A phase II trial of azacitidine with ipilimumab, nivolumab, or ipilimumab and nivolumab in previously untreated myelodysplastic syndrome

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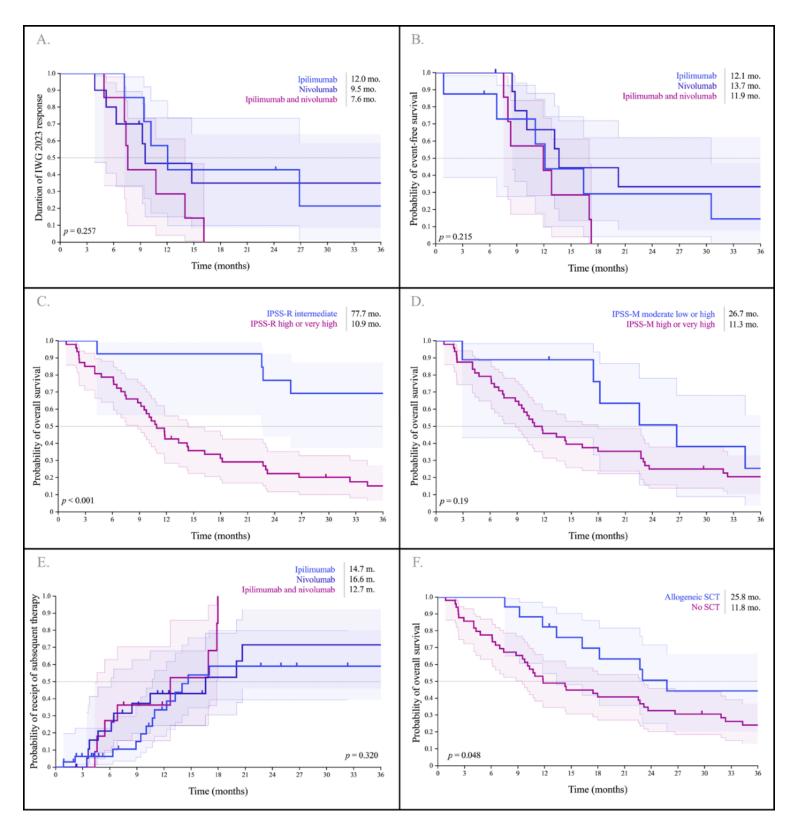
Supplementary Appendix

Subgroup	1	Patients (N = 66)	Hazard Ratio	P Value		
CCI score	•	66	0.99 (0.77–1.27)	0.943		
Marrow blast count	•	66	1.02 (0.88–1.18)	0.802		
Disease risk						
IPSS-M score	⊢■──	64	2.56 (1.35–4.88)	0.004		
IPSS-R score	■ H	66	0.80 (0.51–1.26)	0.334		
Cytogenetic subgroups						
Normal karyotype		13	0.46 (0.09–2.34)	0.348		
Complex karyotype		36	0.26 (0.05–1.47)	0.128		
Monosomy 17 or del(17p)		9	0.65 (0.17–2.42)	0.518		
Monosomy 7 or del(7q)	-	28	1.50 (0.54–4.12)	0.434		
Monosomy 5 or del 5(q)	■-	19	0.24 (0.07–0.83)	0.024		
Molecular subgroups						
ASXL1	—	11	1.44 (0.35–5.90)	0.612		
DNMT3A	-	12	2.75 (0.84–8.93)	0.093		
EZH2	-	3	3.29 (0.37–29.03)	0.284		
KRAS	-	⊣ 3	3.31 (0.61–17.87)	0.164		
NRAS	H H	7	0.64 (0.15–2.84)	0.559		
TET2	—	13	1.32 (0.42–4.11)	0.635		
TP53	-	3 0	19.46 (2.50–151.53)	0.005		
-1	1 5	20				
Survival Better Survival Worse						

Supplementary Figure 1. Forest plot of predictors of overall survival with stem cell transplant as a time-dependent covariate for patients treated with azacitidine-ipilimumab, azacitidine-nivolumab, and azacitidine-ipilimumab-nivolumab. Sixty-four of 66 patients had next-generation sequencing performed prior to treatment.

	Azacitidine-ipilimumab $(N = 33)$	Azacitidine-nivolumab $(N = 20)$	
Hematologic toxicities, grade ≥3 (%)			
Leukopenia	19 (57.6)	15 (75.0)	13 (100.0)
Neutropenia	23 (69.7)	17 (85.0)	13 (100.0)
Lymphocytopenia	14 (42.2)	8 (40.0)	11 (84.6)
Anemia	21 (63.6)	11 (55.0)	9 (69.2)
Thrombocytopenia	25 (75.8)	17 (85.0)	13 (100.0)
Non-hematologic toxicities, grade ≥3 (%)			
Neutropenic fever	6 (18.2)	4 (20.0)	6 (46.2)
Infection	7 (21.2)	9 (45.0)	6 (46.2)
Fatigue	0	0	0
Pneumonia	5 (15.2)	7 (35.0)	2 (15.4)
Pneumonitis	2 (6.1)	0	2 (15.4)
Respiratory failure or hypoxia	4 (12.1)	0	0
Hemorrhage	0	2 (10.0)	1 (7.7)
Abdominal pain	0	0	0
Vomiting	0	0	0
Diarrhea	0	0	0
Colitis	1 (3.0)	1 (5.0)	0
AST elevation	1 (3.0)	3 (15.0)	1 (7.7)
ALT elevation	2 (6.1)	3 (15.0)	2 (15.4)
Bilirubin elevation	0	1 (5.0)	0
Rash	1 (3.0)	0	3 (23.1)
Hyperthyroidism	0	0	0
Hypothyroidism	0	0	0
Creatinine increased	2 (6.1)	0	1 (7.7)
Death during induction (%)			
Death within 30 days	1 (3.0)	0	0
Death between $31 - 60$ days	1 (3.0)	0	0

Supplementary Table 1. Grade ≥ 3 toxicities in patients treated with azacitidine-ipilimumab, azacitidine-nivolumab, and azacitidine-ipilimumab-nivolumab. Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase.



Supplementary Figure 2. Time-to-event analyses for patients treated with azacitidine-ipilimumab, azacitidine-nivolumab, and azacitidine-ipilimumab-nivolumab. (A) Duration of response among IWG 2023 responders for all three cohorts. (B) Probability of event-free survival in all three cohorts. (C) Overall survival stratified by IPSS-R intermediate-risk disease and high or very high-risk disease. All cohorts are pooled. (D) Overall survival stratified by IPSS-M moderate- or high-risk disease. All cohorts are pooled. (E) Median time to the next line of therapy for relapsed or refractory disease for all three cohorts. (F) Non-landmarked analysis of overall survival in patients that underwent SCT for all three cohorts.