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POSTER ABSTRACTS

905.OUTCOMES RESEARCH-LYMPHOID MALIGNANCIES

A Meta-Analysis Comparing the Relative Efficacy of Pediatric-Inspired Regimens Versus Hyper-CVAD for the Treatment of Acute Lymphoblastic Leukemia/Lymphoblastic Lymphoma in Adolescents, Young Adults, and Adults

 Wenqing Su¹, Melisa Stricherz², Alison Martin³, Jonathan Belsey⁴, Eric Kemadjou⁴, Daniel J. DeAngelo⁵
¹ Jazz Pharmaceuticals, Philadelphia, PA

² Jazz Pharmaceuticals, Palo Alto, CA

³ Crystallise Ltd, Stanford-le-Hope, Essex, United Kingdom

⁴ JB Medical Ltd, Sudbury, Suffolk, United Kingdom

⁵ Dana-Farber Cancer Institute, Boston, MA

Background: Acute lymphoblastic leukemia/lymphoblastic lymphoma (ALL/LBL) are rare aggressive hematologic malignancies. Children with ALL/LBL have an overall favorable prognosis; however, adult patients (pts) have a poorer outcome. As a result, pediatric or pediatric-inspired regimens with asparaginase (ASP) have been used in adolescents and young adult (AYA) pts with ALL/LBL with promising results. Unfortunately, there are no prospective randomized studies comparing this approach with hyper-CVAD, a commonly used adult regimen not containing ASP. A meta-analysis was conducted to assess the efficacy of pediatric-inspired ASP-containing regimens compared with hyper-CVAD in treating ALL/LBL in AYA and adult pts.

Methods: We performed a systematic literature review (using databases including PubMed, Embase, and Cochrane Library) to identify relevant studies comparing ASP-containing regimens and hyper-CVAD in pts with ALL/LBL published up to April 21, 2022. The search strategy consisted of title/abstract key words and subject headings describing key concepts of "acute lymphoblastic leukemia," "lymphoblastic lymphoma," "asparaginase," "hyper-CVAD," "refractory," and "minimal residual disease." Abstracts were screened for inclusion to identify full texts that were assessed for eligibility. To determine the effects of intervention on complete response (CR) and overall survival (OS) (2 commonly reported outcomes across identified studies), odds ratios (OR) and hazard ratios (HR) were calculated. A meta-analysis was conducted using both random- and fixed-effects models to estimate the pooled OR and HR, 95% confidence intervals (CIs), and 95% prediction intervals (PIs). Scenario analyses identified potential sources of heterogeneity and bias.

Results: The initial search identified 46 primary publications of potential relevance: 12 studies directly compared ASP-containing regimens and hyper-CVAD, but none were randomized. Based on direct comparison studies, ASP-containing regimens had statistically significant improvement in median OS (4 studies), 2-year OS (1 study), 3-year OS (3 studies), and 5-year OS (1 study) compared with hyper-CVAD. Four studies with comparable demographics were suitable for meta-analysis (n=702 total pts; n=366 ASP-containing regimens; n=336 hyper-CVAD): 2 studies in AYA (aged 13-43 yrs) and 2 in adults of any age (aged > 16 yrs). ASP-containing regimens in the included studies were all based on Berlin-Frankfurt-Münster (BFM) or Cancer and Leukemia Group B (CALGB)-10403 protocols.

Pts treated with ASP-containing regimens had a significantly higher chance of achieving CR (random- and fixed-effects model: OR, 2.04 [95% CI: 1.31, 3.18]) and improved OS (random-effects model: HR, 1.76 [95% CI: 1.36, 2.29]; fixed-effects model: HR, 1.75 [95% CI: 1.36, 2.24]) than those treated with hyper-CVAD. There was a low level of heterogeneity among studies for both CR ($I^2=0\%$, $\tau^2=0.00$, $P=0.86$) and OS ($I^2=0\%$, $\tau^2=0.02$, $P=0.79$) data.

One study evaluated 2 different ASP-containing regimens vs hyper-CVAD. Two separate meta-analyses were executed: 1 pooling results from both treatment arms (base case) and 1 considering them separately (scenario 1). A further analysis was limited to just 2 studies, where the proportionality assumption for the HR was robust and the results consequently most statistically reliable (scenario 2). Compared with the base case, both scenarios yielded similar estimates of treatment effect but with greater heterogeneity and wider PIs.

This analysis has limitations: the type of ASP-containing regimen varied (1 study assessed L-ASP regimens, 2 assessed pegaspargase, and 1 did not specify), the studies each took place in different countries potentially contributing to heterogeneity in cultural, genetic, and healthcare practices, and not all details of pts' clinical characteristics were reported to inform on comparability of the pt populations. Further, without head-to-head studies, there was no way to address whether treatment cost or institutional bias affected the results.

Conclusion(s): Meta-analysis suggests that ASP-containing regimens are associated with improved rates of CR and OS in AYA (median age range 13-43 yrs) and adult (median age range 16-60 yrs) pts.

Disclosures Su: *Jazz Pharmaceuticals*: Current Employment, Current holder of stock options in a privately-held company. **Stricherz:** *Jazz Pharmaceuticals*: Current Employment, Current holder of stock options in a privately-held company. **Martin:** *Crystallise Ltd*: Current Employment. **Belsey:** *JB Medical*: Current Employment. **Kemadjou:** *JB Medical*: Current Employment. **DeAngelo:** *Blueprint*: Honoraria; *GlycoMimetics*: Research Funding; *Blueprint*: Research Funding; *AbbVie*: Research Funding; *Novartis*: Research Funding; *Amgen*: Honoraria; *Autolus*: Honoraria; *Gilead*: Honoraria; *Incyte*: Honoraria; *Jazz*: Honoraria; *Kite*: Honoraria; *Novartis*: Honoraria; *Pfizer*: Honoraria; *Servier*: Honoraria; *Takeda*: Honoraria.

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