

Table S1 WHO grading system for bleeding [1].

	Grade 1	Grade 2	Grade 3
Oral and nasal (ON)	<ul style="list-style-type: none"> Oropharyngeal bleeding – total duration of all episodes in previous 24 hours ≤ 30 minutes* Petechiae of oral mucosa Epistaxis – total duration of all episodes in previous 24 hours ≤ 30 minutes* 	<ul style="list-style-type: none"> Oropharyngeal bleeding – total duration of all episodes in previous 24 hours > 30 minutes* Epistaxis – total duration of all episodes in previous 24 hours > 30 minutes* 	<ul style="list-style-type: none"> Any bleeding requiring RBC transfusion over routine transfusion needs**
Skin, soft tissue, musculoskeletal (ST)	<ul style="list-style-type: none"> Petechiae of skin Purpura ≤ 1 inch diameter One or more spontaneous hematomas in the soft tissue or muscle > 1" 	<ul style="list-style-type: none"> Purpura > 1 inch diameter*** Spontaneous hematoma in deeper tissues Joint bleeding (confirmed by aspiration, imaging study or other accepted technique) 	<ul style="list-style-type: none"> Any bleeding requiring RBC transfusion over routine transfusion needs**
Gastrointestinal (GI)	<ul style="list-style-type: none"> Positive stool occult blood test 	<ul style="list-style-type: none"> Melanotic stool Hematochezia – visible red blood mixed in stool, not requiring a transfusion Hematemesis – Grossly visible blood in emesis or in nasogastric drainage tube (not related or secondary to swallowed blood) 	<ul style="list-style-type: none"> Any bleeding requiring RBC transfusion over routine transfusion needs**
Genitourinary (GU)	<ul style="list-style-type: none"> Any biochemical or microscopic Hb/RBCs without red urine Abnormal vaginal bleeding [Unexpected bleeding out of normal cycle OR Bleeding heavier than normal OR Breakthrough bleeding (patient on hormonal therapy to prevent bleeding)] with spotting 	<ul style="list-style-type: none"> Gross/visible hematuria without need for transfusion Abnormal vaginal bleeding [Unexpected bleeding out of normal cycle OR Bleeding heavier than normal OR Breakthrough bleeding (patient on hormonal therapy to prevent bleeding)] more than spotting 	<ul style="list-style-type: none"> Any bleeding requiring RBC transfusion over routine transfusion needs**

Pulmonary (PL)	<ul style="list-style-type: none"> • Hemoptysis – Visible blood • Blood in broncho-pulmonary lavage, or blood tinged sputum (excluding those with nose or oropharyngeal bleeding) 	<ul style="list-style-type: none"> • Any bleeding requiring RBC transfusion over routine transfusion needs**
Body Cavity (BC)	<ul style="list-style-type: none"> • Visible blood in body cavity fluid (e.g. red cells apparent in fluid aspirate) short of criteria for Grade 3 or 4 	<ul style="list-style-type: none"> • Grossly bloody body cavity fluids and organ dysfunction with symptoms, and/or need to intervene (e.g. to aspirate), and/or need for transfusion
Central Nervous System (CNS)	<ul style="list-style-type: none"> • Retinal bleeding without visual impairment • Lumbar puncture with blood (>5 RBC/μL in CSF on microscopic analysis and non-traumatic tap), no symptoms and no visible red color 	<ul style="list-style-type: none"> • Lumbar puncture with visible red color in absence of symptoms, and non-traumatic tap
Invasive Sites (IS)	<ul style="list-style-type: none"> • Bleeding at invasive sites (venipuncture sites, intravenous lines or catheter exit sites): active oozing at site for a cumulative total of > 1 hour in the previous 24 hours 	<ul style="list-style-type: none"> • Any bleeding requiring RBC transfusion over routine transfusion needs**
Hemodynamic Instability (HD)		<ul style="list-style-type: none"> • Any bleeding associated with moderate hemodynamic instability (hypotension; >30mmHg fall or >30% decrease in either systolic or diastolic blood pressure) and requiring RBC transfusion over routine transfusion needs**

GRADE 4:

- Any bleeding associated with severe hemodynamic instability (hypotension; >50mm/Hg fall or >50% decrease in either systolic or diastolic blood pressure, with associated tachycardia (heart rate increase of > 20% for 20 minutes) and requiring RBC transfusion over routine transfusion needs
- Fatal bleeding from any source
- Retinal bleeding with visual impairment (Visual impairment is defined as a field deficit, and patients with suspected visual impairment require an ophthalmologic consult for documentation)
- CNS symptoms with non-traumatic bloody lumbar puncture
- CNS bleeding on imaging study with or without dysfunction

*Count actual bleeding (i.e. "running out" or need for basin, Kleenex, towel, etc.) not minor bleeding.

