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POSTER ABSTRACTS

614.ACUTE LYMPHOBLASTIC LEUKEMIAS: THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Delaying Pegaspargase Administration during Induction in Adults with Acute Lymphoblastic Leukemia

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Background
Pegaspargase (PEG-asparaginase) is a key drug in pediatric-inspired regimens that is utilized frequently in young adults with acute lymphoblastic leukemia (ALL). Pegaspargase has unique toxicities including hypersensitivity, hepatotoxicity, pancreatitis, thrombosis and hypertriglyceridemia. Hepatotoxicity occurs frequently during the induction cycle in newly diagnosed (ND) adults with ALL, and although it is usually reversible, its prolonged persistence may cause interruptions in the treatment. We analyzed two approaches for pegaspargase administration in ND adults with ALL; early administration on day 4 and delayed administration on day 15 that were utilized in our treatment protocols.We hypothesized that later administration of pegaspargase is associated with lower risk of toxicity while maintaining similar response rate.

Methods
This is a retrospective analysis of adult patients (age:19-71) with ND ALL that received pegaspargase during their first induction chemotherapy cycle. Patients were stratified into two groups, the early (day 4) and delayed (day 15) pegaspargase group. The primary objective was to assess differences in toxicities, including hepatotoxicity, hypertriglyceridemia, thrombosis, and pancreatitis. Adverse events were graded using NCI Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Key secondary outcomes included differences in minimal residual disease (MRD), complete remission (CR) rates, and induction related mortality. Statistical analysis was done with descriptive statistics, Mann Whitney U test, Pearson chi-squared test, and multivariate analysis (p-value < 0.05).

Results
Of 117 patients analyzed, there were 72 (62%) patients who received early pegaspargase (EP) while 45 (38%) patients received delayed pegaspargase (DP). The median age of patients was younger in the EP cohort (31.5 vs. 38, p=0.03) and there was no significant difference in gender (p=0.36), BMI (p=0.42), or median pegaspargase dose (p=0.12). CALGB10403 was the most common chemotherapy regimen in the EP cohort and in 20% of DP cohort, while modified BFM was the most common chemotherapy regimen in DP cohort (80%).
Grade 3/4 transaminitis occurred more frequently in EP compared to DP cohort (15% vs 2%; p=0.02), however, other grade 3/4 toxicities were not statistically different: hyperbilirubinemia (21% vs 11%; p=0.17), hypertriglyceridemia (3% vs 9%; p=0.14), and pancreatitis (4% vs 2%; p=0.57), respectively. The CR rate (88% vs 80%; p= 0.18) and end of induction MRD negative rate (60% vs 61%; p=0.86) were similar for EP and DP cohorts, respectively. There was no significant difference in the rates of documented infections during induction (10% vs 9%; p=0.88) and 90-day mortality (2% vs 0%; p=0.42) between EP and DP cohorts, respectively. Post-pegaspargase dose modifications to induction chemotherapy were only observed in the EP cohort (18% vs 0%; p=0.002), with modifications including reduction (5%), delays (6%), and discontinuation (5%) of other chemotherapy agents. In multivariable logistic regression analysis, only older age (OR 1.05; p=0.025) and EP administration (OR 4.58; p=0.007) predicted increased risk of grade 3/4 hepatotoxicity (transaminitis and/or hyperbilirubinemia).

Conclusions
Delaying pegaspargase administration from day 4 to day 15 during induction cycle in adults with ALL was associated with lower rate of high-grade hepatotoxicity and subsequent treatment dose modifications. Delaying pegaspargase had no negative impact on CR or MRD-negativity rates at the end of induction.

Disclosures Stein: *Sanofi:* Current Employment, Current holder of *stock options* in a privately-held company. **Koller:** *NOVARTIS:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *takeda:* Consultancy, Speakers Bureau; *treadwell therapuetics:* Consultancy, Other: safety review committee. **Pullarkat:** *Pfizer:* Consultancy, Speakers Bureau; *Jazz Pharmaceuticals:* Consultancy, Speakers Bureau; *Novartis:* Consultancy, Speakers Bureau; *Servier:* Consultancy, Speakers Bureau; *Amgen:* Consultancy, Speakers Bureau; *Genentech:* Consultancy, Speakers Bureau; *AbbVie:* Consultancy, Speakers Bureau. **Aldoss:** *KiTE:* Consultancy; *Amgen:* Consultancy, Honoraria; *Takeda:* Consultancy; *Pfizer:* Consultancy; *Jazz:* Consultancy; *Sobi:* Consultancy.

