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POSTER ABSTRACTS

612.ACUTE LYMPHOBLASTIC LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Treatment Outcomes for Adults with Mixed Phenotypic Acute Leukemia: A Large Single-Center Retrospective Study

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Introduction:
Mixed phenotype acute leukemia (MPAL) is a rare subtype of acute leukemia characterized by differentiation along more than one lineage. In the absence of eosinophilia and/or stereotypical tyrosine kinase gene fusions, there is no established optimal therapy for adults with MPAL. Typical treatments include acute myeloid leukemia (AML)-type, acute lymphoblastic leukemia (ALL)-type or hybrid-type therapy approaches. We conducted a retrospective comparison of different induction chemotherapy strategies at our institution to help clarify the optimal initial chemotherapy for patients with MPAL.

Methods:
Patients evaluated at the University of Washington/Fred Hutchinson Cancer Center diagnosed with MPAL from 1/2005 to 9/2022 were identified through our IRB-approved institutional repository. MPAL diagnosis was confirmed by independent pathology review (AE and XC). Lineage assignment used the 2022 World Health Organization criteria based on initial diagnostic immunophenotype or genetic features. Treatment was classified as either AML-type (anthracycline + cytarabine with or without purine analogs, e.g. 7+3, CLAG-M or FLAG-IDA), ALL-type (anthracycline + cyclophosphamide + steroid + vincristine, e.g. hyperCVAD, or CALGB 10403) or hybrid-type regimens (most often CLAG-M + vincristine + dexamethasone). Log-rank survival and Cox proportional hazards were used to compare survival.

Results:
We identified a total of 49 patients with MPAL who received induction chemotherapy at our institution. These included 14 patients (28.6%) treated with ALL-type therapies, 9 patients (18.4%) treated with AML-type therapies and 26 patients (53.1%) treated with hybrid-type therapies. The proportions of B/myeloid, T/myeloid and rare B/T phenotypes were similar among the 3 treatment groups, though patients treated with ALL-type regimens were significantly younger (Table 1). The overall proportion of patients who achieved complete remission (CR) was high (67%) with a non-statistically significant trend for non-AML-type treatments (ALL-type = 10/14, 71.4%; AML-type = 5/9, 55.6%; hybrid-type = 21/26, 80.8%; p = 0.22).
Overall, patients had similar survival regardless of induction therapy type with 43.8% of patients treated with ALL-type therapy, 50.0% of patients treated with AML-type therapy, and 39.0% of patients treated with hybrid-type therapy alive 48 months post-induction treatment (p=0.68) (Figure 1). Compared to patients treated with ALL-type therapy, the Cox proportional hazard for death among patients treated with AML-type therapy was 1.5 (95% CI 0.4 - 5.3, p = 0.5) and for those who received hybrid-type therapy was 1.5 (95% CI 0.6 - 39, p = 0.4). Among 36 patients who achieved complete response after induction chemotherapy, there was a trend toward longer survival among patients who were found to be measurable residual disease (MRD) negative by flow cytometry compared to MRD+ with 63.1% in the MRD- group alive at 48 months compared to 33.3% in the MRD+ group (p = 0.07). Compared to the MRD- group, the MRD+ Cox proportion hazard ratio for survival was 2.6 (95% CI 0.9 - 7.9, p = 0.07).
The proportion of patients subsequently transplanted was similar in each treatment group (28 patients total; Table 1). Patients who received HSCT lived longer. In a landmark analysis of patients who survived a minimum of 100 days following initiation of induction therapy, 57.8% of HSCT recipients were still alive at 48 months compared to 20.2% of patients who did not undergo HSCT (p = 0.001). Compared to patients who did not receive a HSCT, the Cox proportion hazard ratio for survival for those receiving HSCT was 0.25 (95% CI 0.1 - 0.61, p < 0.003).

Conclusion:

Although our data showed a non-statistically significant trend toward a higher CR rate with ALL-type regimens for patients with MPAL regardless of immunophenotype, it failed to show a survival benefit at 48 months based on choice of ALL-, AML- or hybrid-type induction regimens. Despite being one of the largest cohorts reported of patients with MPAL, this study was limited by sample size and its retrospective nature. Clinical trials are needed to better determine optimal induction regimens. A survival benefit was seen for patients receiving HSCT consolidation; therefore, HSCT should be encouraged for all eligible patients with MPAL.