**Red cell transfusion must be specifically related to treatment of bleeding within 24 hours of onset of bleeding.

***Grade 2A excludes skin bleeding.

Table S2A Multi-predictor logistic regression analyses of predictor variables for ON, ST, GI, GU and PL organ system bleeding.

Predictor	ON OR (95% CI)	P value	ST OR (95% CI)	P value	GI OR (95% CI)	P value	GU OR (95% CI)	P value	PL OR (95% CI)	P value
Stratum		<0.001		0.65		<0.001		<0.001		0.001
ALLO vs AUTO	3.48 (2.03,5.97)	<0.001	1.27 (0.53,3.05)	0.59	1.71 (1.21,2.42)	0.002	2.79 (1.71,4.56)	<0.001	2.26 (1.41,3.62)	<0.001
CHEMO vs AUTO	1.10 (0.58,2.08)	0.77	0.90 (0.32,2.52)	0.84	0.96 (0.62,1.51)	0.87	1.87 (1.08,3.21)	0.02	1.11 (0.62,1.99)	0.71
ALLO vs CHEMO	3.17 (1.96,5.11)	<0.001	1.41 (0.65,3.06)	0.38	1.78 (1.22,2.59)	0.003	1.50 (0.97,2.30)	0.07	2.03 (1.22,3.37)	0.01
Gender		0.26		0.16		0.11		<0.001		0.61
Male	1.28 (0.83,1.96)	0.26	0.58 (0.28,1.23)	0.16	0.79 (0.59,1.06)	0.11	0.28 (0.19,0.40)	<0.001	1.11 (0.75,1.64)	0.61
Female	1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)	

Age	0.99 (0.97,1.00) 0.03	1.01 (0.98,1.05) 0.45	1.00 (0.99,1.01) 0.70	0.97 (0.96,0.99) <0.001	1.00 (0.99,1.02)	0.75
Dose Group	0.22	0.01	0.79	0.92		0.67
Low	1.58 (0.95,2.63)0.08	0.82 (0.35,1.92) 0.64	0.91 (0.63,1.33) 0.63	0.99 (0.63,1.55)0.96	1.12 (0.68,1.86)	0.65
Medium	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	
High	1.16 (0.70,1.91)0.57	0.24 (0.08,0.73) 0.01	1.03 (0.73,1.46) 0.85	1.08 (0.68,1.70)0.75	0.91 (0.57,1.43)	0.67
Hematocrit	0.15	0.56	0.27	0.67		0.88
HMC≤25	1.41 (0.98,2.03)0.07	1.53 (0.61,3.85) 0.37	1.20 (0.94,1.52) 0.13	1.11 (0.88,1.39)0.39	0.93 (0.68,1.27)	0.63
25<HMC≤29	1.22 (0.89,1.66)0.22	1.02 (0.40,2.62) 0.97	1.12 (0.93,1.35) 0.24	1.06 (0.89,1.27)0.51	0.95 (0.72,1.25)	0.7
HMC>29	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	
Morning Platelet Count	<0.001	0.001	0.003	0.01		0.58
1-10x10 ⁹ /L	6.10 (1.90,19.57) 0.002	2.44 (0.62,9.60) 0.2	1.99 (1.33,2.99) <0.001	1.61 (1.03,2.52)0.04	0.90 (0.51,1.62)	0.73
11-20x10 ⁹ /L	9.25 (2.88,29.64) <0.001	1.28 (0.34,4.74) 0.71	1.77 (1.19,2.64) 0.01	1.59 (1.05,2.42)0.03	1.01 (0.57,1.78)	0.98
21-40x10 ⁹ /L	4.63 (1.36,15.80) 0.01	0.13 (0.01,1.20) 0.07	1.44 (0.97,2.13) 0.07	1.70 (1.15,2.52)0.01	1.16 (0.68,1.96)	0.59
41-60x10 ⁹ /L	4.15 (1.21,14.24) 0.02	0.98 (0.19,5.10) 0.99	1.50 (1.01,2.23) 0.04	1.84 (1.23,2.75)0.003	1.05 (0.60,1.83)	0.86
≥61x10 ⁹ /L	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	

Table S2B Multi-predictor logistic regression analyses of predictor variables for BC, CNS, IS, and HD organ system bleeding.

