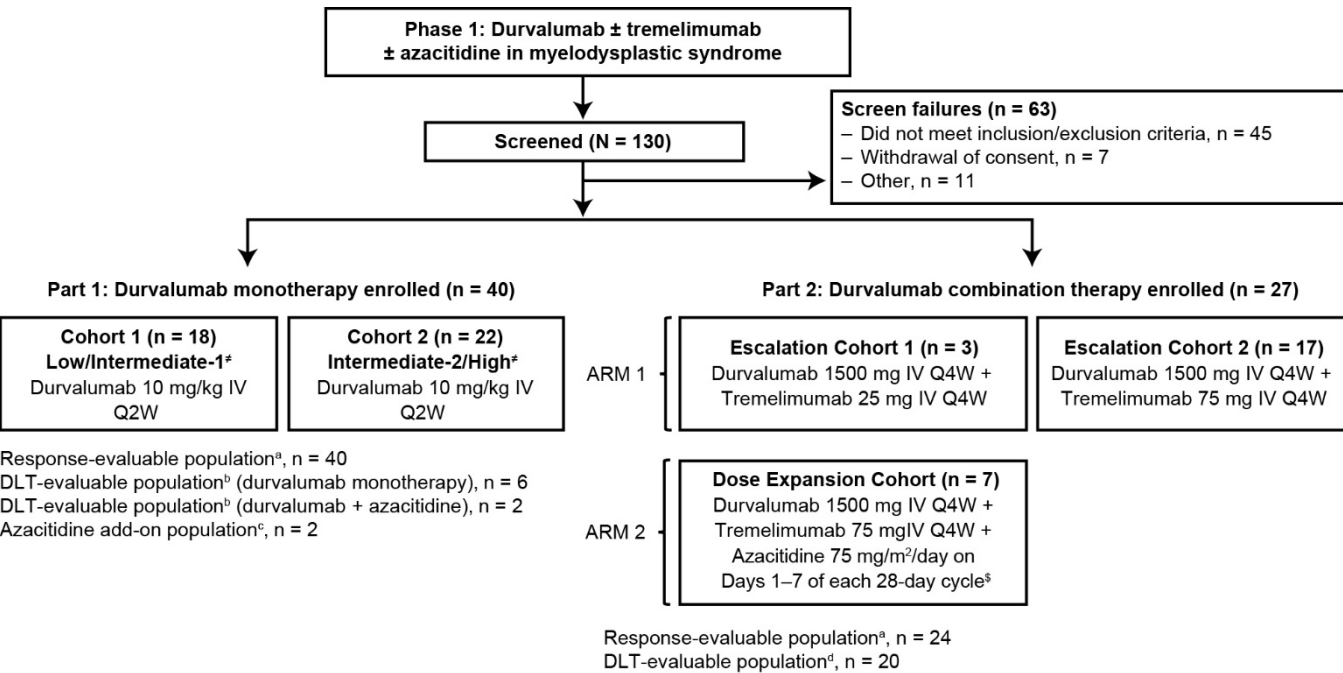


Supplementary Figures and Tables

Online Resource 1.



Online Resource 1. Study design. ^aIPSS risk status; * SC injection. ^aResponse-evaluable population includes patients in the as-treated population who had ≥ 1 post-baseline bone marrow biopsy, who died from any cause, or who discontinued due to clinical PD prior to any post-baseline bone marrow biopsy. ^bThe initial 6 patients enrolled in the study who received ≥ 2 protocol-assigned doses of durvalumab and completed the safety follow-up through the DLT evaluation period or experienced a DLT during the DLT evaluation period. ^cAzacitidine add-on population includes patients in part 1 who received durvalumab and azacitidine (75 mg/m²/day on days 1 to 7 of each 28-day cycle) after initial treatment with durvalumab monotherapy. ^dDLT-evaluable population includes all patients entered in the dose-escalation phase who received ≥ 2 doses of durvalumab and completed the safety follow-up through the DLT evaluation period (through the administration of the third dose of durvalumab and tremelimumab with or without azacitidine) or experienced any DLT.

DLT dose-limiting toxicity, *durva* durvalumab, *IPSS* International Prognostic Scoring System, *IV* intravenous, *PD* progressive disease, *Q2W* every 2 weeks, *Q4W* every 4 weeks, *SC* subcutaneous.

