

Outcomes of different haploidentical transplantation strategies from the Taiwan Blood and Marrow Transplantation Registry

Xavier Cheng-Hong Tsai,^{1,2,3} Tzu-Ting Chen,⁴ Jyh-Pyng Gau,⁵ Po-Nan Wang,⁶ Yi-Chang Liu,^{7,8} Ming-Yu Lien,⁴ Chi-Cheng Li,^{9,10} Ming Yao,^{1,3} Bor-Sheng Ko^{1,3}

¹Division of Hematology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan

²Genome and Systems Biology Degree Program, National Taiwan University, Taipei, Taiwan

³Department of Hematological Oncology, National Taiwan University Cancer Center, Taipei, Taiwan

⁴Division of Hematology and Oncology, Department of Medicine, China Medical University Hospital, Taichung, Taiwan

⁵Division of Hematology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan

⁶Division of Hematology, Department of Internal Medicine, Chang Gung Medical Foundation, Linkou Branch, Taoyuan, Taiwan

⁷Division of Hematology-Oncology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

⁸College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

⁹Tai-Cheng Cell Therapy Center, National Taiwan University, Taiwan

¹⁰Department of Hematology and Oncology, Buddhist Tzu-Chi General Hospital, Hualien, Taiwan.

Supplementary Table	2
Supplementary Figure Legend	4
Supplementary Figures.....	5

Supplementary Table S1. Post hoc test for CD34 dose

	Mean difference	Std. Error	P value
mGIAC vs PTCy with ATG	-2.51	0.56	<0.001
mGIAC vs PTCy without ATG	-3.39	0.67	<0.001
PTCy with ATG vs. PTCy without ATG	-0.87	0.76	0.489

Abbreviations: ATG, anti-thymocyte globulin

Supplementary Table S2. Comparison of clinical characteristics among patients with different haplo-HSCT approaches after propensity-score matching

Variables	Total (n = 129)	Modified GIAC (n = 86, 66.7%)	PTCy without ATG (n = 16, 12.4%)	PTCy with ATG (n = 27, 20.9%)	P value
Sex ^α					0.341
Male	62 (48.1%)	40 (46.5%)	6 (37.5%)	16 (59.3%)	
Female	67 (51.9%)	46 (53.5%)	10 (62.5%)	11 (40.7%)	
Age, years ^β	42.1 (18.7-69.2)	42.0 (18.7-69.2)	42.0 (21.8-63.7)	44.9 (18.9-68.3)	0.700
Disease ^α					
AML	70 (54.3%)	51 (59.3%)	5 (31.3%)	14 (51.9%)	0.113
MDS	9 (7.0%)	7 (8.1%)	0 (0%)	2 (7.4%)	0.500
MDS/MPN	4 (3.1%)	1 (1.2%)	2 (12.5%)	1 (3.7%)	0.055
ALL	26 (20.2%)	18 (20.9%)	3 (18.8%)	5 (18.5%)	0.953
MPAL	2 (1.6%)	2 (2.3%)	0 (0%)	0 (0%)	0.602
CML	4 (3.1%)	1 (1.2%)	1 (6.3%)	2 (7.4%)	0.195
NHL	10 (7.8%)	3 (3.5%)	5 (31.3%)	2 (7.4%)	0.001
HL	3 (2.3%)	2 (2.3%)	0 (0%)	1 (3.7%)	0.738
Myeloma	1 (0.8%)	1 (1.2%)	0 (0%)	0 (0%)	0.777
Conditioning ^α					0.833
Myeloablative	28 (21.7%)	20 (23.3%)	3 (18.8%)	5 (18.5%)	
Reduced intensity	101 (78.3%)	66 (76.7%)	13 (81.3%)	22 (81.5%)	
ATG dose per kilogram ^γ	6.0 (2.0-7.5)	6.0 (5.0-7.5)	0	4.0 (2.0-7.5)	<0.001
Stem cell source ^α					<0.001
BM + mobilized PB	86 (66.7%)	86 (100%)	0 (0%)	0 (0%)	
Mobilized PB	43 (33.3%)	0 (0%)	16 (100%)	27 (100%)	
Donor relationship ^α					0.584
Child	53 (41.1%)	35 (40.7%)	7 (43.8%)	11 (40.7%)	
Parent	37 (28.7%)	27 (31.4%)	2 (12.5%)	8 (29.6%)	
Sibling	39 (30.2%)	7 (27.9%)	7 (43.8%)	8 (29.6%)	
Donor-recipient sex combination ^α					0.736
Female donor to male recipient	33 (25.6%)	22 (25.6%)	3 (18.8%)	8 (29.6%)	
Other combinations	96 (74.4%)	64 (74.4%)	13 (81.2%)	19 (70.4%)	
Recipient CMV serostatus ^{αδ}					0.898
Negative	11 (8.5%)	8 (9.3%)	1 (9.1%)	2 (18.2%)	
Positive	118 (91.5%)	78 (90.7%)	15 (93.8%)	25 (92.6%)	
Missing	1 (0.8%)	0 (0%)	0 (0%)	1 (3.7%)	
CD34 (10⁶/kg) ^{ve}	5.1 (1.3-21.2)	5.0 (2.4-8.3)	5.3 (3.0-13.5)	5.9 (1.3-21.2)	
Disease Risk Index ^α					0.136
Low	8 (6.2%)	5 (5.8%)	0 (0%)	3 (11.1%)	
Intermediate	52 (40.3%)	32 (37.2%)	6 (37.5%)	14 (51.9%)	
High	56 (43.4%)	40 (46.5%)	10 (62.5%)	5 (22.2%)	
Very high	13 (10.1%)	9 (10.5%)	0 (0%)	4 (14.8%)	
Year of HSCT	2016 (2011-2019)	2016 (2013-2019)	2016 (2014-2019)	2017 (2011-2019)	

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; ATG, anti-thymocyte globulin; BM, bone marrow; CMV, cytomegalovirus; CR, complete remission; HL, Hodgkin lymphoma; MDS, myelodysplastic syndrome; MPAL, mixed phenotypic acute leukemia; NHL, non-Hodgkin lymphoma; PB, peripheral blood

α Number of patients (%)

β Mean (range)

γ Median (range)

δ Based on patients with available data

ε Combination of bone marrow and peripheral stem cell doses

Supplementary Table S3. Causes of death among patients receiving different haplo-HSCT

strategies

Cause of death	Modified GIAC (n = 110)	PTCy without ATG (n = 26)	PTCy with ATG (n = 42)	P value
Overall	54	20	23	
Relapse	32 (59.3%)	10 (50%)	12 (52.2%)	0.620
Infection	12 (22.2%)	5 (25%)	8 (34.8%)	0.309
GvHD	5 (9.3%)	2 (10%)	1 (4.3%)	0.589
Graft failure	2 (3.7%)	2 (10%)	0 (%)	0.102
Interstitial pneumonia	1 (1.9%)	0 (%)	1 (4.3%)	0.625
Intracerebral hemorrhage	0 (0%)	1 (5%)	0 (0%)	0.053
Other	2 (3.7%)	0 (%)	1 (4.3%)	0.748

