Outcomes of Tagraxofusp (SL-401) in Older Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

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BPDCN: Aggressive Hematologic Malignancy

• Rare, aggressive hematologic malignancy often with cutaneous manifestations (~80% of patients present with skin lesions)
  - Lymph nodes and viscera may also be involved

• Cell of origin: plasmacytoid dendritic cell (pDC)

• Historically, has been misdiagnosed as AML, NHL, and other heme malignancies

• Diagnostic signature triad: CD123 / CD4 / CD56. Think “123456” - aids in the correct diagnosis

• Historically poor prognosis - median overall survival of 8-12 months with chemotherapy

Tagraxofusp: First Drug Approved in BPDCN

- Tagraxofusp is a targeted therapy directed to CD123
- CD123 overexpressed on BPDCN and other hematologic cancers
- Tagraxofusp potent against BPDCN in vitro and in vivo
- Tagraxofusp FDA-approved in December 2018 for treatment of adult and pediatric patients, 2 years and older, with BPDCN
- MAA under review in Europe
### Stage 1
(Dose Escalation)
- BPDCN (treatment-naïve and previously-treated)
- Tagraxofusp (7 or 12 mcg/kg) via IV infusion, days 1-5 of a 21-day cycle*
- Key objectives: To determine the recommended phase 2 dose (RP2D)

### Stage 2
(Expansion)
- BPDCN (treatment-naïve and previously-treated)
- Tagraxofusp (12 mcg/kg) via IV infusion, days 1-5 of a 21-day cycle*
- Key objectives: To further define safety and efficacy of the RP2D

### Stage 3
(Pivotal, Confirmatory)
- BPDCN (treatment-naïve)
- Tagraxofusp (12 mcg/kg) via IV infusion, days 1-5 of a 21-day cycle*
- Key objective: To confirm efficacy for regulatory decision making

*BPCDN patients were enrolled in an additional cohort, Stage 4, to ensure continued access during regulatory review

#### Select inclusion criteria
- Patient population: treatment-naïve or previously-treated
- Age ≥18
- ECOG PS 0-2
- Adequate organ function including: LVEF ≥ lower limit of normal, creatinine ≤1.5 mg/dL, albumin ≥3.2 g/dL, bilirubin ≤1.5 mg/dL, AST/ALT ≤2.5×ULN

#### Select exclusion criteria
- Persistent clinically significant toxicities from prior chemotherapy
- Received chemotherapy or other investigational therapy within the prior 14 days
- Clinically significant cardiopulmonary disease
- Receiving immunosuppressive therapy

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BPDCN, blastic plasmacytoid dendritic cell neoplasm; ECOG PS, Eastern Cooperative Oncology Group performance status; LVEF, left ventricular ejection fraction; ULN, upper limit of normal; FDA, Food and Drug Administration

*The study design allowed for a 10-day treatment window in which patients could receive the total of five drug infusions, to allow for dose interruptions, if needed.
## Tagraxofusp: Demographics By Age Group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Patients N=44</th>
<th>Age ≥ 70 years N=20</th>
<th>Age &lt; 70 years N=24</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>36 (82)</td>
<td>18 (90)</td>
<td>18 (75)</td>
</tr>
<tr>
<td>Female</td>
<td>8 (18)</td>
<td>2 (10)</td>
<td>6 (25)</td>
</tr>
<tr>
<td><strong>Race, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>2 (5)</td>
<td>1 (5)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>White</td>
<td>40 (91)</td>
<td>19 (95)</td>
<td>21 (88)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>1 (4)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>68.5 (22, 84)</td>
<td>75 (70, 84)</td>
<td>61.5 (22, 69)</td>
</tr>
<tr>
<td><strong>ECOG, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>20 (46)</td>
<td>7 (35)</td>
<td>13 (54)</td>
</tr>
<tr>
<td>1</td>
<td>24 (54)</td>
<td>13 (65)</td>
<td>11 (46)</td>
</tr>
</tbody>
</table>

BPDCN, blastic plasmacytoid dendritic cell neoplasm; ECOG, Eastern Cooperative Oncology Group.
Performance-status scores on the ECOG scale range from 0 to 5, with 0 indicating no symptoms and higher scores indicating an increasing severity of symptoms. Per inclusion criteria, can range from 0-2.
Tagraxofusp: Safety and Tolerability in Older Patients

