Evaluation of minimal residual disease positivity rates in adult acute lymphoblastic leukemia patients treated with asparaginase versus non-asparaginase containing regimens

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Background
- Acute lymphoblastic leukemia (ALL) is predominantly a disease of children, with a second peak of incidence in older adults. A prospective multicenter study of 368 ALL patients aged 15 to 65 years found an age greater than 35 years to be a statistically significant negative prognostic factor.1
- The regimens currently used at Duke University Hospital to treat adult ALL include:

<table>
<thead>
<tr>
<th>Asparaginase</th>
<th>Non-asparaginase</th>
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<tr>
<td>CALGB 10403</td>
<td>HyperCVAD</td>
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<tr>
<td>CALGB 19802</td>
<td>R-HyperCVAD</td>
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<tr>
<td>CALGB 8811</td>
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- Administration of asparaginase is associated with well documented toxicities that included pancreatitis, hyperglycemia, thromboembolism, and hepatotoxicity.2
- The clinical significance of minimal residual disease (MRD) has been shown in childhood and adult ALL and is an independent prognostic factor for relapse in these patient populations.3
- In most studies, MRD positivity is defined by a presence of 0.01% or more ALL cells. Risk of relapse is proportional to the level of MRD, especially when measured at the end of induction therapy.4,5

Objectives

Primary Objective
- To determine whether choice of induction therapy between asparaginase and non-asparaginase containing regimens had an impact on the rate of MRD positivity in adult ALL patients treated at Duke University Hospital.

Secondary Objective
- Determine differences in:
  - Treatment delays
  - Adverse effects
  - Overall survival rates

Methods

Study Design
- IRB-approved, single-center, retrospective cohort study
- MRD results will be divided based on use of 4-color flow cytometry and 8-color flow cytometry.

Table 1. Study Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
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<td>Age ≥ 18 years of age</td>
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<tr>
<td>Diagnosis of acute lymphoblastic leukemia</td>
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<td>Treatment at Duke University Hospital by adult oncology team</td>
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<td>Treatment initiation before October 1, 2014</td>
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<table>
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<th>Exclusion Criteria</th>
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<td>Prior history of chemotherapy</td>
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<td>Treatment in the setting of a clinical trial</td>
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Subject Selection
- All potential subjects for inclusion will be identified via a query of the Duke Enterprise Data Unified Content Explorer (DEDUCE) database.

Endpoints

Primary Endpoint
- Rate of post-induction minimal residual disease positivity, defined as having MRD greater than 0.01% per standard flow cytometry assay.

Secondary Endpoints
- Overall two year survival from start of induction treatment
- Rate of hepatotoxicity, defined as AST/ALT 3x upper limit of normal (ULN) or conjugated bilirubin 1.5x ULN
- Rate of neuropathy, defined as requiring initiation of treatment with gabapentin or pregabalin or a chemotherapy dose reduction documented as neuropathy-related
- Average days of treatment delays in overall treatment regimen
- Number of patients who required re-induction

Data Collection and Analysis

Data Collection
- Data collection will include data from January 1, 2002 to October 1, 2016.
- Demographic and clinical data including age at diagnosis, sex, and race will be collected.
- Data collection and analysis are currently in process.

Statistical Analysis
- Descriptive statistics will be used to summarize the sample.
- Association between the rates of post-induction MRD positivity will be examined via a 2 by 2 table using Chi-squared tests or Fisher’s exact test.
- Two-year mortality between treatment choices will be assessed utilizing Kaplan-Meier curves and log-rank tests.
- Rates of different toxicities, differences in rates of patients needing re-induction treatment, and presence or absence of treatment delays between the treatment regimens will be examined using Chi-squared tests or Fisher’s exact test.
- Statistical significance will be examined at alpha=0.05.
- Statistical analyses will be performed using SAS 0.4 statistical software (SAS Institute Inc., Cary NC).

References

Disclosures: Authors have no conflicts of interests regarding personal or financial relationships with commercial entities that may have influenced the content or subject matter of this presentation.