Clinical Trial Availability in Adolescent and Young Adults with Non-Hodgkin Lymphoma

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Disclosures

• No relevant financial disclosures
Introduction

• Adolescent and young adult cancer patients (AYAs) have not benefitted from the improvements in survival seen by pediatric patients, or patients over 40 years of age.

• In non-Hodgkin lymphoma: increased relapse rates and increased mortality.
Pediatric patients and trial enrollment

• Participation in protocols often cited as a reason for improved survival rates
  – Single institution enrollments vary, but range from 30% to 81.1%
AYAs in Clinical Trials

• AYAs between the ages of 15-19 enrolled in clinical trials: 10%
  – Only 2% of patients between ages of 20-30 years of age
• Possibly due to patient factors and regulatory factors
Methods

• Keyword search of “Non-Hodgkin lymphoma” on Clinical Trials.gov yielded record of 726 trials

• Exclusions:
  – Trials not containing a novel agent (e.g. tissue banking)
  – Trials focused only on conditioning regimen
Methods

• 404 trials of novel agents
  – 17 categories of novel agents identified.

• Collected data on any novel agent contained within a trial protocol
  – Age groups, sample size, and information on study agent
  – Lymphoma subtypes included in a trial
  – Whether study sites maintained affiliation with Children’s Oncology Group
Results

• 404 trials of novel agents in patients with Hodgkins disease
  – 61 studies open to patients under 18 years of age
  – 227 trials studying novel agents in patients with the six most common subtypes of lymphoma in the AYA population.
Table 1: Clinical Trials by Age Inclusion and Phase

<table>
<thead>
<tr>
<th></th>
<th>Studies which include patients &lt; 18 years of age</th>
<th>Studies including only patients ≥18 years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total # of trials</td>
<td>61</td>
<td>343</td>
</tr>
<tr>
<td>Total # of patients included</td>
<td>5656</td>
<td>32473</td>
</tr>
<tr>
<td># trials by phase (average no. enrolled subjects +/- SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase I</td>
<td>25</td>
<td>116</td>
</tr>
<tr>
<td></td>
<td>(50 +/- 53)</td>
<td>(88 +/- 71)</td>
</tr>
<tr>
<td>Phase I/II</td>
<td>2</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>(141 +/- 142)</td>
<td>(136 +/- 117)</td>
</tr>
<tr>
<td>Phase II</td>
<td>29</td>
<td>162</td>
</tr>
<tr>
<td></td>
<td>(129 +/- 86)</td>
<td>(113 +/- 87)</td>
</tr>
<tr>
<td>Phase III</td>
<td>3</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>(785 +/- 494)</td>
<td>(192 +/- 90)</td>
</tr>
<tr>
<td>Phase IV</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>(40 +/- 57)</td>
<td></td>
</tr>
<tr>
<td>Phase not specified</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>(76 +/- 90)</td>
<td>(18 +/- 12)</td>
</tr>
</tbody>
</table>
Results

• All agent classes were represented in trials open to patients who were at least 18 years old.
• In the under-18 subset, three agent classes had no listed trials
  – BiTE immunotherapy
  – Pleiomorphic pathway modifiers
  – PI3K inhibitors
• Immunotherapy class with only 1 trial enrolling patients under 18 years of age.
Table 2: Clinical Trials by Agent Class, Age of Inclusion and Availability at Children's Oncology Group Inclusion

<table>
<thead>
<tr>
<th>Agent Class</th>
<th>Allows enrollment of patients &lt; 18 years old</th>
<th>Limited to patients ≥ 18 years old</th>
<th>COG availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytotoxic T lymphocytes</td>
<td>9</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>HDAC inhibitor</td>
<td>3</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>Small molecule</td>
<td>7</td>
<td>92</td>
<td>51</td>
</tr>
<tr>
<td>Monoclonal antibody</td>
<td>5</td>
<td>63</td>
<td>24</td>
</tr>
<tr>
<td>CAR T cell</td>
<td>12</td>
<td>22</td>
<td>19</td>
</tr>
<tr>
<td>Checkpoint inhibitors vaccine)</td>
<td>1</td>
<td>42</td>
<td>28</td>
</tr>
<tr>
<td>mTOR inhibitor</td>
<td>3</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>TKI (all, including BTK)</td>
<td>7</td>
<td>46</td>
<td>27</td>
</tr>
<tr>
<td>Donor cells</td>
<td>4</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Antibody-drug conjugate</td>
<td>3</td>
<td>35</td>
<td>15</td>
</tr>
<tr>
<td>Proteasome inhibitor</td>
<td>3</td>
<td>22</td>
<td>17</td>
</tr>
<tr>
<td>iMID</td>
<td>3</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Radioimmunotherapy</td>
<td>1</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>BITE</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>PI3K inhibitor</td>
<td>0</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>Pleiomorphic Pathway Modifier</td>
<td>0</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Miscellaneous*</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
</tbody>
</table>

*Includes single agents not included in any other class
Results

• 178 of the 343 trials which excluded patients under the age of 18 had at least one listed study site listed as an affiliate of the Children’s Oncology Group
Why is AYA enrollment so low?

• Decreased knowledge about clinical trial availability
• Patient concerns about clinical trial participation
• Difficulty accessing clinical trials
AYA HOPE Study

• Reviewed medical records and evaluated self-administered surveys
  – Patient knowledge of clinical trial availability
  – Assessed reasons for non-participation
AYA HOPE Study

• 515 Patients evaluated
  – 63% not aware that clinical trials were available
  – 17% of study participants were aware of trials for their type and stage of cancer.
  – 8% were aware of a specific trial available of type and stage of cancer
ASH HOPE Study

• Stated concerns for non-involvement:
  – Insufficient testing
  – Potential adverse effects
  – Feeling like a guinea pig
  – Concerns about receiving placebo
  – Concerns about changing physicians
  – Not feeling like a trial would help
  – Problems with access (too ill to enroll, no trials nearby, insurance or other access issues)
Improving Access to Clinical Trials

• Pediatric trials for drugs may not be initiated for years until after initial FDA approval in adults

• Not eligible for trials designed for adult oncology patients
  – Delays utilization of drugs that become standard of care in adult diseases
Regulatory safeguards

- Children are viewed as vulnerable subjects who require additional protection
  - Sufficient information must be given before obtaining consent of parents and children
  - Risk undertaken in a clinical trial must be justified in terms of anticipated benefits.
Rituximab

• First approved as a single agent treatment in adults with relapsed and refractory NHL in 1997

• 20 years later, no approved indication in the pediatric setting
  – Completed and ongoing studies in pediatric patients.
Blinatumomab

• Approved for treatment of Philadelphia chromosome negative relapsed or refractory B-cell precursor ALL

• Phase I data with anti-lymphoma activity in adult patients with relapsed/refractory NHL, with durable responses.

• To date, no studies of blinatumomab for patients with NHL in the under-18 population.
Specific barriers in the subset of AYAs who are under 18 years old

- Disease processes which may behave more like adult counterparts
- Excluded from clinical trials of novel agents in adult patients
- Delay of access to agents that have already been FDA approved in treatment of adult NHL
• Most NHL trials which enroll patients over the age of 18 occur at Children’s Oncology Group member institutions
  – Patients over the age of 18 have access to clinical trials regardless of whether they are treated in an adult or pediatric setting.
  – Access is limited to younger patients at the same institution.

• No data accrued on proportion of AYA patients enrolled in trials of NHL patients.
• In institutions which treat both adult and pediatric patients, and in adult centers which may open trials to pediatric populations
  – Cooperation between providers in pediatric and adult oncology to meet requirements of pediatric patients
  – Build trials that overcome additional regulatory barriers
Take Home Points

• Most patients who enroll NHL patients over the age of 18 occur at COG member institutions

• Greater need to build trials which enroll all patients who might benefit from them
  – Working to meet regulatory barriers for pediatric clinical trials

• For AYA patients, address concerns that lead to avoidance of clinical trials.
References


Thank you!

References available on request.

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