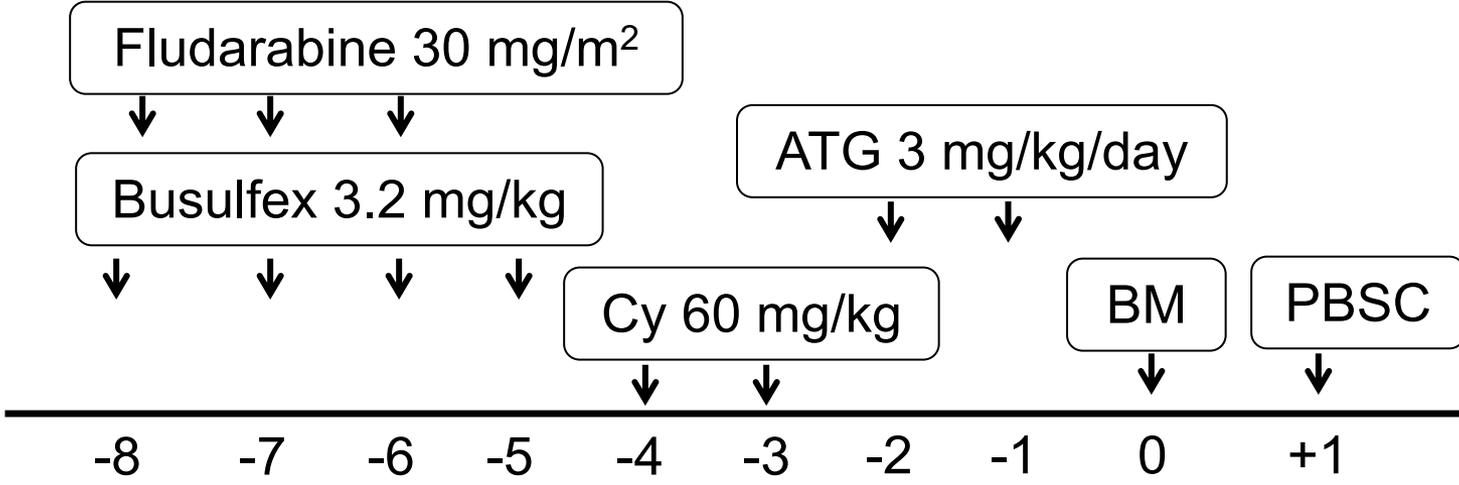
Supplementary Figure S1. Modified GIAC protocol for myeloablative conditioning (A) and reduced intensity conditioning (B).

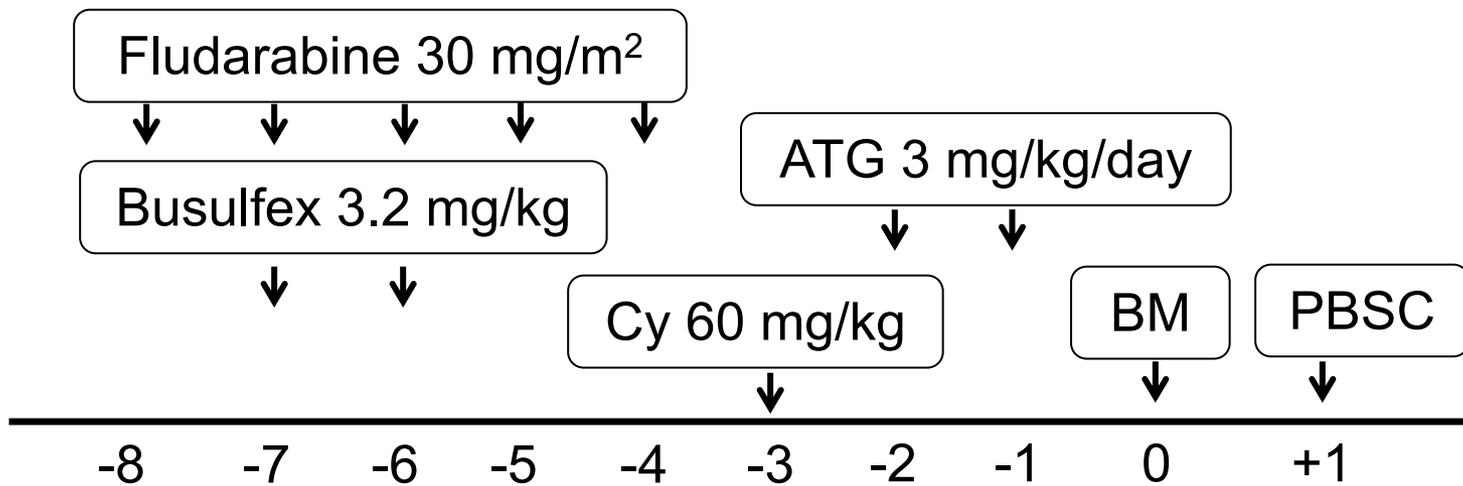
Supplementary Figure S2. The outcome analyses of patients receiving haplo-HSCT after propensity score matching, including cumulative incidence of relapse (A), nonrelapse mortality (B), overall survival (C), and GvHD/relapse-free survival (D).

Supplementary Figure S3. (A) The univariate analysis of cumulative incidence of relapse (CIR) yielded that advanced disease status and grade III-IV acute GvHD were significant prognostic factors. (B) In the univariate analysis of nonrelapse mortality (NRM), the variables had no prognostic impact. (C) The univariate analysis of GvHD/relapse-free survival (GRFS) yielded advanced disease status, grade III-IV acute GvHD, and extensive chronic GvHD were significant prognostic factors. (D) The univariate analysis of overall survival (OS) yielded advanced disease status, grade III-IV acute GvHD, extensive chronic GvHD, stem cell source, and recipient CMV serostatus were significant prognostic factors.

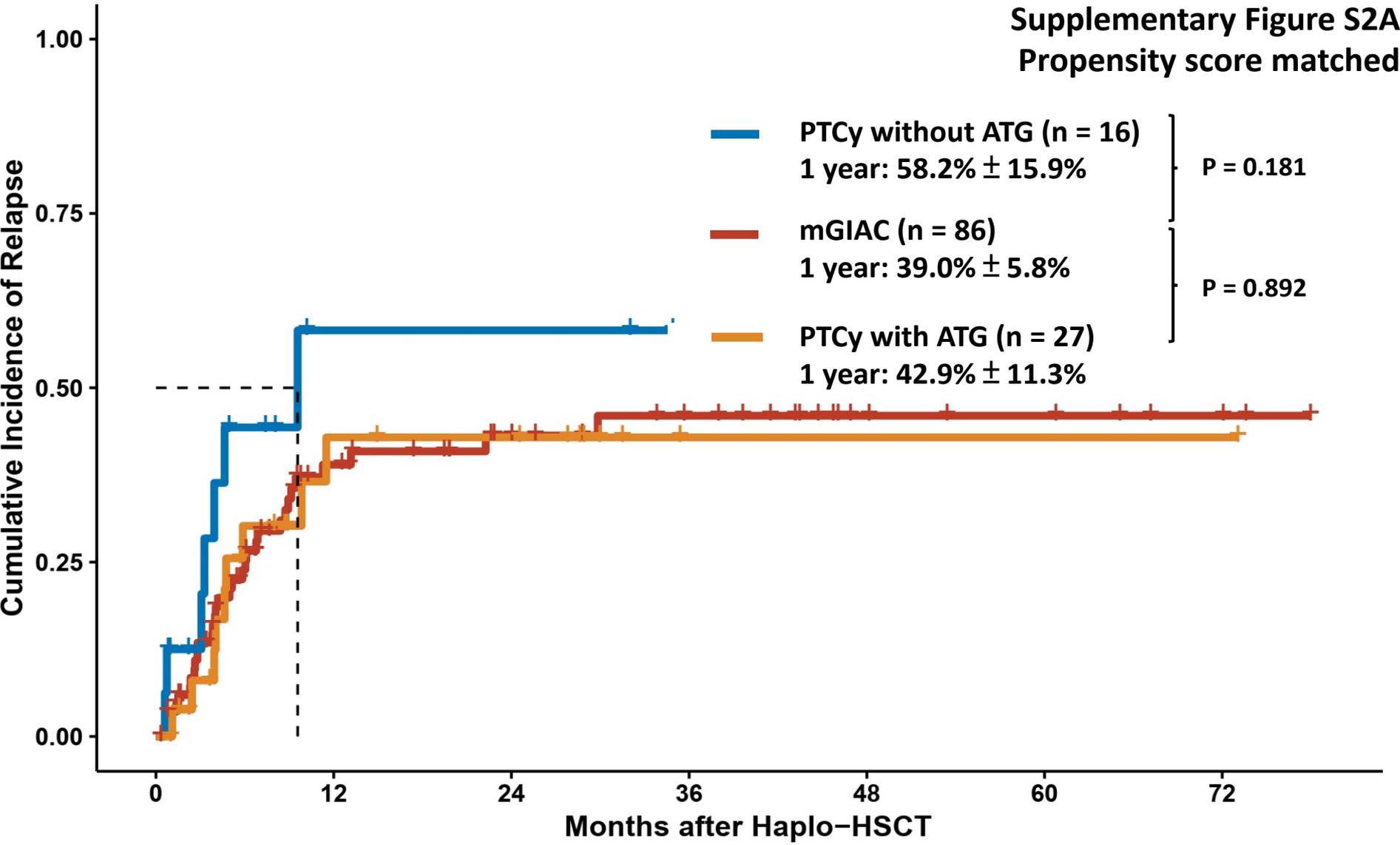
Supplementary Figure S4. Comparison of nonrelapse mortality (A) and cumulative incidence of relapse (B) in patients with low/intermediate-risk diseases receiving haplo-HSCT.

