.

End point type	Secondary

End point timeframe:

From first dose and until death, loss to follow-up, withdrawal of consent for further data collection, or study closure (Up to 91 months)

End point values	Stable Disease (SD) Cohort: Oral Azacitidine	Progressive Disease (PD) Cohort: Oral Azacitidine	Stable Disease Cohort: Oral Azacitidine and Durvalumab	Progressive Disease Cohort: Oral Azacitidine and Durvalumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	22	6	5
Units: Percentage of Participants				
number (not applicable)	31.3	18.2	33.3	60.0

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Time to Progression to AML

End point title	Kaplan-Meier Estimate of Time to Progression to AML

End point description:

Time to AML progression was defined as the time from the date of first dose of IP until the date the participant had documented progression to AML.

End point type	Secondary

End point timeframe:

From first dose and until death, loss to follow-up, withdrawal of consent for further data collection, or study closure (Up to 91 months)

End point values	Stable Disease (SD) Cohort: Oral Azacitidine	Progressive Disease (PD) Cohort: Oral Azacitidine	Stable Disease Cohort: Oral Azacitidine and Durvalumab	Progressive Disease Cohort: Oral Azacitidine and Durvalumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	22	6	5
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)	21.47 (1.68 to 99999)	6.21 (1.64 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Participants with Treatment Emergent Adverse Events (TEAEs)

End point description:

TEAEs were defined as AEs occurring or worsening on or after the date of the first dose of oral aza or durva and within 28 days after last dose of oral aza or 90 days after last dose of durva A serious adverse event (SAE) is any: • Death; • Life-threatening event; • Any inpatient hospitalization or prolongation of existing hospitalization; • Persistent or significant disability or incapacity; • Congenital anomaly or birth defect; • Any other important medical event The severity of an AE was evaluated by the investigator according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) (Version 4.0) where Grade 1 = Mild, Grade 2 = Moderate, Grade 3 = Severe, Grade 4 = Life-threatening and Grade 5 = Death.

End point type	Secondary

End point timeframe:

From first dose, until 28 days after the last dose of CC-486 (90 days after the last dose of durvalumab) or the last study visit, whichever date is later (Up to 91 months)

End point values	Stable Disease (SD) Cohort: Oral Azacitidine	Progressive Disease (PD) Cohort: Oral Azacitidine	Stable Disease Cohort: Oral Azacitidine and Durvalumab	Progressive Disease Cohort: Oral Azacitidine and Durvalumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	22	6	5
Units: Participants				
≥ 1 TEAE	32	22	6	5
≥ 1 TEAE Related to (R/T) Oral Azacitidine (AZA)	28	20	6	4
≥ 1 TEAE R/T Durvalumab (Durva)	0	0	5	4
≥ 1 TEAE R/T Oral AZA or Durva	28	20	6	4

≥ 1 Serious TEAE	25	15	4	5
≥ 1 Serious TEAE R/T Oral AZA	4	3	2	1
≥ 1 Serious TEAE R/T Durva	0	0	1	1
≥ 1 Serious TEAE R/T Oral AZA or Durva	4	3	2	1
≥ 1 NCI CTC Grade (GR) 3 or 4 TEAE	32	19	5	5
≥ 1 NCI CTC GR 3 or 4 TEAE R/T Oral AZA	18	10	4	3
≥ 1 NCI CTC GR 3 or 4 TEAE R/T Durva	0	0	2	2
≥ 1 NCI CTC GR 3 or 4 TEAE R/T AZA or Durva	18	10	4	3
≥ 1 TEAE Leading to Death	4	4	2	0
≥ 1 TEAE Leading to Death R/T Oral AZA	0	0	0	0
≥ 1 TEAE Leading to Death R/T Durva	0	0	0	0
≥ 1 TEAE Leading to Death R/T AZA or Durva	0	0	0	0
≥ 1 TEAE Leading to Dose Reduction of AZA	10	8	1	0
≥ 1 TEAE Leading to Reduction of Durva	0	0	0	0
≥ 1 TEAE Leading to Reduction of AZA or Durva	10	8	1	0
≥1 TEAE Leading to Interruption of AZA	21	13	3	4
≥1 TEAE Leading to Interruption of Durva	0	0	2	0
≥1 TEAE Leading to Interruption of AZA or Durva	21	13	3	4
≥ 1 TEAE Leading to Discontinuation (D/C) of AZA	15	8	4	4
≥ 1 TEAE Leading to D/C of Durva	0	0	3	3
≥ 1 TEAE Leading to D/C of AZA or Durva	15	8	4	4

