Immunosuppressive therapy for pediatric aplastic anemia: a North American Pediatric Aplastic Anemia Consortium study

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Supplemental Table 1: Baseline factors and response. Reference groups for the analysis are as follows: IST treatment, age at second treatment >=10 years, male gender, lymphocyte count at diagnosis >=1000 /uL.

Baseline	Comparison	All subjects					
		OR		DR		CR	
		N(%)	p-value	N(%)	p-value	N(%)	p-value
PNH clone	Absent vs.Present	61 (72%) v. 41 (75%)	0.85	59 (69%) v. 40 (73%)	0.71	58 (68%) v. 34 (62%)	0.47
MCV, fL	<100 vs. >= 100	153 (71%) v.46 (74%)	0.64	149 (69%) v.42 (68%)	0.88	135 (62%) v.36 (58%)	0.56
Telomere length Flow FISH							
Total Lymphocytes <1st%	No vs Yes	58 (67%) v. 6 (100%)	0.17	58 (67%) v. 5 (83%)	0.66	52 (60%) v. 4 (67%)	0.99
Total Lymphocytes <10th%	No vs Yes	48 (70%) v. 16 (70%)	0.99	48 (70%) v. 15 (65%)	0.8	43 (62%) v. 13 (57%)	0.63
Granulocytes <10th %	No vs Yes	27 (64%) v. 37 (74%)	0.37	27 (64%) v. 36 (72%)	0.5	24 (57%) v. 32 (64%)	0.53
Lymph and Gran <10th%	No vs. Yes	51 (68%) v. 13 (76%)	0.57	51 (68%) v. 12 (71%)	0.99	46 (61%) v. 10 (59%)	0.99

* Median time from diagnosis to treatment by a) OR (yes vs. no) is 24 vs. 23 days (p=0.29), b) DR (yes vs. no) is 24 vs. 24 days (p=0.88) and c) CR (yes vs. no) is 23 vs. 26 days (p=0.76).

Baseline	Comparison	hATG/CYA					
		OR		DR		CR	
		N(%)	p-value	N(%)	p-value	N(%)	p-value
PNH clone	Absent vs.Present	45 (74%) v. 35 (73%)	0.99	43 (70%) v. 34 (71%)	0.99	42 (69%) v. 29 (60%)	0.42
MCV, fL	<100 vs. >= 100	130 (70%) v.36 (75%)	0.59	125 (68%) v.33 (69%)	0.99	114 (62%) v.26 (54%)	0.41
Telomere length Flow FISH							
Total Lymphocytes <1st%	No vs Yes	54 (68%) v. 6 (100%)	0.17	54 (68%) v. 5 (83%)	0.66	48 (60%) v. 4 (67%)	0.99
Total Lymphocytes <10th%	No vs Yes	45 (69%) v. 15 (71%)	0.99	45 (69%) v. 14 (67%)	0.99	40 (62%) v. 12 (57%)	0.8
Granulocytes <10th %	No vs Yes	24 (65%) v. 36 (73%)	0.48	24 (65%) v. 35 (71%)	0.64	21 (57%) v. 31 (63%)	0.66
Lymph and Gran <10th%	No vs. Yes	48 (69%) v. 12 (75%)	0.77	48 (69%) v. 11 (69%)	0.99	43 (61%) v. 9 (56%)	0.78

* Median time from diagnosis to treatment by a) OR (yes vs. no) is 23 vs. 23 days (p=0.78), b) DR (yes vs. no) is 23 vs. 23 days (p=0.43) and c) CR (yes vs. no) is 22 vs. 24 days (p=0.32).