	BC		CNS		IS		HD	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Stratum		<0.001		0.4		0.39		0.93
ALLO vs AUTO	7.71 (0.90,66.16)	0.06	1.65 (0.45,6.02)	0.45	0.86 (0.42,1.75)	0.67	0.93 (0.28,3.02)	0.9
CHEMO vs AUTO	17.00 (2.35,123.14)	0.01	2.17 (0.58,8.11)	0.25	0.59 (0.27,1.28)	0.18	0.80 (0.24,2.71)	0.72
ALLO vs CHEMO	0.45 (0.17,1.24)	0.12	0.76 (0.30,1.96)	0.57	1.45 (0.78,2.69)	0.24	1.16 (0.42,3.21)	0.78
Gender		0.17		0.44		0.51		0.42
Male	1.90 (0.75,4.80)	0.17	1.41 (0.59,3.37)	0.44	0.81 (0.42,1.53)	0.51	0.65 (0.23,1.85)	0.42
Female	1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)	
Age	0.98 (0.96,1.00)	0.07	0.99 (0.96,1.02)	0.38	1.02 (1.00,1.05)	0.10	1.06 (1.02,1.10)	0.01
Dose Group		0.49		0.67		0.51		0.47
Low	0.47 (0.15,1.48)	0.20	1.65 (0.53,5.15)	0.39	1.18 (0.60,2.34)	0.63	0.91 (0.28,2.97)	0.88
Medium	1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)	
High	0.45 (0.14,1.41)	0.17	1.23 (0.41,3.64)	0.71	0.76 (0.37,1.57)	0.46	0.46 (0.11,1.92)	0.28
Hematocrit		0.46		0.21		0.02		0.01
HMC≤25	0.50 (0.16,1.55)	0.23	2.33 (0.98,5.56)	0.06	1.34 (0.82,2.19)	0.24	6.05 (1.68,21.79)	0.01
25<HMC≤29	0.49 (0.19,1.25)	0.14	1.12 (0.46,2.75)	0.8	0.77 (0.46,1.29)	0.32	1.22 (0.26,5.66)	0.8
HMC>29	1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)	
Morning Platelet Count		0.97		0.08		0.37		0.34
1-10x10 ⁹ /L	0.68 (0.16,2.82)	0.59	0.19 (0.05,0.69)	0.01	0.67 (0.36,1.26)	0.22	2.65 (0.33,21.42)	0.36
11-20x10 ⁹ /L	0.60 (0.14,2.49)	0.48	0.46 (0.17,1.25)	0.13	0.68 (0.38,1.22)	0.20	1.48 (0.16,13.44)	0.73
21-40x10 ⁹ /L	0.82 (0.27,2.46)	0.72	0.29 (0.08,1.08)	0.06	0.92 (0.51,1.66)	0.79	0.88 (0.08,9.23)	0.92
41-60x10 ⁹ /L	0.74 (0.17,3.12)	0.68	0.74 (0.21,2.55)	0.63	0.58 (0.30,1.12)	0.11	1.73 (0.14,20.85)	0.67
≥61x10 ⁹ /L	1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)		1.00 (Ref.)	