Supplementary Figure S5. Comparison of cumulative incidence of relapse (A) and nonrelapse mortality (B) in patients with high/very-high-risk diseases receiving haplo-HSCT.





Supplementary Figure S2A
Propensity score matched

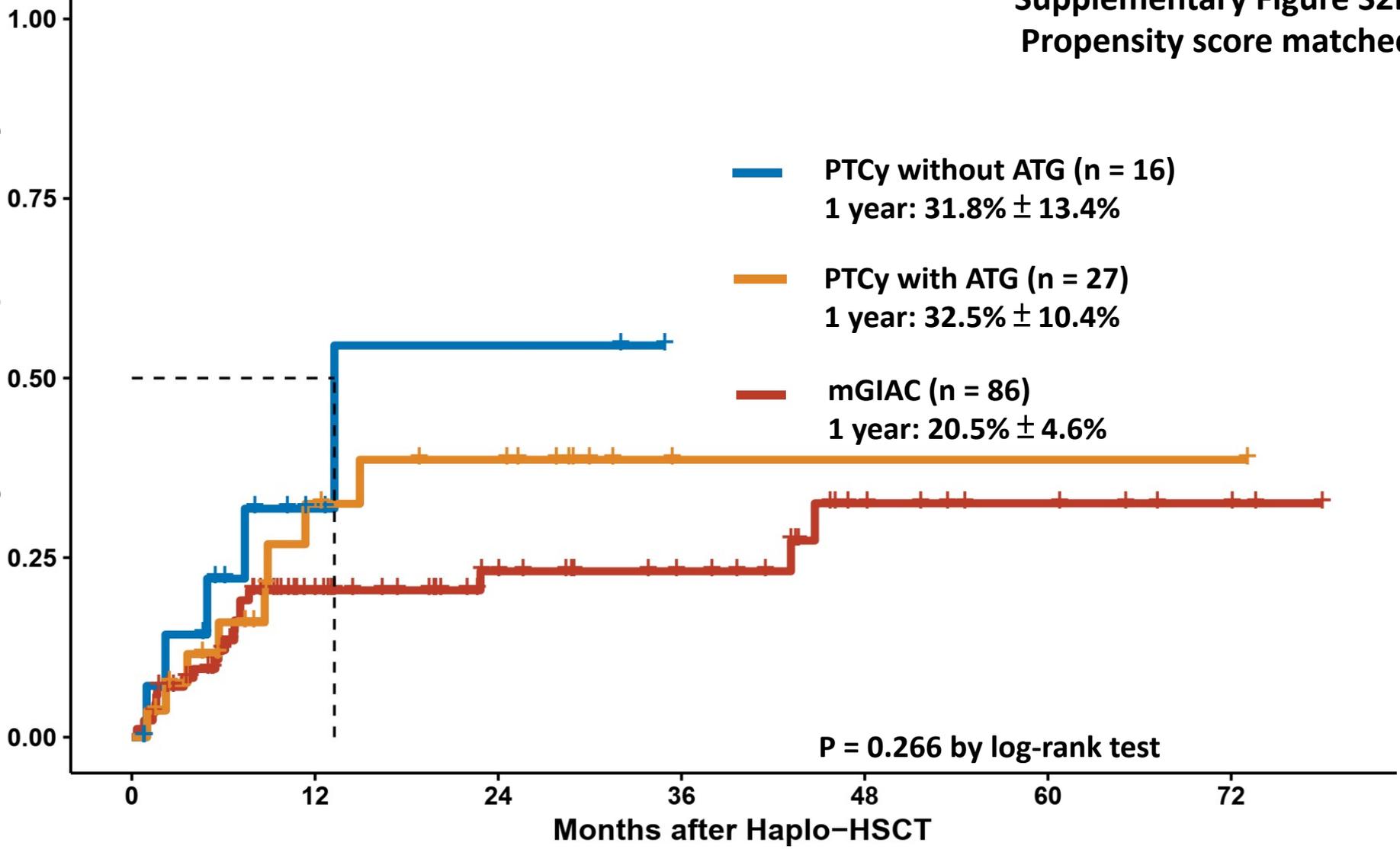


No. at risk:

█	86	34	23	17	8	6	3
█	16	2	2	0 ₇	0	0	0
█	27	9	8	1	1	1	1

Supplementary Figure S2B
Propensity score matched

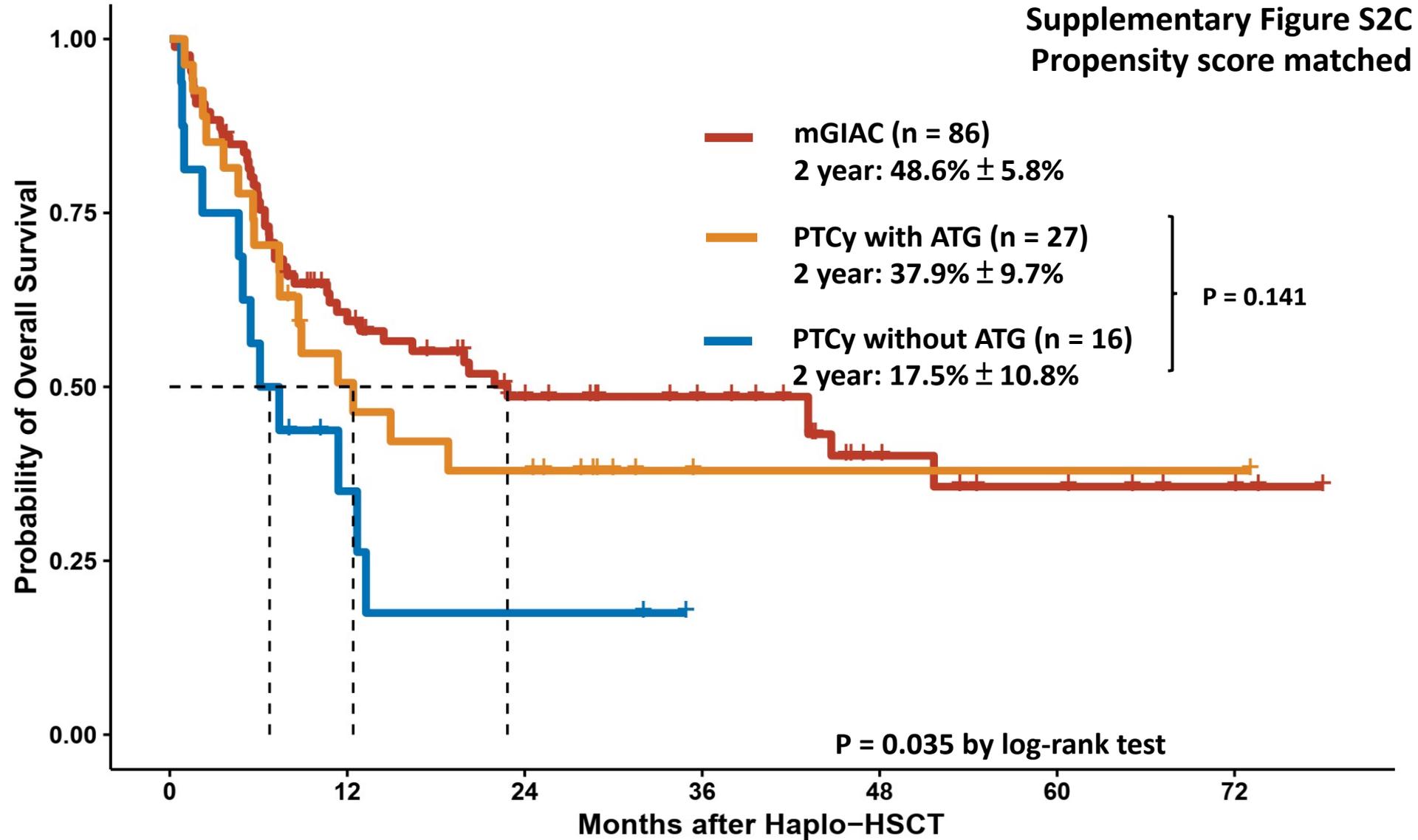
Probability of Non-relapse Mortality



No. at risk:

█	86	45	28	21	10	6	3
█	16	4	2	0 ₈	0	0	0
█	27	12	9	1	1	1	1

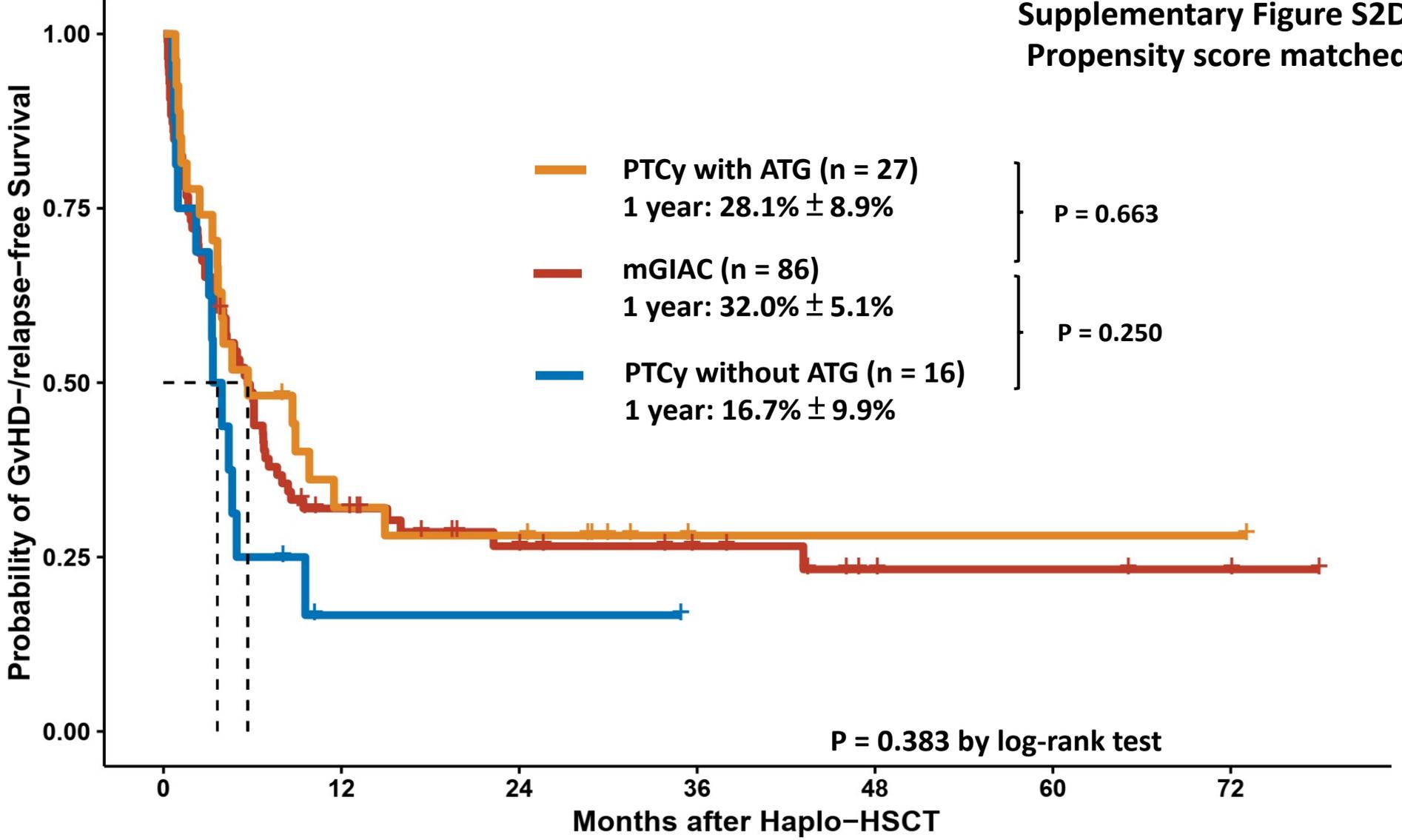
Supplementary Figure S2C
Propensity score matched



No. at risk:

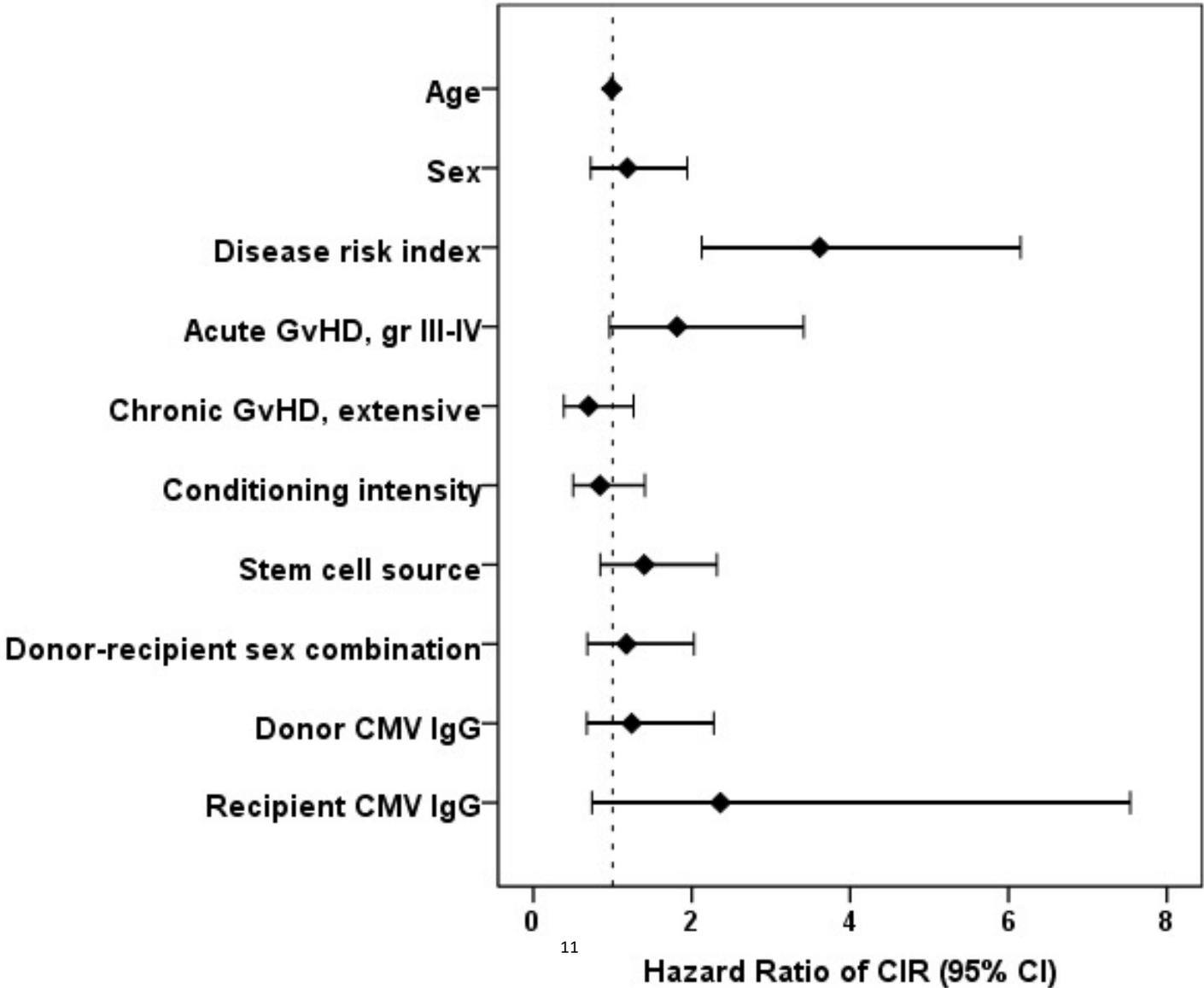
—	86	45	28	21	10	6	3
—	16	4	2	0 ₉	0	0	0
—	27	12	9	1	1	1	1

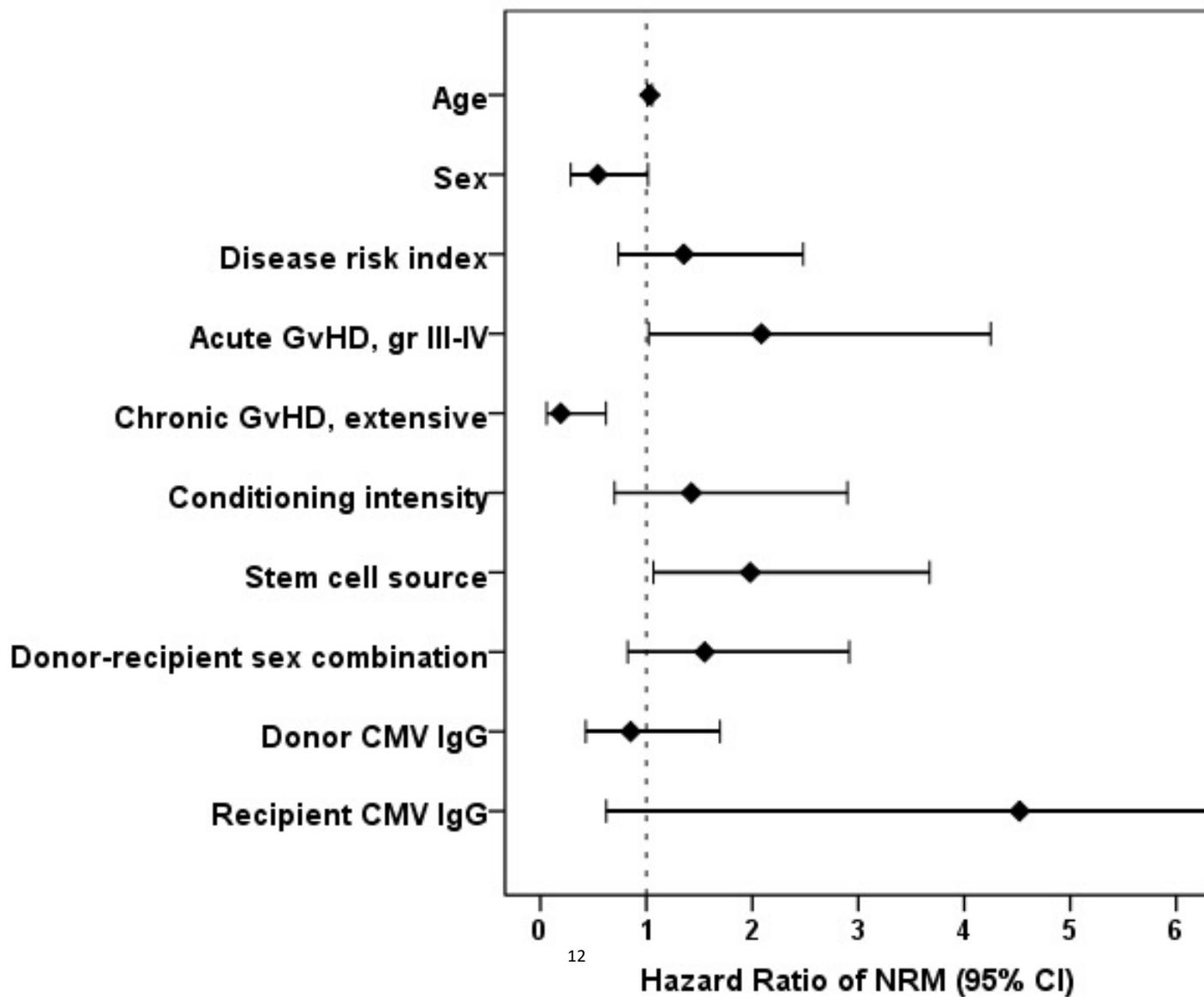
Supplementary Figure S2D
Propensity score matched