Table 1. Baseline Characteristics and Induction Outcomes and Safety Analysis of Early vs Delayed Pegaspargase Administration in Newly Diagnosed ALL

	Early pegaspargase (n=72)	Delayed pegaspargase (n=45)	p-value
Gender, n (%)			
• Male	42 (58)	25 (55)	0.36
Median age, yrs (range)	31.5 (19-71)	38 (21-60)	0.03
Ethnicity, n (%)			
• Hispanic	46 (64)	27 (60)	0.67
• Caucasian	17 (24)	13 (29)	0.52
• Asian	8 (11)	1 (2)	0.07
• African American	0 (0)	3 (7)	0.02
• Other	1 (1)	1 (2)	0.73
Elevated total bilirubin or AST/ALT at baseline	21 (29)	22 (48)	0.03
Primary Diagnosis			
• Ph-like B-ALL	18 (25)	12 (27)	0.84
• Ph negative B-ALL	34 (47)	25 (56)	0.38
• Ph positive B-ALL	1 (1)	0 (0)	0.42
• T-cell ALL	17 (24)	6 (13)	0.17
• Mixed Phenotype Acute Leukemia	2 (3)	2 (4)	0.62
Baseline WBC, median (Range)	4.95 (0.3-280)	6.8 (0.3-268)	0.07
BMI, median (range)	26.7 (16.9-44.6)	28 (17-50.8)	0.42
Median pegaspargase dose IU	3750	3580	0.12
Backbone Regimen, n(%)			
• CALGB10403	72 (100)	9 (20)	<0.001
• Modified BFM	0 (0)	36 (80)	<0.001
Response to treatment, n (%)			
• CR	64/72 (88)	36/45 (80)	0.28
○ MRD positive	26/64 (40)	14/36 (39)	
○ MRD negative	38/64 (60)	22/36 (61)	0.86
Incidence of non-hematologic Grade 3 or 4 adverse event, n (%)			
• Transaminitis	11 (15)	1 (2)	0.02
• Hyperbilirubinemia	15 (21)	5 (11)	0.17
• Hypersensitivity	1 (2)	0 (0)	0.43
• Pancreatitis	3 (4)	1 (2)	0.57
• Hypertriglyceridemia	2 (3)	4 (9)	0.15
• Thromboembolic events	4 (6)	4 (9)	0.48
Dose Modifications to Chemotherapy after PEG, n(%)	13 (18)	0 (0)	0.002
• Dose reduction	4 (5)	0 (0)	
• Dose delays	6 (8)	0 (0)	
• Dose discontinuation	4 (5)	0 (0)	
Neutropenia, n(%)			
• Grade 3 or higher	60 (83)	42 (93)	0.13
• Febrile Neutropenia	8 (11)	11 (24)	0.057
Documented Infection, n (%)	7 (10)	4 (9)	0.88
30-day mortality, n (%)	0 (0)	0 (0)	NA
90-day mortality, n (%)	1 (2)	0 (0)	0.42

Table 2. Multivariate logistic regression analysis of grade 3 or higher hepatotoxicity (transaminitis or hyperbilirubinemia)

Predictor	OR (CI)	p-value
Age	1.05 (1.01 – 1.11)	0.025
Gender		
• Male	0.85 (0.33 – 2.19)	0.74
Ethnicity (non-Hispanic)		
• Hispanic	2.28 (0.76 – 6.81)	0.13
BMI	1.05 (0.98 – 1.12)	0.15
Early vs Delayed Pegaspargase		
• Early group	4.58 (1.5 – 13.95)	0.007
Dose Capping to 3750 units (one vial)		
• Yes	2.9 (0.92 – 9.15)	0.06
Elevated total bilirubin or transaminases at baseline		
• Yes	0.89 (0.32 – 2.42)	0.82

Figure 1

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