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Blood 142 (2023) 1456–1457

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

612.ACUTE LYMPHOBLASTIC LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Venous Thromboembolism in Adolescents and Young Adults with Acute Lymphoblastic Leukemia Treated on a Pediatric-Inspired Regimen

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Introduction

Adolescent and young adult (AYA) patients (pts) with acute lymphoblastic leukemia (ALL) can be effectively treated with pediatric-inspired ALL regimens which incorporate asparaginase (ASP). Asparaginase is associated with increased venous thromboembolic (VTE) complications. We examined the incidence of and risk factors for VTE events as well as the impact of VTE events on outcomes of AYA pts treated on Dana-Farber Cancer Institute (DFCI) ALL Consortium Protocols.

Methods

We identified pts aged 15-50 years diagnosed with Philadelphia chromosome negative (Ph-neg) ALL treated on 4 multicenter DFCI Consortium protocols (Pediatric 00-001, Pediatric 05-001, Adult 01-175, and Adult 06-254), or treated as per these protocols between 2000-2021. All regimens included an ASP containing induction, 30 weeks of continuous ASP exposure during consolidation and a continuation phase without ASP. The use of a pegylated vs non-pegylated ASP formulation varied between protocols. As ASP exposure is associated with both VTE and survival, it may confound the association between VTE and survival; thus, to ameliorate confounding, all survival associated outcomes were conducted on pts who remained on protocol for at least 1 year (encompassing ASP exposure). Overall survival (OS) and event free survival (EFS) were presented with Kaplan Meier curves and comparisons were made by the log-rank test. Cumulative incidence of VTE, relapse (CIR) and non-relapse mortality (NRM) were estimated by the cumulative incidence method with the appropriate competing risks, and comparisons were made by the Gray test. Cox regression analysis was fit to evaluate the effect of covariates on OS and EFS.

Results

Among 341 Ph-neg AYA ALL pts aged 15-50 years, 109 (32%) experienced one or more VTE events. The baseline characteristics did not differ between pts who experienced a VTE and those who did not experience a VTE, except for a higher rate of VTE among overweight/obese pts (BMI≥25 kg/m ^{2}, n=56, 38%) vs normal BMI (n=53, 27%, p=0.04) and a lower rate of VTE in patients with hyperdiploid vs non-hyperdiploid karyotype (n=4, 12% vs n=105, 34%, p<0.01).

Of the 109 pts with VTE, 9 (8%) experienced sinus vein thrombosis (2.6% in the overall cohort) and 19 (17%) experienced at least one additional VTE. Most initial VTE events occurred during consolidation (n=78, 72%), followed by induction (n=22, 20%), and continuation/follow-up (n=9, 8%). The 2-yr cumulative incidence of VTE was 32% (95% CI, 27%-37%) and was similar between patients who were treated with non-pegylated ASP vs. pegylated ASP (n=43, 30% vs n=65, 35%, p=0.35). The 2-yr cumulative incidence of VTE was higher in the BMI ≥ 25 kg/m ^{2} group compared to those with normal BMI (38% vs 28%, p=0.035, **Figure 1**) and was the only covariate associated with increased VTE risk in the univariate regression model (HR 1.49, 95% CI, 1.03-2.17).

Among pts who completed ≥ 1 year of protocol therapy (n=220), the 4-year OS was 92%, and did not differ between pts who experienced VTE vs. not (94% vs 90%, p=0.99, **Figure 2**). Similarly, there were no differences in 4-year CIR (14% vs 11%,

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p=0.50), NRM (0% vs 3%, p=0.37), and EFS (86% vs 86%, p=0.79). In univariate analysis for OS, obese BMI (>30 kg/m ^{2}), higher WBC, B-cell immunophenotype, and fewer weeks on ASP therapy were associated with worse OS; all remained predictive in the multivariable model. In the uni- and multivariable analysis for EFS, higher WBC and B-cell immunophenotype were associated with worse EFS. Notably, VTE was not associated with worse OS or EFS in all regression analyses.

Conclusion

Among AYAs treated on DFCI ALL Consortium protocols, VTE events were frequent, occurred mostly during consolidation phase and were more common among pts with overweight/obese BMI vs normal BMI. Sinus vein thrombosis was rare. VTE incidence did not impact CIR, NRM, EFS or OS, suggesting that VTE is a manageable toxicity.

Disclosures Raman: *Genentech Inc.:* Consultancy. **Valtis:** *EastRx:* Consultancy. **Place:** *Triterpenoid Therapuetics:* Current equity holder in private company; *Novartis:* Research Funding; *Servier:* Research Funding; *AbbVie:* Research Funding. **Silverman:** *Servier Pharmaceuticals:* Membership on an entity's Board of Directors or advisory committees; *Jazz Pharmaceuticals:* Membership on an entity's Board of Directors or advisory committees. **Sallan:** *Servier:* Honoraria; *Jazz:* Honoraria. **Brunner:** *GSK:* Research Funding; *Celgene/BMS:* Consultancy, Research Funding; *AstraZeneca:* Research Funding; *Taiho:* Consultancy; *Novartis:* Consultancy, Research Funding; *Takeda:* Consultancy; *Agios:* Consultancy, Research Funding; *Keros Therapeutics:* Consultancy; *Janssen:* Research Funding; *Acceleron:* Consultancy; *Gilead:* Consultancy. **Neuberg:** *Madrigal Pharmaceuticals:* Current equity holder in private company. **Garcia:** *Servier:* Consultancy; *Pfizer:* Research Funding; *New Wave:* Research Funding; *AbbVie:* Consultancy, Research Funding; *Astellas:* Consultancy; *Genentech:* Consultancy, Research Funding; *Bristol Myers Squibb:* Consultancy; *Gilead:* Consultancy; *AstraZeneca:* Research Funding; *Prelude:* Research Funding. **Winer:** *Curis Inc:* Consultancy; *Abbvie:* Consultancy. **Stone:** *Jazz:* Consultancy; *Kura One:* Consultancy; *AvenCell:* Consultancy; *Aptevo:* Other: DSMB; *Epizyme:* Other: DSMB; *Hermavant:* Consultancy; *Amgen:* Consultancy; *Rigel:* Consultancy; *Syntrix:* Other: DSMB; *GSK:* Consultancy; *Cellularity:* Consultancy; *BerGenBio:* Consultancy; *Takeda:* Other: DSMB; *Lava Therapeutics:* Consultancy; *Ligand Pharma:* Consultancy; *CTI Biopharma:* Consultancy; *Abbvie:* Consultancy. **Connors:** *CSL Behring:* Research Funding; *Abbott, Anthos, Alnylam, Bristol-Myers Squibb, Five Prime Therapeutics, Pfizer, Roche, Sanofi, Werfen:* Consultancy, Other: Scientific advisory boards. **DeAngelo:** *Amgen:* Honoraria; *Blueprint:* Research Funding; *Novartis:* Research Funding; *Incyte:* Honoraria; *AbbVie:* Research Funding; *Gilead:* Honoraria; *Blueprint:* Honoraria; *Autolus:* Honoraria; *GlycoMimetics:* Research Funding; *Jazz:* Honoraria; *Kite:* Honoraria; *Novartis:* Honoraria; *Pfizer:* Honoraria; *Servier:* Honoraria; *Takeda:* Honoraria. **Luskin:** *Novartis:* Research Funding; *Novartis:* Honoraria; *Pfizer:* Honoraria; *Jazz:* Honoraria; *AbbVie:* Research Funding.

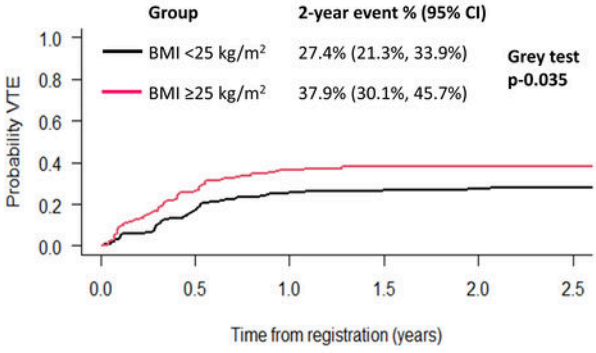

Figure 1. Cumulative incidence of VTE with death as competing risk among AYAs with ALL (n=341). VTE – venous thromboembolism; BMI – body mass index; CI – confidence interval; AYA – Adolescents and young adults; ALL – acute lymphoblastic leukemia

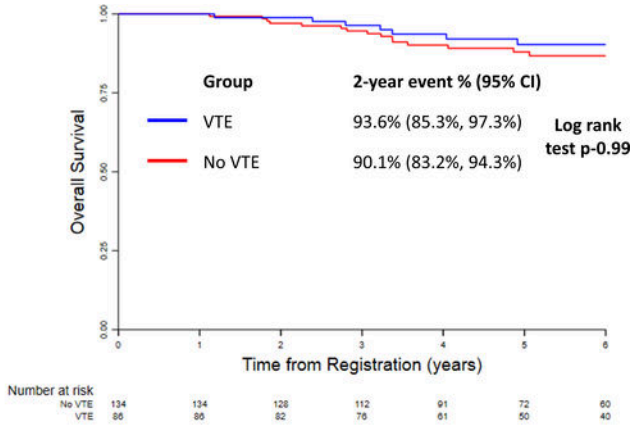

Figure 2. Overall survival in AYAs with ALL who completed one year on protocol (n=220), stratified by VTE events.
AYA – Adolescents and young adults; ALL – acute lymphoblastic leukemia; VTE – venous thromboembolism

Figure 1

https://doi.org/10.1182/blood-2023-178353

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