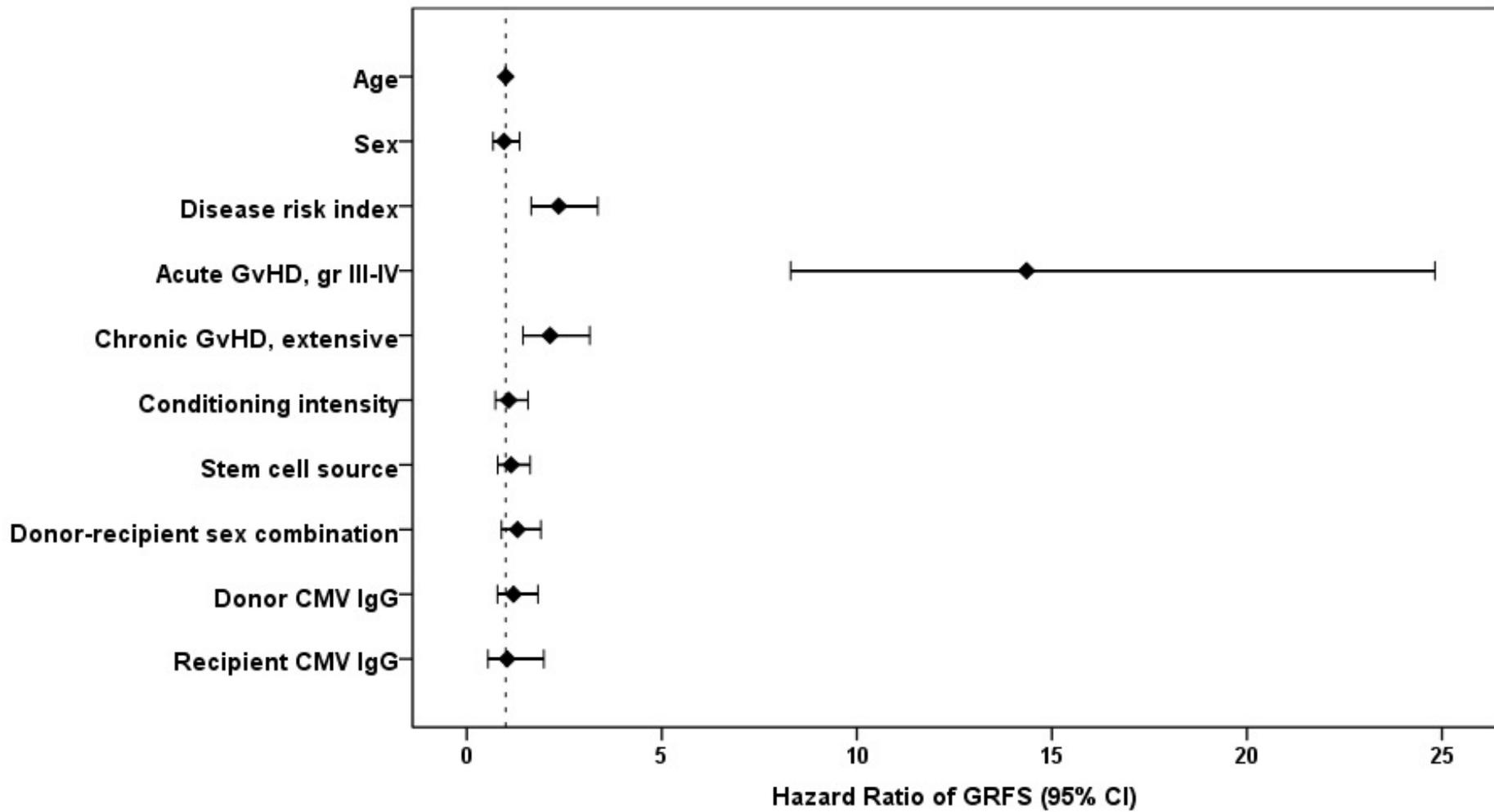


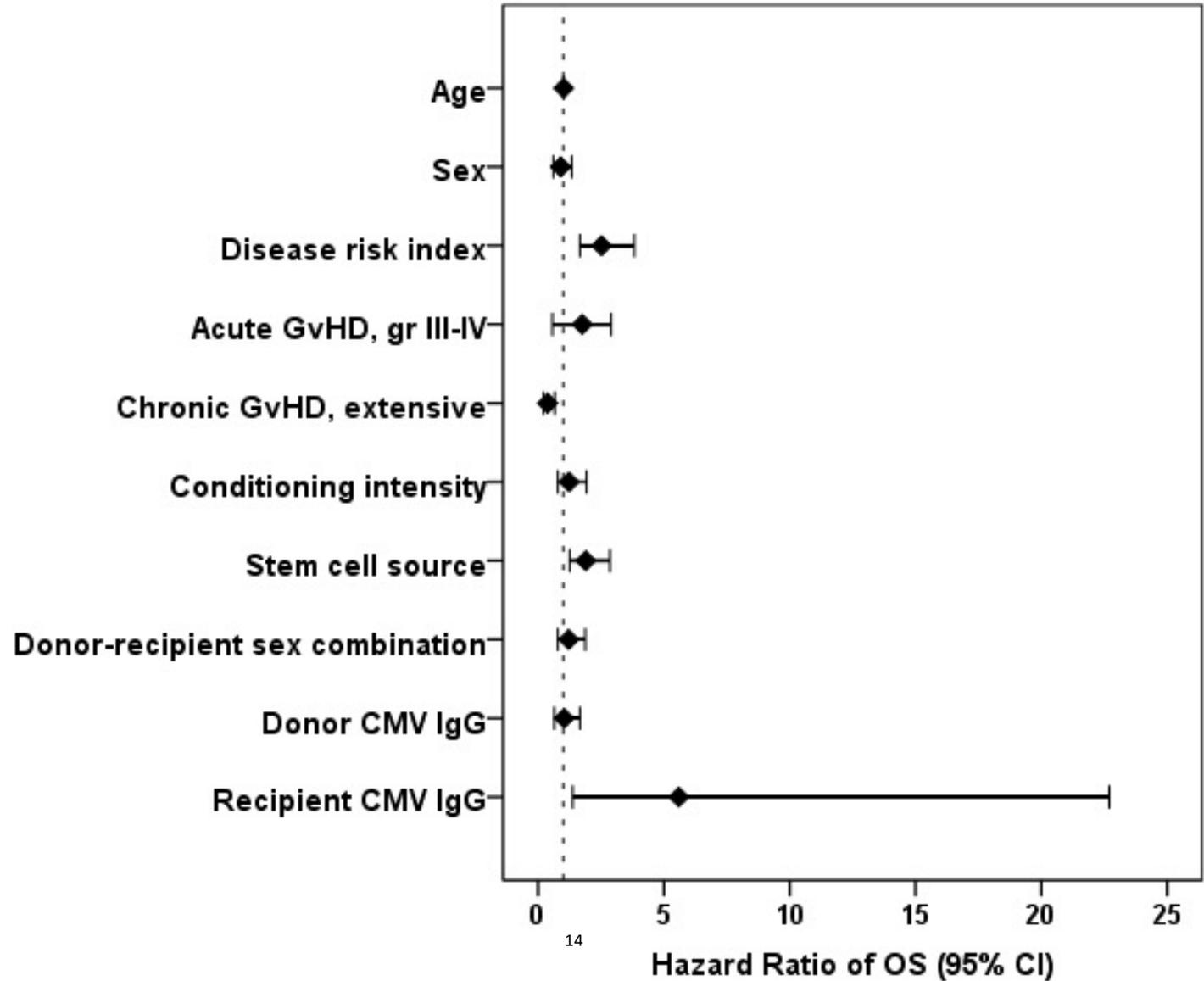
No. at risk:

—	86	22	13	9	4	3	2
—	16	1	1	0 ₁₀	0	0	0
—	27	8	7	1	1	1	1

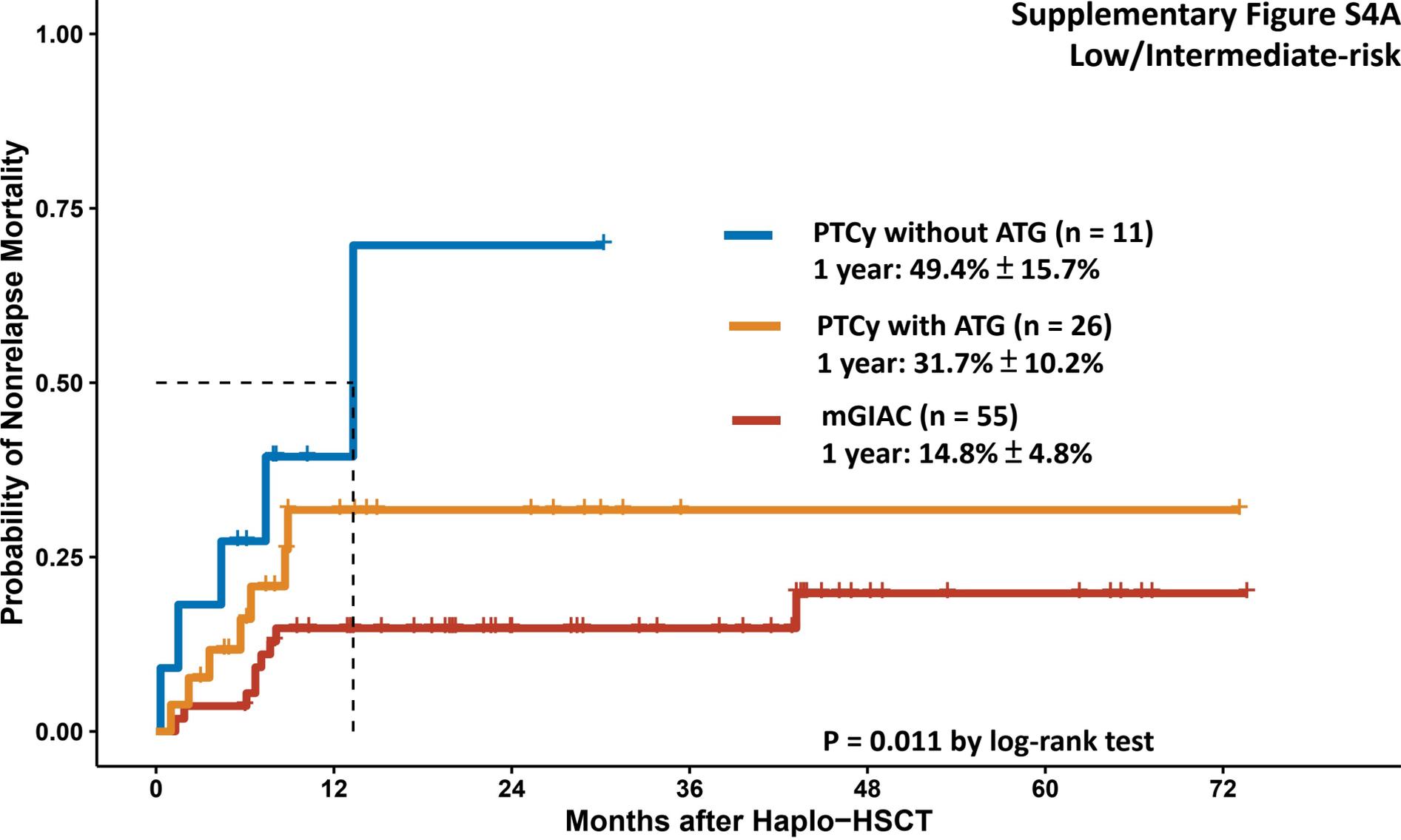








Supplementary Figure S4A
Low/Intermediate-risk

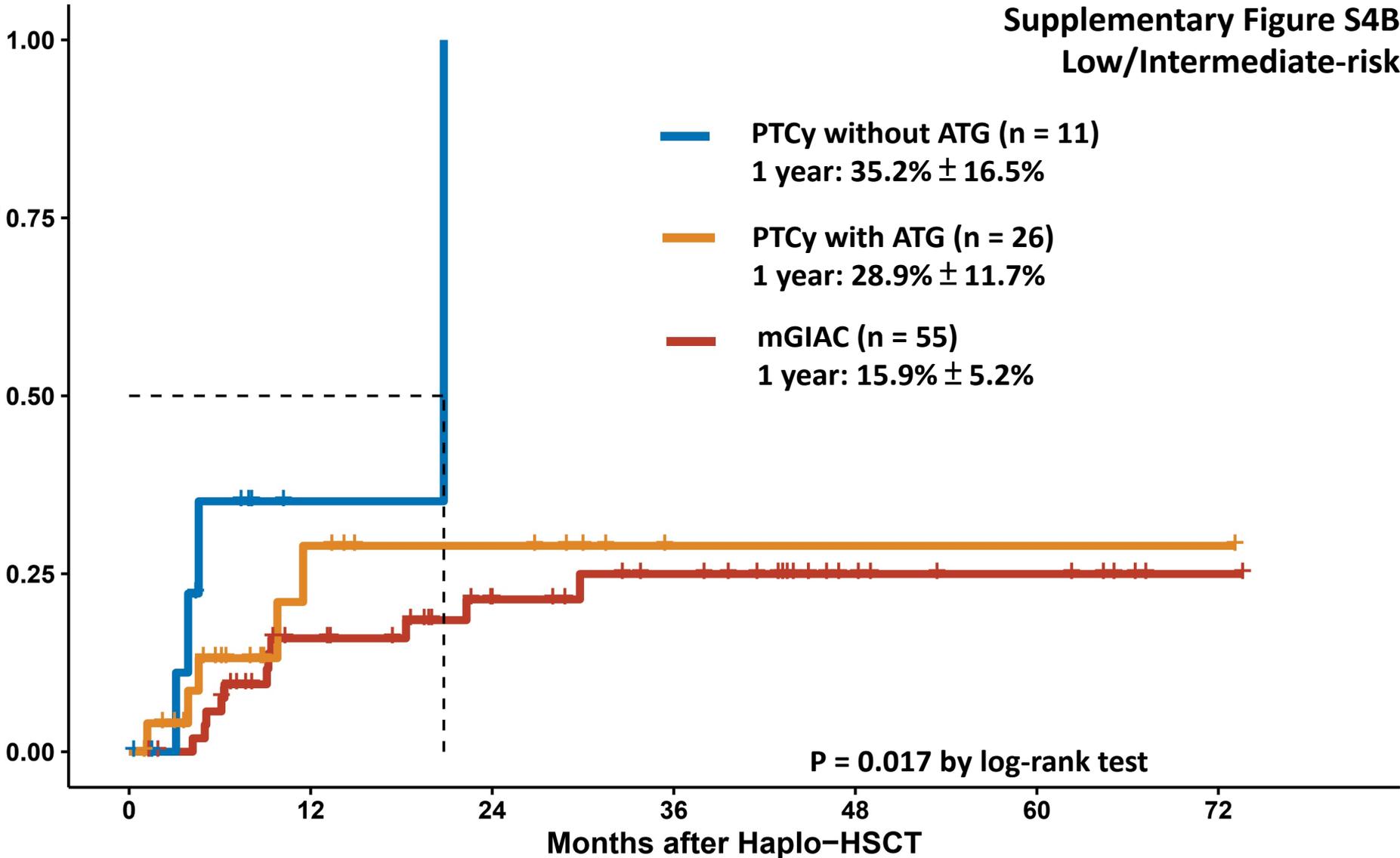


No. at risk:

█	55	42	27	21	9	6	1
█	11	2	1	0 ₁₅	0	0	0
█	26	11	7	1	1	1	1

Supplementary Figure S4B
Low/Intermediate-risk

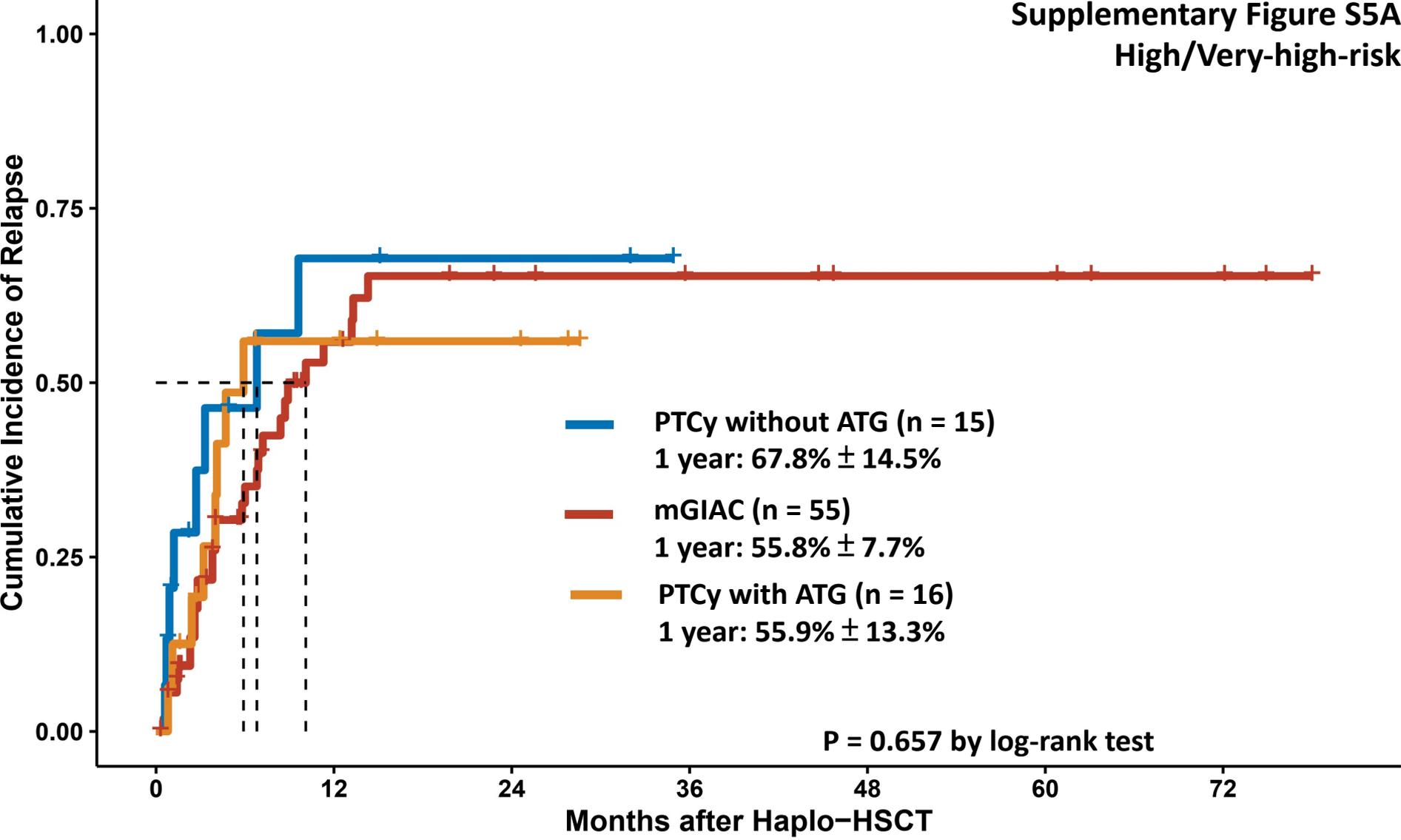
Cumulative Incidence of Relapse



No. at risk:

—	55	36	25	19	9	6	1
—	11	1	0	0 ₁₆	0	0	0
—	26	9	6	1	1	1	1

Supplementary Figure S5A
High/Very-high-risk

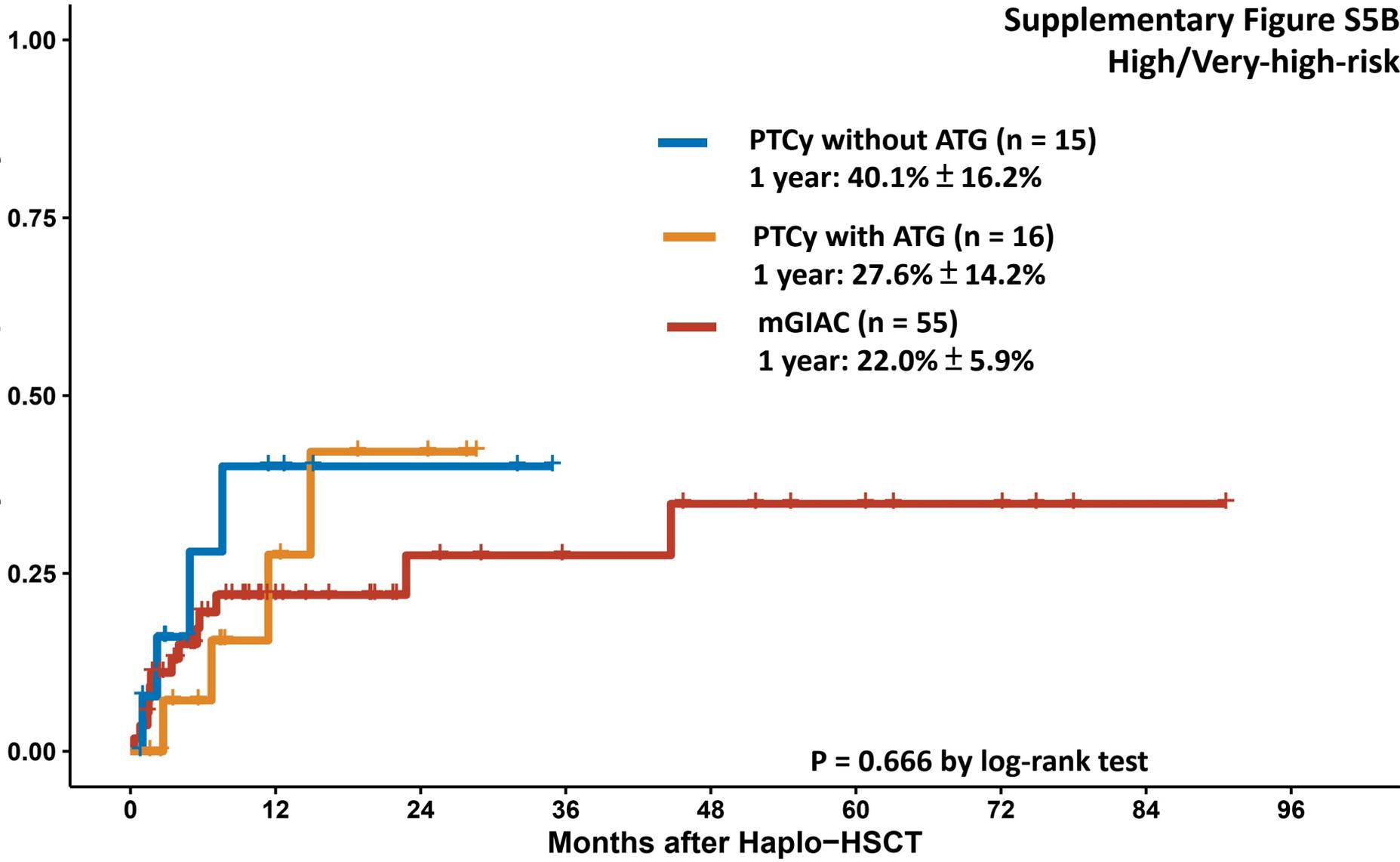


No. at risk:

—	55	15	9	7	5	5	3
—	15	3	2	0 ₁₇	0	0	0
—	16	5	3	0	0	0	0

Supplementary Figure S5B
High/Very-high-risk

Probability of Nonrelapse Mortality



No. at risk:

—	55	24	13	10	8	6	4	1	0
—	15	4	2	0	0	0	0	0	0
—	16	6	3	0	0	0	0	0	0