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAE and Non-SAEs were collected from first dose, until 28 days after the last dose of CC-486 (90 days after the last dose of durvalumab) or the last study visit, whichever date is later. (Up to 91 months)

Adverse event reporting additional description:

The number at Risk for All-Cause Mortality represents all enrolled participants. The number at risk for Serious Adverse Events and Other (Not Including Serious) Adverse Events represents safety population that include all enrolled subjects who have received at least 1 dose of IP and had at least 1 post-dose safety assessment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Stable Disease (SD) Cohort: Oral Azacitidine
Reporting group description: -	
Reporting group title	Stable Disease Cohort: Oral Azacitidine and Durvalumab
Reporting group description: -	
Reporting group title	Progressive Disease Cohort: Oral Azacitidine and Durvalumab
Reporting group description: -	
Reporting group title	Progressive Disease (PD) Cohort: Oral Azacitidine
Reporting group description: -	

Serious adverse events	Stable Disease (SD) Cohort: Oral Azacitidine	Stable Disease Cohort: Oral Azacitidine and Durvalumab	Progressive Disease Cohort: Oral Azacitidine and Durvalumab
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 32 (81.25%)	4 / 6 (66.67%)	5 / 5 (100.00%)
number of deaths (all causes)	22	3	5
number of deaths resulting from adverse events	4	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Glioma			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Transformation to acute myeloid leukaemia			

subjects affected / exposed	8 / 32 (25.00%)	1 / 6 (16.67%)	3 / 5 (60.00%)
occurrences causally related to treatment / all	0 / 8	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sarcoma			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 32 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Pyrexia			
subjects affected / exposed	2 / 32 (6.25%)	1 / 6 (16.67%)	2 / 5 (40.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Respiratory distress			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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

Pulmonary oedema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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			
White blood cell count increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ejection fraction decreased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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			
Femur fracture			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 32 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Ataxia			

subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Dementia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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			
Leukocytosis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Neutropenia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Febrile neutropenia			
subjects affected / exposed	2 / 32 (6.25%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperleukocytosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Thrombocytopenia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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			
Haematemesis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Diarrhoea			

subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Constipation			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Intestinal ischaemia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Rectal haemorrhage			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Nausea			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 6 (16.67%)	0 / 5 (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
Autoimmune hepatitis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 6 (16.67%)	0 / 5 (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
Skin and subcutaneous tissue disorders			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Erythema			

subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Pyoderma gangrenosum			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Haematuria			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Urinary retention			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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			
Neck pain			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Myositis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Joint effusion			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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

Bone pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Back pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Bacteraemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Fungaemia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			

subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis gangrenous			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Cellulitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Diverticulitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Gastroenteritis norovirus			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Oral herpes			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Pneumonia			

subjects affected / exposed	9 / 32 (28.13%)	0 / 6 (0.00%)	2 / 5 (40.00%)
occurrences causally related to treatment / all	1 / 10	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Pseudomonal sepsis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	3 / 32 (9.38%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serratia bacteraemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (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
Upper respiratory tract infection			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Metabolism and nutrition disorders			
Tumour lysis syndrome			

subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Dehydration			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (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
Failure to thrive			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Serious adverse events	Progressive Disease (PD) Cohort: Oral Azacitidine		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 22 (68.18%)		
number of deaths (all causes)	18		
number of deaths resulting from adverse events	4		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Glioma			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transformation to acute myeloid leukaemia			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Sarcoma			

subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pyrexia			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pulmonary oedema			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Respiratory failure			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
White blood cell count increased			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ejection fraction decreased			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dementia			

subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperleukocytosis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Haematemesis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			

subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal ischaemia				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatitis				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Autoimmune hepatitis				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Acute febrile neutrophilic dermatosis				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erythema				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyoderma gangrenosum				

subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myositis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint effusion			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Back pain				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Appendicitis				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthritis infective				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial sepsis				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fungaemia				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis gangrenous				

subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis norovirus				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Neutropenic sepsis				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oral herpes				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	2 / 22 (9.09%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				

subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pseudomonal sepsis				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 22 (9.09%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 1			
Serratia bacteraemia				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection enterococcal				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Tumour lysis syndrome				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				

subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Failure to thrive			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Stable Disease (SD) Cohort: Oral Azacitidine	Stable Disease Cohort: Oral Azacitidine and Durvalumab	Progressive Disease Cohort: Oral Azacitidine and Durvalumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 32 (100.00%)	6 / 6 (100.00%)	5 / 5 (100.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Hypertension			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Hypotension			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	3 / 5 (60.00%)
occurrences (all)	1	0	3
Superficial vein thrombosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	7 / 32 (21.88%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	10	3	2
Generalised oedema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Fatigue			

subjects affected / exposed	10 / 32 (31.25%)	2 / 6 (33.33%)	4 / 5 (80.00%)
occurrences (all)	33	3	7
Chills			
subjects affected / exposed	1 / 32 (3.13%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Catheter site erythema			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	9 / 32 (28.13%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	9	0	0
Oedema peripheral			
subjects affected / exposed	6 / 32 (18.75%)	1 / 6 (16.67%)	3 / 5 (60.00%)
occurrences (all)	6	1	4
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Penile pain			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Oedema genital			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	3 / 32 (9.38%)	0 / 6 (0.00%)	2 / 5 (40.00%)
occurrences (all)	4	0	2
Dyspnoea exertional			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	4	0	0
Dyspnoea			
subjects affected / exposed	9 / 32 (28.13%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	13	0	0

Cough			
subjects affected / exposed	7 / 32 (21.88%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	7	0	2
Hypoxia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	3 / 32 (9.38%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	4	0	0
Pleural effusion			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Productive cough			
subjects affected / exposed	3 / 32 (9.38%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	6 / 32 (18.75%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	7	0	1
Depression			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Delirium			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	5
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	9
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	4	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	3 / 32 (9.38%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	5	0	0
Cardiac murmur			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Platelet count decreased			
subjects affected / exposed	0 / 32 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Serum ferritin increased			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Urine output decreased			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Weight decreased			
subjects affected / exposed	10 / 32 (31.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	11	0	0
White blood cell count increased			

subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 32 (15.63%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	7	0	0
Skin wound			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Spinal compression fracture			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Transfusion reaction			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	1
Contusion			
subjects affected / exposed	5 / 32 (15.63%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	14	0	0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Atrial fibrillation			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	2 / 5 (40.00%)
occurrences (all)	1	0	2
Tricuspid valve disease			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Sinus bradycardia			

subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Nervous system disorders			
Somnolence			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Sciatica			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Headache			
subjects affected / exposed	4 / 32 (12.50%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	12	4	0
Dysgeusia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	6 / 32 (18.75%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	14	0	0
Lethargy			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	3 / 32 (9.38%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	4	0	1
Neutropenia			
subjects affected / exposed	12 / 32 (37.50%)	1 / 6 (16.67%)	2 / 5 (40.00%)
occurrences (all)	42	1	4
Anaemia			
subjects affected / exposed	12 / 32 (37.50%)	1 / 6 (16.67%)	3 / 5 (60.00%)
occurrences (all)	40	1	18
Splenomegaly			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Thrombocytopenia			