- No apparent cumulative AEs, including in the bone marrow, over multiple cycles

- CLS most serious adverse reaction
  - CLS largely cycle 1-related and manageable with monitoring and pre-emptive measures

- Across all patients treated at prescribed dose, 55% of patients experienced CLS\(^1\), including Grades 1-2 in 46% (43/94), Grade 3 in 6% (6/94), Grade 4 in 1% (1/94), and 2 fatal events (2%; 2/94)

### Adverse Reactions in ≥ 30% of Patients ≥ 70 years

<table>
<thead>
<tr>
<th></th>
<th>All Grades (%)</th>
<th>Grade ≥ 3 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT Increase</td>
<td>69</td>
<td>51</td>
</tr>
<tr>
<td>AST Increase</td>
<td>67</td>
<td>46</td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>62</td>
<td>3</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>54</td>
<td>3</td>
</tr>
<tr>
<td>Nausea</td>
<td>49</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>41</td>
<td>10</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>41</td>
<td>36</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>36</td>
<td>0</td>
</tr>
<tr>
<td>Weight Increase</td>
<td>36</td>
<td>0</td>
</tr>
<tr>
<td>Anemia</td>
<td>33</td>
<td>23</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>33</td>
<td>18</td>
</tr>
<tr>
<td>Hypotension</td>
<td>33</td>
<td>5</td>
</tr>
<tr>
<td>Chills</td>
<td>31</td>
<td>3</td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>31</td>
<td>0</td>
</tr>
</tbody>
</table>

\(^1\)Defined as any event reported as CLS during treatment with tagraxofusp or the occurrence of at least 2 of the following CLS manifestations within 7 days of each other: hypoalbuminemia, edema, hypotension.

AE, Adverse Events; CLS, Capillary leak syndrome; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase.

Analysis includes patients treated with AML and BPDCN treated with tagraxofusp at 12 μg/kg
### Tagraxofusp: Clinical Activity Across Age Groups

**Response Rates in BPDCN Patients (Tagraxofusp at 12 mcg/kg)**

<table>
<thead>
<tr>
<th>Efficacy Measures</th>
<th>Treatment-Naïve Patients</th>
<th>Previously-Treated Patients</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>All ages N=29</td>
<td>Age ≥ 70 years N=10</td>
</tr>
<tr>
<td>ORR, % (n)</td>
<td>90% (26)</td>
<td>100% (10)</td>
</tr>
<tr>
<td>CR/CRc rate, % (n)</td>
<td>72% (21)</td>
<td>70% (7)</td>
</tr>
<tr>
<td>Bridged to SCT, % (n)</td>
<td>45% (13)</td>
<td>20% (2)</td>
</tr>
</tbody>
</table>

CR, complete response; CRc (clinical CR), complete response with minimal residual skin abnormalities not indicative of active disease; ORR, overall response rate; SCT, stem cell transplant
Tagraxofusp: Representative Skin Response

- 71 year old female with BPDCN
- Treatment-naïve; extensive skin and bone marrow (BM) involvement
- Received six cycles of tagraxofusp at 12 mcg/kg
- Bridged to stem-cell transplantation after CR and 6 cycles of tagraxofusp
Tagraxofusp: Overall Survival (OS)

First-line BPDCN (12 mcg/kg) - Stages 1, 2, and 3 (n=29)

- Median OS: Not reached
- Long-term survivors
  (median follow up: 25 months)

Data cutoff: September 1, 2018
Tagraxofusp: Bone Marrow Responses

BPDCN (12 mcg/kg); Stages 1, 2, and 3
BPDCN: historically poor outcomes

Tagraxofusp, a novel targeted therapy directed to CD123, demonstrated high levels of clinical activity across age cohorts in patients with BPDCN
- Treatment-naïve patients, age ≥ 70 years (N=10)
  - 100% ORR; 70% CR/CRc; 20% bridged to receive SCT
- Previously-treated patients, age ≥ 70 years (N=10)
  - 70% ORR; 10% CR/CRc

Tagraxofusp has a predictable and manageable safety profile in patients with BPDCN
- Most serious adverse reaction is CLS
- Most common adverse reactions in patients ≥ 70 years are AST/ALT increase, hypoalbuminemia and peripheral edema

First medication approved for BPDCN
- U.S. FDA approved for adult and pediatric patients with BPDCN on December 21, 2018
- Marketing Authorization Application (MAA) for BPDCN under review by the European Medicines Agency (EMA)
Acknowledgements

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