Disclosures Appelbaum: *2seventy bio:* Research Funding. **Halpern:** *Abbie, Notable Labs, Agios:* Consultancy; *Imago Bioscience, Bayer, Gilead, Jazz, Incyte, Karyopharm Therapeutics, Disc Medicine:* Research Funding. **Cassaday:** *Jazz:* Consultancy, Honoraria; *Vanda Pharmaceuticals:* Research Funding; *Servier:* Research Funding; *Pfizer:* Consultancy, Honoraria, Research Funding; *Merck:* Research Funding; *Incyte:* Research Funding; *Kite/Gilead:* Consultancy, Honoraria, Research Funding; *Amgen:* Consultancy, Honoraria, Research Funding; *Autolus:* Membership on an entity's Board of Directors or advisory committees; *PeproMene Bio:* Membership on an entity's Board of Directors or advisory committees; *Seagen:* Other: Spouse was employed by and owned stock in Seagen within the last 24 months.. **Walter:** *ImmunoGen, Jura:* Consultancy, Research Funding; *Amgen, Aptevo, Celgene, Janssen, Jazz, MacroGenics, Pfizer:* Research Funding; *Abbvie, Adicet, Amphivena, BerGenBio, Bristol Myers Squibb, GlaxoSmithKline, Orum:* Consultancy. **Percival:** *Pfizer:* Research Funding; *Glycomimetics:* Research Funding; *Telios:* Research Funding; *BMS:* Research Funding; *Biosight:* Research Funding; *Astex:* Research Funding; *Ascentage:* Research Funding; *Abbvie:* Research Funding.

Table 1: Patient baseline characteristics.

	ALL-Type Therapy (N=14)	AML-Type Therapy (N=9)	Hybrid-Type Therapy (N=26)	p-value
Age				
Mean (SD)	43.9 (15.5)	62.7 (14.1)	50.5 (17.1)	0.0257
Median [Min, Max]	38.5 [24.0, 66.0]	68.0 [38.0, 76.0]	48.0 [18.0, 77.0]	
Sex				
Female	6 (42.9%)	2 (22.2%)	9 (34.6%)	0.598
Male	8 (57.1%)	7 (77.8%)	17 (65.4%)	
Race				
American Indian or Alaska Native	1 (7.1%)	0 (0%)	1 (3.8%)	0.507
Asian	1 (7.1%)	0 (0%)	4 (15.4%)	
Black or African American	1 (7.1%)	1 (11.1%)	1 (3.8%)	
Native Hawaiian or Other Pacific Islander	1 (7.1%)	0 (0%)	1 (3.8%)	
Unavailable or Unknown	1 (7.1%)	2 (22.2%)	0 (0%)	
White	9 (64.3%)	6 (66.7%)	19 (73.1%)	
ECOG Performance Status				
0	1 (7.1%)	0 (0%)	1 (3.8%)	0.776
1	10 (71.4%)	7 (77.8%)	19 (73.1%)	
2	1 (7.1%)	2 (22.2%)	4 (15.4%)	
3	2 (14.3%)	0 (0%)	1 (3.8%)	
Unknown	0 (0%)	0 (0%)	1 (3.8%)	
Phenotype				
B/myeloid	10 (71.4%)	3 (33.3%)	12 (46.2%)	0.122
B/T/myeloid	1 (7.1%)	0 (0%)	0 (0%)	
T/myeloid	3 (21.4%)	6 (66.7%)	14 (53.8%)	
WBC Count				
Mean (SD)	67.5 (90.8)	17.2 (19.7)	31.8 (78.8)	0.251
Median [Min, Max]	23.9 [0.600, 295]	14.8 [1.24, 63.7]	4.72 [0.730, 397]	
HSCT				
No	6 (42.9%)	6 (66.7%)	9 (34.6%)	0.246
Yes	8 (57.1%)	3 (33.3%)	17 (65.4%)	

AML – acute myeloid leukemia. ALL – acute lymphoblastic leukemia. ECOG – Eastern Cooperative Oncology Group. WBC – white blood cell. HSCT – hemopoietic stem cell transplant.

Figure 1: Survival by treatment type.

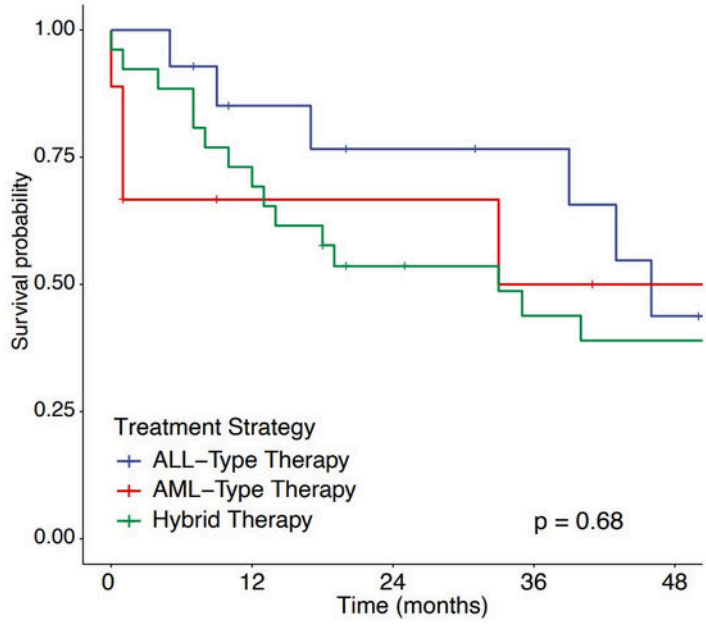

Figure 1

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