subjects affected / exposed	8 / 32 (25.00%)	1 / 6 (16.67%)	4 / 5 (80.00%)
occurrences (all)	11	2	11
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hypoacusis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Ear pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Eye haemorrhage			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	21 / 32 (65.63%)	4 / 6 (66.67%)	2 / 5 (40.00%)
occurrences (all)	41	4	2
Constipation			
subjects affected / exposed	13 / 32 (40.63%)	1 / 6 (16.67%)	2 / 5 (40.00%)
occurrences (all)	25	1	3
Dry mouth			
subjects affected / exposed	1 / 32 (3.13%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Abdominal pain upper			
subjects affected / exposed	3 / 32 (9.38%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	12	0	0
Abdominal pain			
subjects affected / exposed	3 / 32 (9.38%)	2 / 6 (33.33%)	1 / 5 (20.00%)
occurrences (all)	6	2	2
Abdominal distension			

subjects affected / exposed	3 / 32 (9.38%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	4	0	0
Anal erythema			
subjects affected / exposed	0 / 32 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			
subjects affected / exposed	2 / 32 (6.25%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	4	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	4	0	1
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	3 / 32 (9.38%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Dysphagia			
subjects affected / exposed	2 / 32 (6.25%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	2	2	0
Dyspepsia			
subjects affected / exposed	1 / 32 (3.13%)	2 / 6 (33.33%)	1 / 5 (20.00%)
occurrences (all)	1	3	1
Duodenogastric reflux			
subjects affected / exposed	0 / 32 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Stomatitis			
subjects affected / exposed	4 / 32 (12.50%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	4	1	1
Periodontal disease			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Oral mucosa haematoma			

subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	24 / 32 (75.00%)	2 / 6 (33.33%)	2 / 5 (40.00%)
occurrences (all)	34	6	3
Mouth haemorrhage			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	2 / 5 (40.00%)
occurrences (all)	1	0	2
Vomiting			
subjects affected / exposed	18 / 32 (56.25%)	2 / 6 (33.33%)	3 / 5 (60.00%)
occurrences (all)	25	3	5
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	1 / 32 (3.13%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Petechiae			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	10	0	0
Pruritus			
subjects affected / exposed	5 / 32 (15.63%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	6	0	0
Rash			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Dermatitis bullous			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	1 / 32 (3.13%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0

Rash maculo-papular			
subjects affected / exposed	3 / 32 (9.38%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	3	1	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	2
Pollakiuria			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Dysuria			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	5	0	0
Renal cyst			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	2	0	1
Urinary tract obstruction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Urinary retention			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Urinary incontinence			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Renal disorder			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 32 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	4 / 32 (12.50%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	7	0	2

Muscle spasms			
subjects affected / exposed	2 / 32 (6.25%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Joint effusion			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Back pain			
subjects affected / exposed	7 / 32 (21.88%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	9	0	1
Arthralgia			
subjects affected / exposed	5 / 32 (15.63%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	7	0	0
Polyarthritis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	3 / 32 (9.38%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	3	5	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 32 (6.25%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Folliculitis			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Diverticulitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Cellulitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	3 / 32 (9.38%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	6	0	0
Upper respiratory tract infection			

subjects affected / exposed	6 / 32 (18.75%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	13	1	0
Staphylococcal infection			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	3 / 32 (9.38%)	0 / 6 (0.00%)	2 / 5 (40.00%)
occurrences (all)	3	0	3
Oral herpes			
subjects affected / exposed	5 / 32 (15.63%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	5	0	0
Oral candidiasis			
subjects affected / exposed	3 / 32 (9.38%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	4	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	15 / 32 (46.88%)	1 / 6 (16.67%)	2 / 5 (40.00%)
occurrences (all)	23	1	2
Dehydration			
subjects affected / exposed	2 / 32 (6.25%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Gout			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	4	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	9	0	2
Hypophosphataemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Hypomagnesaemia			
subjects affected / exposed	3 / 32 (9.38%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	3	0	3
Hypokalaemia			
subjects affected / exposed	4 / 32 (12.50%)	0 / 6 (0.00%)	2 / 5 (40.00%)
occurrences (all)	4	0	8
Hypocalcaemia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	3
Hyperuricaemia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Hyperphosphataemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