Supplemental Table 2: Causes of death

Study ID	Initial treatment	Survival time (months)	Subsequent IST	Subsequent BMT	Cause of Death
ID-02-12	hATG/CYA	21.3	Yes	No	CMV viremia, disseminated fungal disease
ID-02-14	hATG/CYA	6.7	Yes	No	Necrotizing pneumonia, CMV
ID-02-20	hATG/CYA	55.4	Yes X2	Yes	Auto accident
ID-03-05	hATG/CYA	10.9	No	Yes	Diffuse alveolar damage (DAD)
ID-03-06	hATG/CYA	11.1	No	Yes	Diffuse alveolar damage
ID-03-28	hATG/CYA	35.5	No	No	Septic shock due to fungemia
ID-04-03	hATG/CYA	1.6	No	No	Disseminated fungus
ID-05-04	hATG/CYA	25.7	Yes	Yes	Septic shock
ID-05-15	hATG/CYA	51.8	Yes	No	Aseptic shock contributed by cardiomyopathy related to iron overload, AML
ID-05-20	hATG/CYA	14.4	No	Yes	Multi-organ failure
ID-05-31	hATG/CYA	75.3	Yes	Yes	AML, Multi-organ failure
ID-07-03	hATG/CYA	108.3	Yes X3	No	Respiratory failure
ID-07-08	hATG/Tacro	123	Yes	Yes	Multi-organ failure
ID-07-14	hATG/Tacro	29.5	Yes	Yes	Respiratory failure secondary to adenoviral infection
ID-08-05-KJ	hATG/CYA	17.7	No	Yes	Respiratory failure
ID-09-17	hATG/CYA	73.6	No	Yes	Severe GVHD
ID-11-07	CTX	9	No	Yes	ARDS, renal failure
ID-11-08	CTX	25.9	No	Yes	Pneumonia
ID-11-09	CTX	1.9	No	No	Gram negative sepsis with Cupriavadis gilardii
ID-13-09	rATG/CYA	NE	No	No	Pancytopenia, refractory aplastic anemia
ID-13-11	rATG/CYA	5.7	No	No	
ID-13-13	rATG/CYA/Tacro	105.6	No	No	
ID-13-14	hATG/CYA	0.3	No	No	
ID-15-02	hATG/CYA	5.9	No	No	Disseminated rhizopus mucormycosis pneumonia
ID-15-11	hATG/CYA	69.2	Yes	No	Unspecified cause
ID-20-02	hATG/CYA	3.5	No	No	Respiratory failure
ID-20-15	rATG/Tacro	15.8	No	Yes	Respiratory failure
ID-20-17	hATG/CYA	9.7	No	Yes	Respiratory failure
ID-24-03	hATG/CYA	32.4	Yes	No	Infection and aplasia following induction therapy for B lineage ALL
ID-24-12	hATG/CYA	108.3	No	Yes	AML and failure to engraft with second transplant

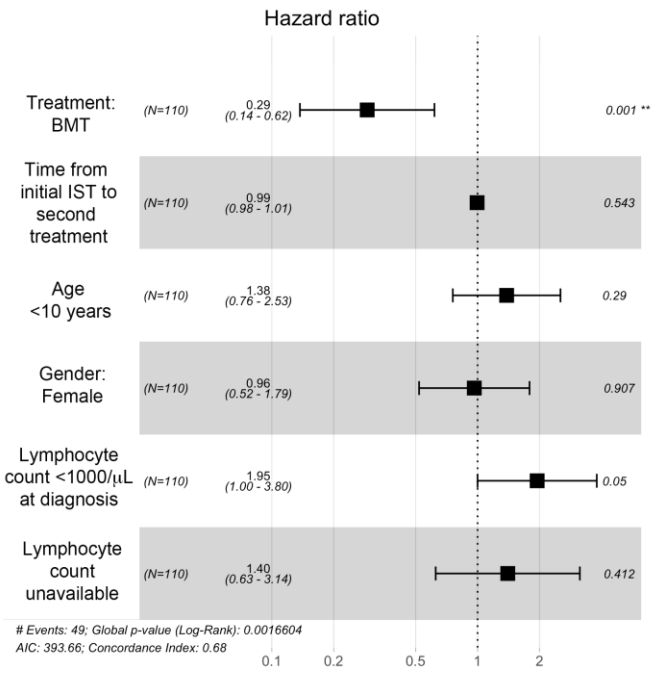
Supplemental Table 3: Outcomes of second IST and initial response to initial hATG/CYA

	Required additional 3rd line treatment post-second IST, n=33	
	Response at 3m after first IST	Response at 6 m post first IST
CR	1	1
VGPR		3
PR	1	3
NR	27	10
Additional Rx	3	15
NE	1	1
Total	33	33

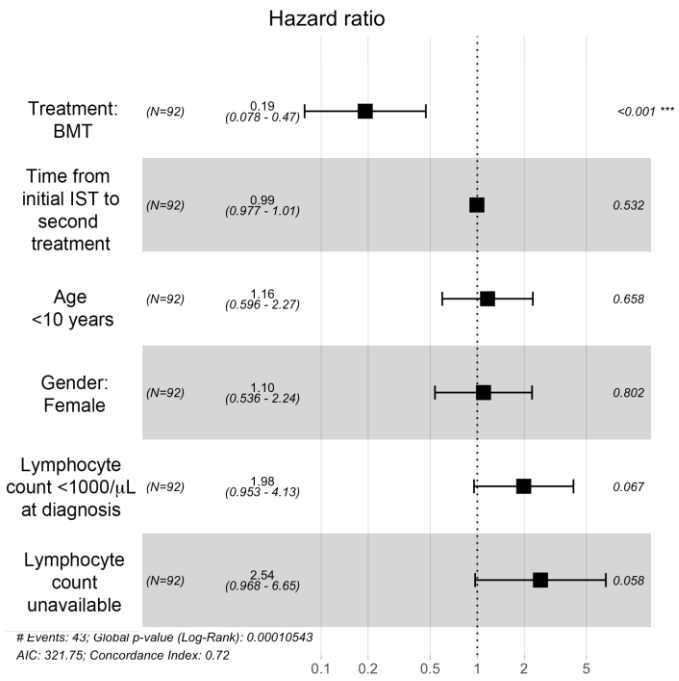
	No additional treatment post-second IST, n=19	
	Response at 3m after first IST	Response at 6 m post first IST
CR		
VGPR	1	1
PR		2
NR	17	10
Additional Rx	1	6
NE		
Total	19	19

Supplemental Figure 1: Cox proportional hazards model of EFS after second treatment

A. All subjects

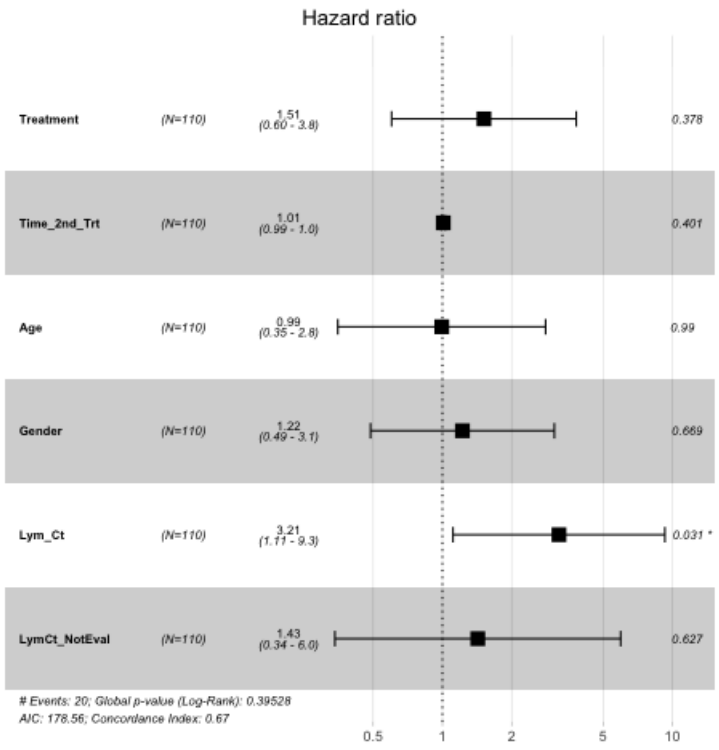


B. hATG/CYA treatment group



Supplemental Figure 2: Cox proportional hazards model of OS after second treatment

A. All subjects



B. hATG/CYA treatment group