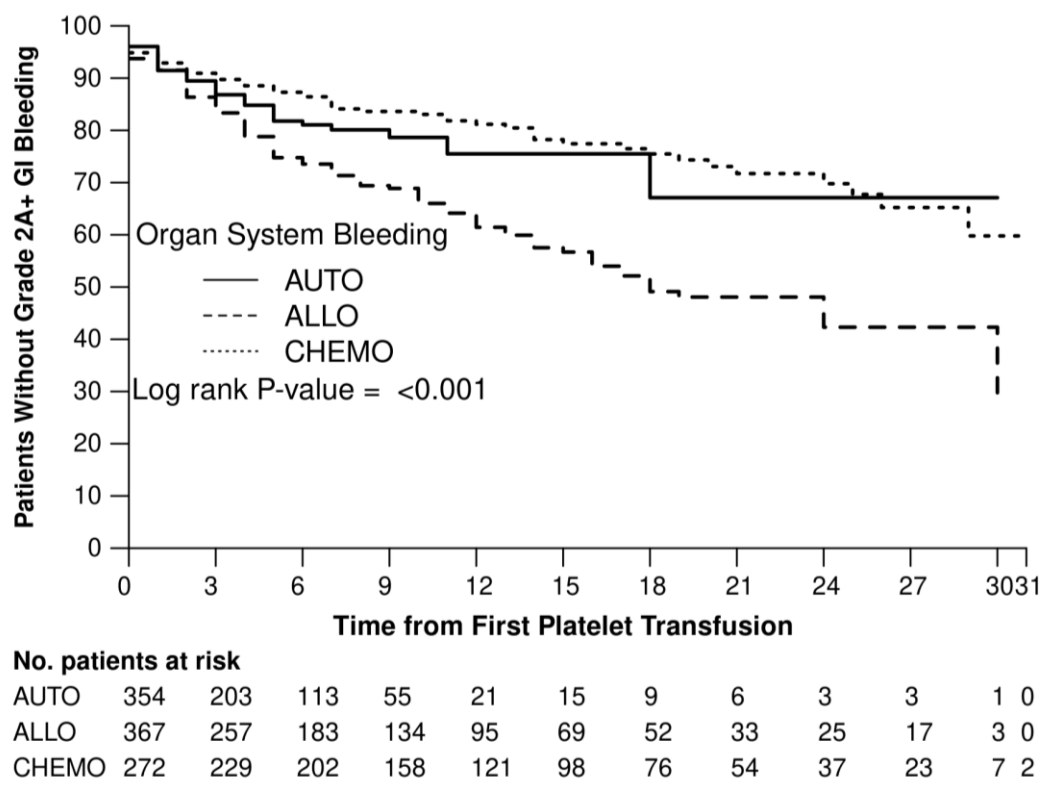


Figure S1A Time from first platelet transfusion to G2A+ GI bleeding.

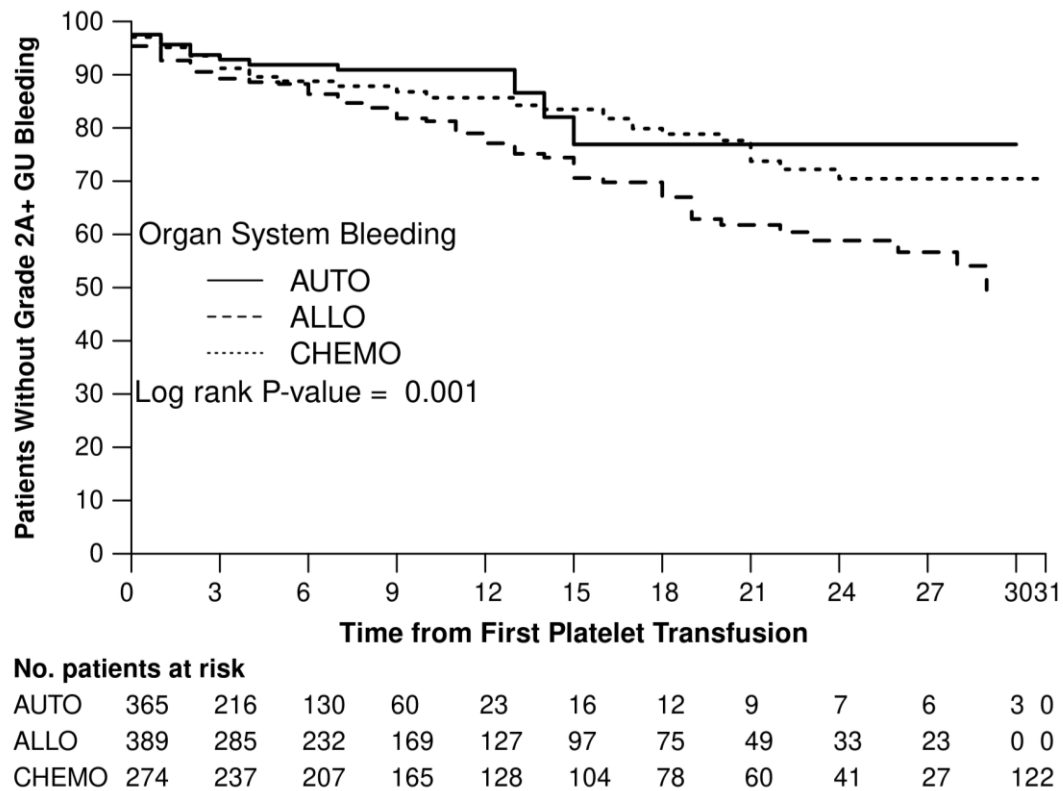


Figure S1B Time from first platelet transfusion to G2A+ GU bleeding.

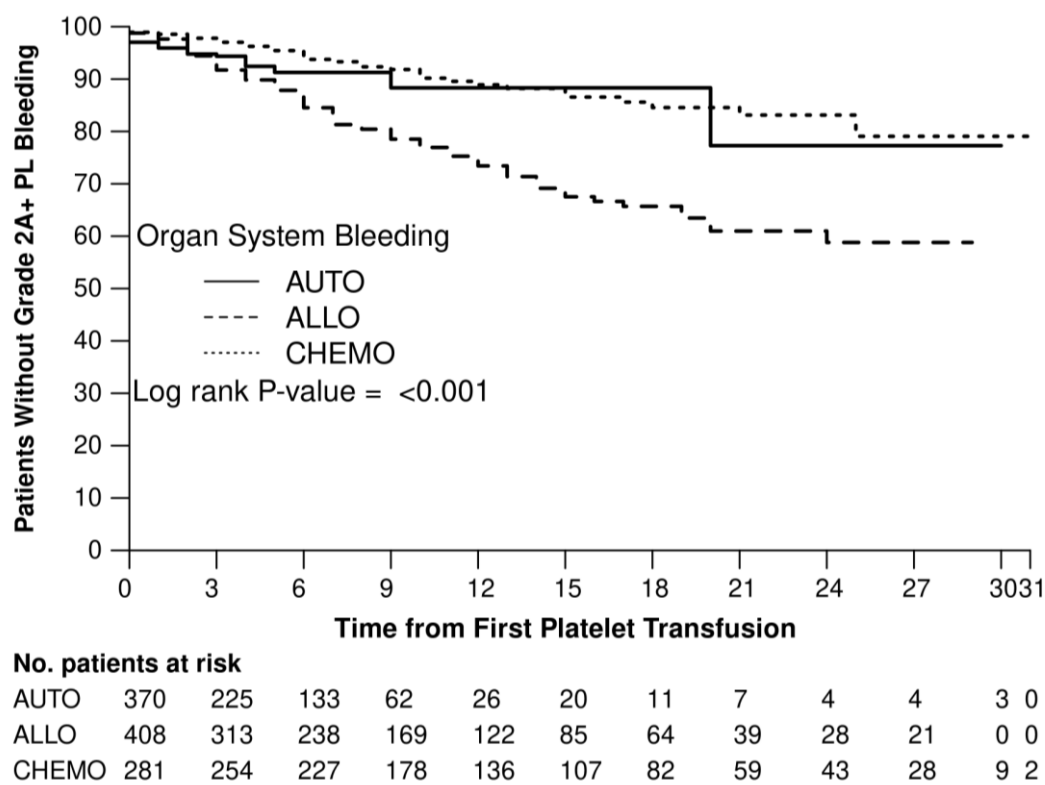


Figure S1C Time from first platelet transfusion to G2A+ PL bleeding.

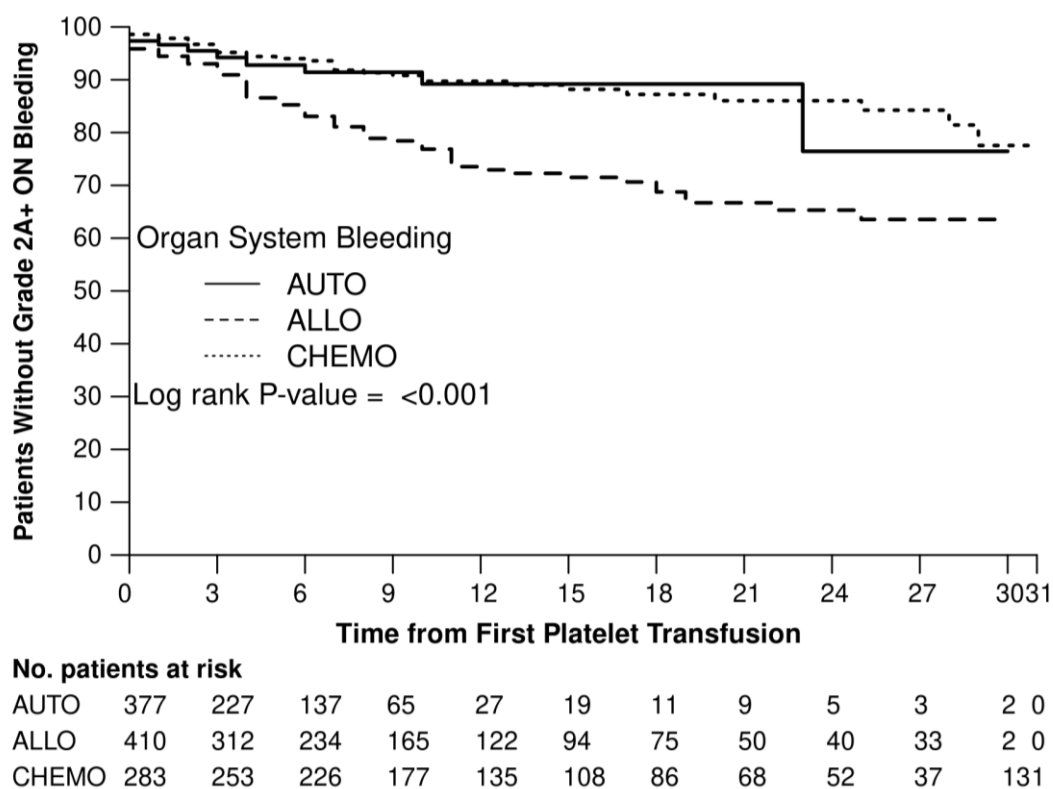


Figure S1D Time from first platelet transfusion to G2A+ ON bleeding.

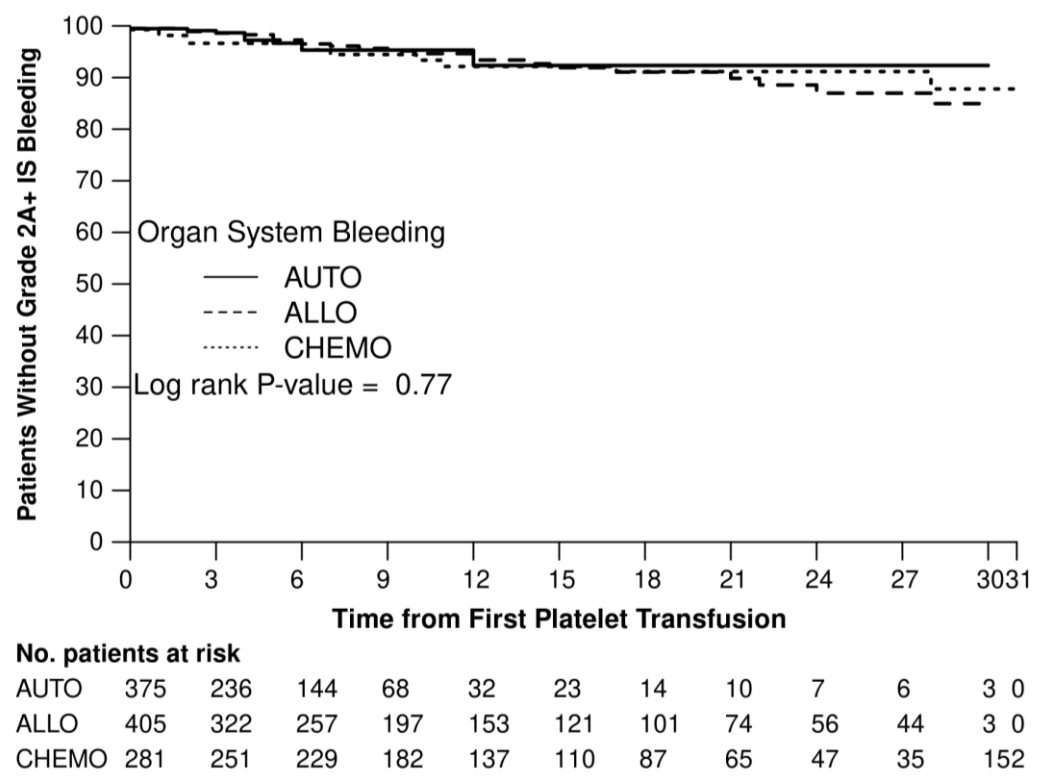


Figure S1E Time from first platelet transfusion to G2A+ IS bleeding.

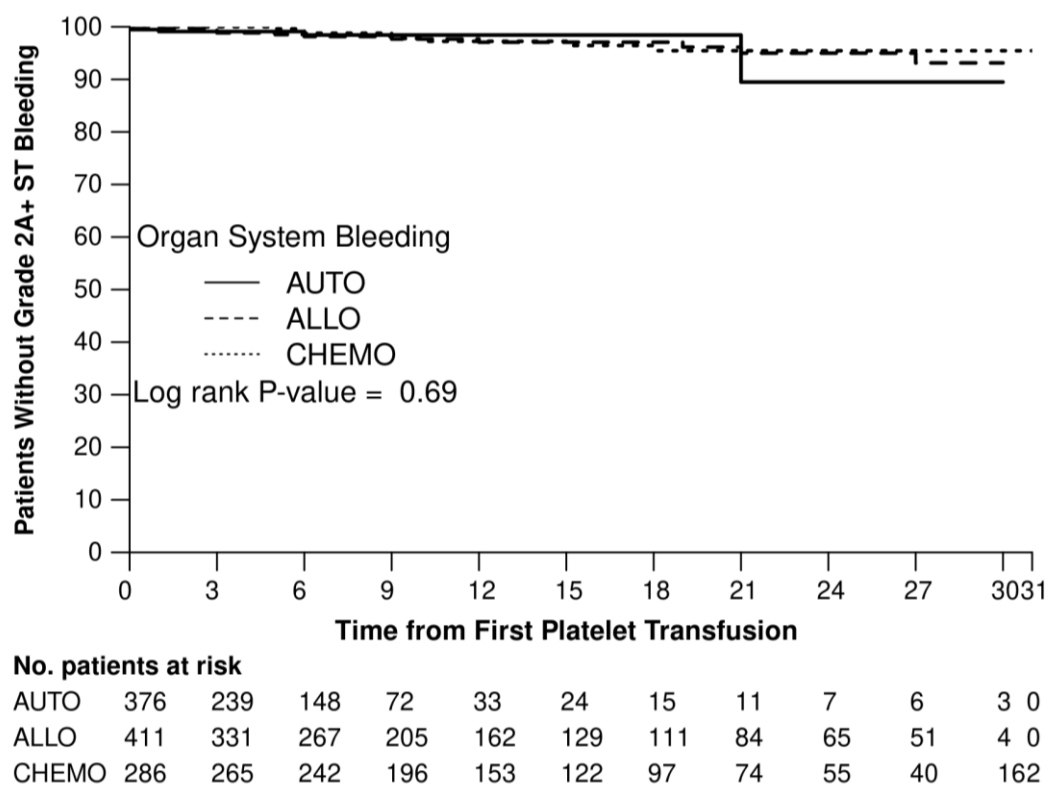


Figure S1F Time from first platelet transfusion to G2A+ ST bleeding.

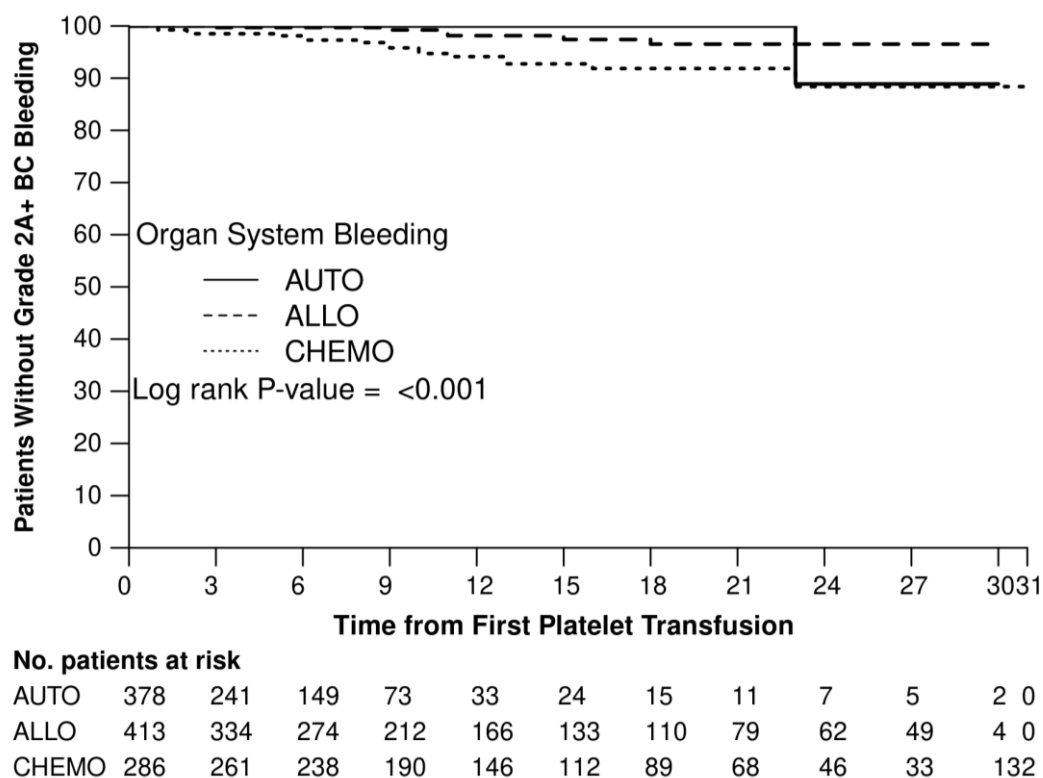


Figure S1G Time from first platelet transfusion to G2A+ BC bleeding.