Non-serious adverse events	Progressive Disease (PD) Cohort: Oral Azacitidine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 22 (100.00%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Superficial vein thrombosis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	5		
Generalised oedema			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	6 / 22 (27.27%)		
occurrences (all)	6		
Chills			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Catheter site erythema			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	5		
Oedema peripheral			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Penile pain			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Oedema genital			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			

subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Dyspnoea exertional			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	4		
Cough			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	4		
Hypoxia			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Pleural effusion			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Pulmonary hypertension			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		

Depression			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Delirium			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	4		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Cardiac murmur			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Serum ferritin increased			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Urine output decreased			

subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	6 / 22 (27.27%)		
occurrences (all)	6		
White blood cell count increased			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Skin wound			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Spinal compression fracture			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Transfusion reaction			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Contusion			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Atrial fibrillation			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Tricuspid valve disease			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Tachycardia			

subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Sinus bradycardia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Nervous system disorders			
Somnolence subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Sciatica subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Headache subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Dysgeusia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Dizziness subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Lethargy subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Blood and lymphatic system disorders			
Febrile neutropenia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Neutropenia subjects affected / exposed occurrences (all)	6 / 22 (27.27%) 18		
Anaemia			

subjects affected / exposed	10 / 22 (45.45%)		
occurrences (all)	28		
Splenomegaly			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	6 / 22 (27.27%)		
occurrences (all)	6		
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Hypoacusis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Ear pain			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Eye haemorrhage			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	11 / 22 (50.00%)		
occurrences (all)	26		
Constipation			
subjects affected / exposed	9 / 22 (40.91%)		
occurrences (all)	12		
Dry mouth			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			

subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
Abdominal pain				
subjects affected / exposed	2 / 22 (9.09%)			
occurrences (all)	2			
Abdominal distension				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
Anal erythema				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
Gingival bleeding				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
Gastrointestinal haemorrhage				
subjects affected / exposed	2 / 22 (9.09%)			
occurrences (all)	2			
Flatulence				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
Dysphagia				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
Dyspepsia				
subjects affected / exposed	3 / 22 (13.64%)			
occurrences (all)	3			
Duodenogastric reflux				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
Haemorrhoids				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
Stomatitis				

subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
Periodontal disease			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Oral mucosa haematoma			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	12 / 22 (54.55%)		
occurrences (all)	17		
Mouth haemorrhage			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	11 / 22 (50.00%)		
occurrences (all)	25		
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Petechiae			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Decubitus ulcer			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		

Dermatitis bullous subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Rash maculo-papular subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Renal and urinary disorders			
Acute kidney injury subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 2		
Pollakiuria subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Dysuria subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Renal cyst subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Urinary tract obstruction subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Urinary retention subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 3		
Urinary incontinence subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Renal disorder subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Endocrine disorders			

Hypothyroidism			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Joint effusion			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
Polyarthritis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Folliculitis			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
Diverticulitis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Cellulitis			

subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Staphylococcal infection			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Rash pustular			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Oral herpes			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Oral candidiasis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 22 (36.36%)		
occurrences (all)	8		
Dehydration			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Gout			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	5		

Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Hypophosphataemia subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 3		
Hypomagnesaemia subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Hypocalcaemia subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Hyperuricaemia subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Hyperphosphataemia subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 September 2015	An additional investigational product (IP), anti-PD-L1 monoclonal antibody, durvalumab (MEDI4736) in combination with CC-486 (combination therapy), was to be evaluated in this study in addition to the evaluation of CC-486 as monotheraphy.
27 March 2017	Updated objectives, futility analysis, enrollment period, safety profile, and dosing for clarity and extended trial duration.
28 December 2017	Protocol text was updated to allow the dose escalation of CC-486 after 2 well tolerated cycles (instead of 4 cycles). The safety assessment observed in the Phase 1 safety run-in portion of the trial was based on 2 dosing cycles and most adverse events occurred early in these cycles.
17 June 2019	A description of the Extension Phase was presented in Appendix J and mentioned throughout the protocol. The overall duration of the study was extended during the Extension Phase

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported