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ORAL ABSTRACTS

612.ACUTE LYMPHOBLASTIC LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Risk-Adjusted Therapies Yield Equivalent Outcomes for Adolescents and Young Adults (AYAs) Treated for Newly Diagnosed T-Cell Acute Lymphoblastic Leukemia (T-ALL) on Children's Oncology Group (COG) Studies AALL0434 and AALL1231

Susan I. Colace, MDMSc[1], Meenakshi Devidas, PhD MBA[2], Zhiguo (Bruce) Chen, MS[3], Robert J. Hayashi[4], Brent L. Wood, MD PhD[5], Natia Esiashvili[6], Samir Patel[7], Andrew J Carroll, PhD[8], Nyla A. Heerema, PhD[9], Barbara Asselin, MD[10], Karen R. Rabin, MDPhD[11], Patrick A. Zweidler-McKay, MDPhD[12], Elizabeth A. Raetz, MD[13], Mignon L. Loh, MD[14,15], Naomi J. Winick, MD[16], William L. Carroll, MD[17], David T. Teachey, MD[18], Stuart S. Winter, MD[19], Kimberly P. Dunsmore, MD[20]

[1] Division of Pediatric Hematology/Oncology/BMT, Nationwide Children's Hospital, Galena, OH
[2] St Jude Children's Research Hospital, Memphis, TN
[3] Biostatistics, University of Florida, Gainesville, FL
[4] Division of Pediatric Hematology/Oncology, Washington University School of Medicine, Saint Louis, MO
[5] Department of Pathology and Laboratory Medicine, Children's Hospital Los Angeles, Los Angeles, CA
[6] Department of Radiation Oncology and Winship Cancer Institute, Emory University, Atlanta, GA
[7] Division of Radiation Oncology, University of Alberta, Edmonton, Canada
[8] Department of Genetics, University of Alabama at Birmingham, Birmingham, AL
[9] Ohio State University, Columbus, OH
[10] Golisano Children's Hospital and Wilmot Cancer Institute at the University of Rochester Medical Center, Rochester, NY
[11] Department of Pediatrics, Baylor College of Medicine, Baylor College of Medicine TX Children's Cancer Center, Houston, TX
[12] ImmunoGen, Inc., Waltham, MA
[13] Department of Pediatrics, NYU Langone Health, New York, NY
[14] Ben Towne Center for Childhood Cancer Research, Seattle Children's Hospital, Seattle, WA
[15] Department of Pediatrics, Seattle Children's Hospital, University of Washington, Seattle, WA
[16] Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas, TX
[17] Perlmutter Cancer Center, Department of Pediatrics and Pathology, NYU Grossman School of Medicine, New York, NY
[18] Division of Oncology, Children's Hospital of Philadelphia, Philadelphia, PA
[19] Cancer and Blood Disorders, Children's Minnesota, Minneapolis, MN
[20] University of Virginia Health Sciences Center, Charlottesville, VA

Introduction

Previous clinical trials have reported that adolescent and young adult (AYA) patients treated for T-cell acute lymphoblastic leukemia (T-ALL) have lower disease-free survival (DFS) and overall survival (OS) and increased toxicity as compared to younger patients. Results for the AYA cohort treated on two COG international phase 3 trials for T-ALL are reported here.

Patients and Methods

AALL0434 enrolled 1562 T-ALL patients (2007-2014) and AALL1231 enrolled 615 T-ALL patients (2014-2019) treated on augmented BFM (ABFM) regimens. AYA patients were defined as age ≥16 years of age (AALL0434: n=226; AALL1231: n = 107). Both studies allowed enrollment up to age 31 years.

On AALL0434, participants were randomized to receive escalating dose methotrexate (CMTX) without leucovorin rescue + pegaspargase or high dose MTX (HDMTX) + leucovorin rescue. Intermediate and high-risk patients were randomized to receive or not receive six 5-day courses of nelarabine (Nel). Risk group assignments in AYA vs non-AYA patients can be found in Table 1. On AALL1231, participants were randomized to receive or not receive bortezomib in Induction and Delayed Intensification. Key differences between AALL0434 and AALL1231 ABFM backbones included the use of prednisone in induction in AALL0434 versus dexamethasone in AALL1231, and cranial radiation therapy in the majority of AALL0434 participants versus only in patients with central nervous system involvement in AALL1231.

Results

On AALL0434, the 4-year DFS for AYA was 81% compared to 84% for those <16 years old (P=0.5965), and OS was 88% and 90% respectively (P=0.3478). AYA patients randomized to CMTX (n=70) had a superior DFS compared to those randomized to HDMTX (n=72) with 4-year DFS 96% versus 78% respectively (P=0.0038). No disadvantage was seen among AYA subjects who received nelarabine versus those who did not, as shown by a 4-year DFS 85% versus 89%, respectively (N=54) (P=0.8116), albeit the sample size was small. On AALL1231, the 4-year EFS for AYA (n=107) was 82.7±3.9% compared to 82.2 ±1.7% for non-AYA (n=508) (P=0.727), and OS was 86.5 ±3.5% and 88.4 ±1.5% respectively (P=0.553). No difference in outcome was seen for AYA patients randomized to receive/not receive bortezomib.

Combined outcome data for AALL0434 and AAL1231 demonstrates 4-year EFS for AYA (n=333) of 82.2+2.4% vs 83.9+0.9% for non-AYA (n=1844) (P=0.52) (Figure 1) and OS of 87.5+2.1% vs 90+0.8% respectively (P=0.19).

Significant differences in patient characteristics in AALL0434 were higher initial white blood counts (P=0.0004) and higher risk group category (P=0.0002) for AYA patients. There were no significant differences in the AALL0434 AYA cohort compared to younger patients in CNS disease status, race, ethnicity, remission status at end of induction, or day 29 end of induction minimal residual disease (MRD).

Toxicity rates were not significantly different in non-AYA vs AYA patients with the exception of upper respiratory infection (9.4% vs 1.8%; P=0.0001) and osteonecrosis (4.8% vs 17.7%; P<0.0001) in AALL0434. Rates of sepsis, catheter-related infection, and other infections were not significantly different between AYA and younger patients in AALL0434.

Analysis of patient characteristics and toxicity rates in AALL1231, as well as analysis of the combined toxicity data for AALL0434 and AAL1231, are currently underway and will be presented at the meeting.

Conclusion

COG AALL0434 and AALL1231 show outstanding overall outcomes for AYA patients with no significant difference in survival between AYA and non-AYA patients on either study, despite differences in the ABFM backbones and the higher risk features seen among the AYA group in AALL0434. There were similar occurrences of therapy-related toxicities for AYA and non-AYA study participants on AALL0434. Despite small numbers, CMTX holds a survival advantage for AYA T-ALL patients, with no survival disadvantage seen among AYA T-ALL patients who received Nel. Bortezomib does not offer significant benefit for AYA T-ALL patients.

Disclosures Wood: *Amgen:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Institutional Laboratory Services Agreement; *Kite:* Other: Institutional Laboratory Services Agreement; *Novartis:* Other: Institutional Laboratory Services Agreement; *Beckman-Coulter:* Honoraria; *Becton-Dickinson:* Honoraria; *Beam:* Other: Institutional Laboratory Services Agreement; *Wugen:* Other: Institutional Laboratory Services Agreement; *Macrogenics:* Other: Institutional Laboratory Services Agreement; *Biosight:* Other: Institutional Laboratory Services Agreement. **Zweidler-McKay:** *Immunogen Inc.:* Current Employment. **Raetz:** *Pfizer:* Research Funding; *Bristol Myer Squibb:* Other: DSMC. **Teachey:** *Neoimmune Tech:* Research Funding; *BEAM:* Research Funding; *Sobi:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Jazz:* Membership on an entity's Board of Directors or advisory committees, Research Funding.

Table 1. Patient characteristics in AALL0434 for non-AYA vs AYA T-ALL patients

Patient Characteristics		<16 Years N=1336, n (%)	>=16 Years N=226, n (%)	P-value
Gender	Male	987 (73.9)	174 (77.0)	0.322
	Female	349 (26.1)	52 (23.0)	
WBC (x 1000 per µL)	< 50	542 (40.6)	120 (53.1)	
	≥ 50	794 (59.4)	106 (46.9)	0.0004
CNS	CNS1	967 (72.9)	161 (71.9)	
	CNS2	259 (19.5)	47 (21.0)	0.872
	CNS3	100 (7.6)	16 (7.1)	
Race	White	945 (79.0)	157 (75.8)	
	Black or African American	169 (14.1)	30 (14.5)	0.341
	Other	82 (6.9)	20 (9.7)	
Ethnicity	Hispanic or Latino	188 (14.1)	34 (15.0)	0.619
	Not Hispanic or Latino	1101 (82.4)	180 (79.7)	
AlloHSCT	Yes	62 (5.2)	13 (6.4)	
	No	1136 (94.8)	191 (93.6)	0.482
BM Induction day29	M1	1221 (94.1)	197 (91.2)	
	M2	41 (3.2)	11 (5.1)	0.242
	M3	35 (2.7)	8 (3.7)	
MRD Induction day29	MRD < 0.01%	764 (59.0)	116 (53.7)	
	0.01% <= MRD < 0.1%	83 (6.4)	12 (5.6)	
	0.1% <= MRD < 1.0%	161 (12.4)	28 (13.0)	0.173
	1.0% <= MRD < 10.0%	191 (14.8)	34 (15.7)	
	MRD >= 10%	95 (7.3)	26 (12.0)	
Risk Group	Low Risk	109 (10.6)	0 (0)	
	Intermediate Risk	690 (67.3)	118 (71.9)	
	High Risk	191 (18.7)	38 (23.2)	0.0002
	Induction Failure	35 (3.4)	8 (4.9)	

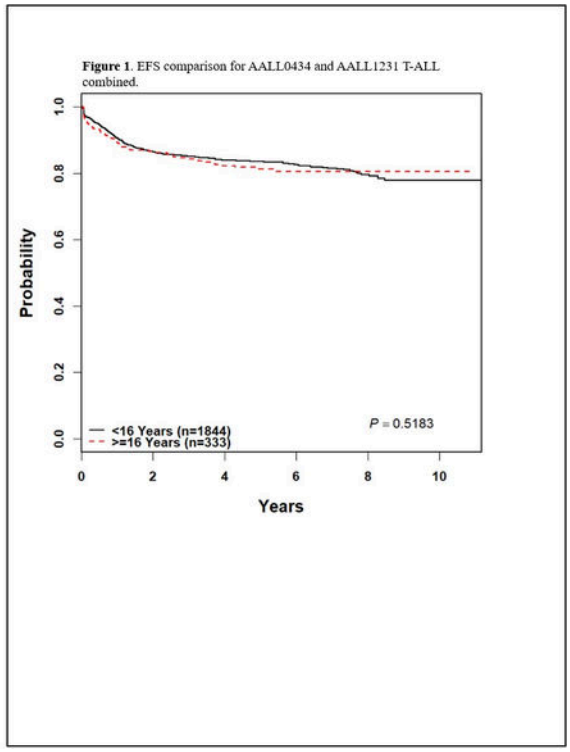

Figure 1

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