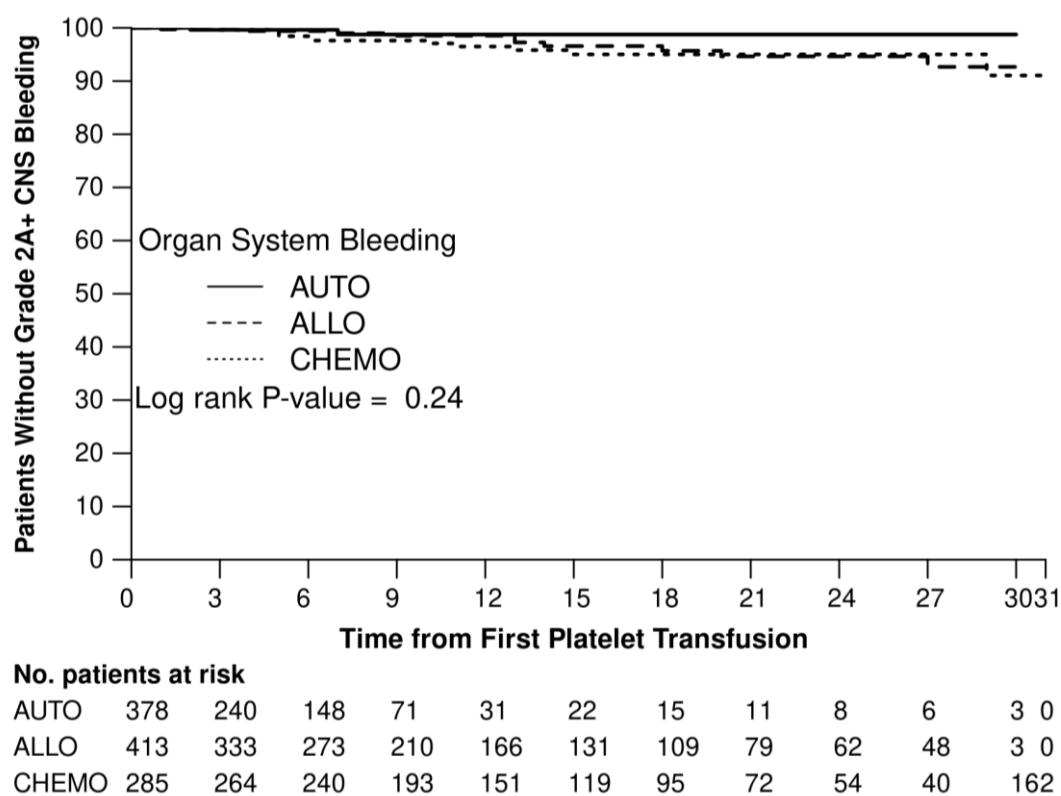


Figure S1H Time from first platelet transfusion to G2A+ CNS bleeding.

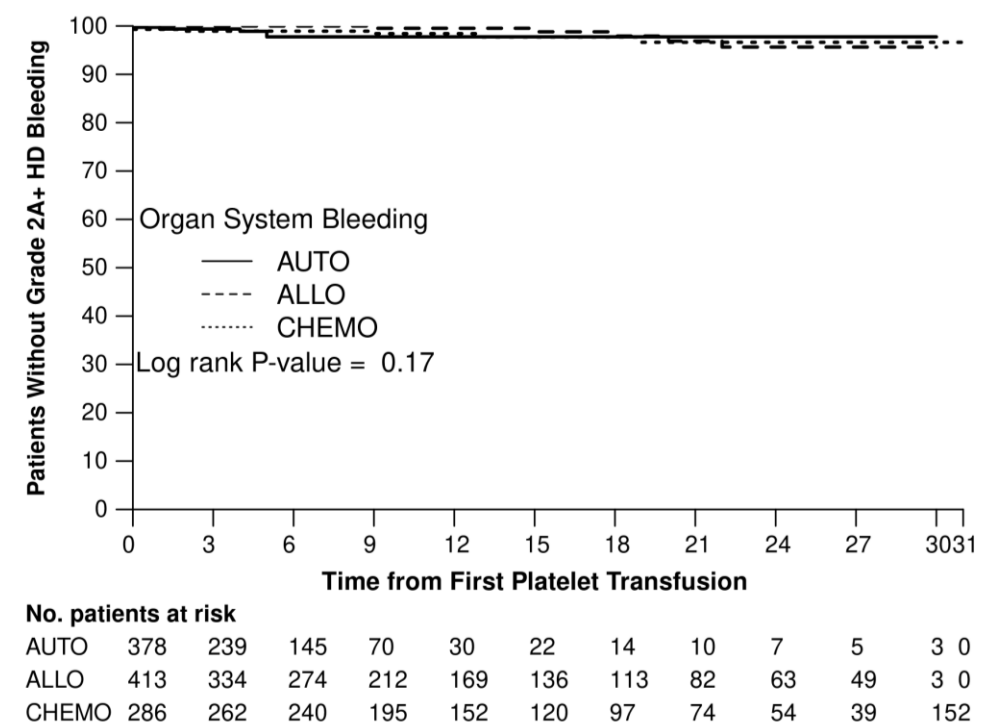


Figure S1I Time from first platelet transfusion to G2A+ HD bleeding.

References

1. Miller AB, Hoogstraten B, Staquet M, Winkler A. Reporting results of cancer treatment. *Cancer*. 1981; 47: 207-214.