Online Resource 2. Duration of exposure, as-treated population.

	Part 1: durvalumab monotherapy			Part 2: durvalumab combination therapy			
	Low/int-1 (n = 18)	Int-2/high (n = 22)	Total (N = 40)	Durva + treme 25 mg (n = 3)	Durva + treme 75 mg (n = 17)	Durva + treme 75 mg + aza (n = 7)	Total (N = 27)
Duration of exposure,^a weeks, median (range)							
Durvalumab	26.2 (6.0, 121.9)	13.0 (4.0, 56.0)	18.0 (4.0, 121.9)	12.3 (12.0, 47.7)	13.0 (4.0, 32.0)	8.0 (4.0, 24.3)	12.0 (4.0, 47.7)
Tremelimumab	-	-	-	12.0 (12.0, 12.3)	13.0 (4.0, 17.1)	8.0 (4.0, 16.0)	12.0 (4.0, 17.1)
Azacitidine	19.7 (19.7, 19.7)	9.0 (9.0, 9.0)	14.4 (9.0, 19.7)	-	-	8.6 (4.7, 25.1)	8.6 (4.7, 25.1)

^aDuration of exposure is defined by the last dose date, plus 28 days, minus the first dose date. For patients who die prior to day 28 of the last cycle, duration is defined as the date of death, minus first dose date, plus 1 day. If the database cutoff occurs prior to day 28 of the last cycle, and the subject remains alive, duration is defined as the date of the database cutoff, minus the dose date, plus 1 day.

Aza azacitidine, *durva* durvalumab, *int* intermediate, *treme* tremelimumab.

Online Resource 3. Treatment-emergent adverse events of any grade in $\geq 20\%$ of all patients in either part 1 or part 2, as-treated population.

System Organ Class ^a Preferred term	Part 1: durvalumab monotherapy			Part 2: durvalumab combination therapy			
	Low/int-1 (n = 18)	Int-2/high (n = 22)	Total (N = 40)	Durva + treme 25 mg (n = 3)	Durva + treme 75 mg (n = 17)	Durva + treme 75 mg + aza (n = 7)	Total (N = 27)
Any treatment-emergent AE	18 (100)	22 (100)	40 (100)	3 (100)	17 (100)	7 (100)	27 (100)
Blood and lymphatic system disorders							
Anemia	4 (22)	8 (36)	12 (30)	1 (33)	7 (41)	2 (29)	10 (37)
Febrile neutropenia	-	-	-	1 (33)	4 (24)	2 (29)	7 (26)
Thrombocytopenia	2 (11)	6 (27)	8 (20)	-	-	-	-
Gastrointestinal disorders							

Abdominal pain	1 (6)	4 (18)	5 (13)	0	5 (29)	1 (14)	6 (22)
Diarrhea	7 (39)	9 (41)	16 (40)	0	4 (24)	2 (29)	6 (22)
Nausea	3 (17)	5 (23)	8 (20)	0	5 (29)	0	5 (19)
General disorders and administration site conditions							
Chills	0	6 (27)	6 (15)	2 (67)	2 (12)	2 (29)	6 (22)
Edema peripheral	4 (22)	7 (32)	11 (28)	0	4 (24)	3 (43)	7 (26)
Fatigue	6 (33)	10 (46)	16 (40)	1 (33)	7 (41)	4 (57)	12 (44)
Pyrexia	4 (22)	11 (50)	15 (38)	0	7 (41)	1 (14)	8 (30)
Metabolism and nutrition disorders							
Hyperglycemia	5 (28)	3 (14)	8 (20)	-	-	-	-
Respiratory, thoracic, and mediastinal disorders							
Cough	3 (17)	9 (41)	12 (30)	1 (33)	5 (29)	1 (14)	7 (26)

Dyspnea	1 (6)	9 (41)	10 (25)	0	5 (29)	1 (14)	6 (22)
Skin and subcutaneous tissue disorders							
Rash maculo-papular	2 (11)	2 (9)	4 (10)	2 (67)	3 (18)	1 (14)	6 (22)

AE adverse event, *Aza* azacitidine, *durva* durvalumab, *int* intermediate, *treme* tremelimumab.

^aPatients were counted once for each System Organ Class and preferred term, regardless of the number of events.

Data are presented as n (%).

MedDRA version 22.0.