Novel Re-Induction and Anti-CD45 Targeted Conditioning with Iodine (¹³¹I) Apamistamab [Iomab-B] Yields Encouraging Results in Older Patients with Active, Relapsed or Refractory Acute Myeloid Leukemia (R/R AML): Safety and Feasibility Data from the Prospective, Randomized Phase III SIERRA Trial

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Iodine ($^{131}$I) apamistamab [Iomab-B] CD45 Targeted Conditioning

- Iodine ($^{131}$I) apamistamab [Iomab-B] is a murine anti-CD45 targeted therapy that was developed at the Fred Hutchinson Cancer Research Center.
- Encouraging Phase II data led to the ongoing SIERRA Phase III trial.
- CD45 is expressed on hematopoietic cells, including leukemia cells, lymphoma cells and all immune cells.
- High doses, such as in the SIERRA trial, deplete hematopoietic stem cells.
- Targets radiation directly to leukemia cells and elicits a direct anti-tumor effect.

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**Leukemic Bone Marrow**

**Post-Iomab-B Myeloablated Bone Marrow**

- B-cell
- Cancer cell
- Cytokines
- Platelets
- RBC
- T-cell
Iomab-B Potential – Background and Rationale

- Compelling prior Phase II clinical data in active, refractory and relapsed AML
- Robust safety and long term efficacy outcomes in multiple populations: 271 patients in 9 Phase I and II clinical trials (AML, ALL, MDS, NHL, MM)

1) Biol Blood Marrow Transplant 15:1431-1438 (2009), MD Anderson outcomes analysis. (Chemo + BMT n=19) (Salvage Chemo n = 95)
2) Iomab-B BMT: Blood 114:5444-5453 (2009) and additional data on file Pagel et. al. (n=36)
SIERRA Phase 3 Trial Design

Study Design (N=150)

Active, relapsed or refractory AML

RANDOMIZED 1:1

Iomab-B → HCT

No CR → CR → dCR

CROSSOVER*

Conventional Chemotherapy**

No CR → CR → HCT

Standard of Care

Physician Choice

dCR

Primary End-point: Durable Complete Response Rate (dCR): morphologic CR lasting ≥180 days
Secondary End-point: 1-year Overall Survival

Key Eligibility Criteria:

Active, relapsed or refractory AML defined as:

- Primary induction failure (PIF) after ≥2 cycles of chemotherapy
- First early relapse after remission < 6 months
- Refractory to salvage combination chemotherapy with high-dose cytarabine
- Second or subsequent relapse

- Bone marrow blast count ≥ 5% or the presence of peripheral blasts
- ≥ 55 years of age
- Karnofsky score ≥ 70
- An 8/8 allele-level, related or unrelated, medically cleared HSC donor matching at HLA-A, HLA-B, HLA-C, and DRB-1
SIERRA Iomab-B Treatment Schedule

Iomab-B Specific

~7 days

Dosimetry
Iomab-B (~10-20 mCi)

Therapy Dose
Iomab-B (24 Gy to liver, mean~600 mCi)

~12 days

Imaging
-12 to HCT

Standard Transplant Procedure

RIC
FLU
30 mg/m²/d

HCT
TBI
200 cGy

Immunosuppression
-4 -3 -2 -1 0

RIC: Reduced Intensity Conditioning      FLU: Fludarabine      TBI: Total Body Irradiation      HCT: Hematopoietic Cell Transplant

Therapy dose individualized and calculated based on upper limit of 24 Gy liver exposure
**SIERRA Trial: Demographics Highlights**

- ASH presentation based on safety data from first 25% of patients enrolled. Updated results for this cohort being presented at today’s session.
- Additional protocol defined safety updates at 50% and 75% of planned enrollment.

### Ongoing Phase 3 SIERRA Trial (N=38)

<table>
<thead>
<tr>
<th>Study Arm</th>
<th>Randomized to Iomab-B (N=19)</th>
<th>Randomized to Conventional Care (N=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong> (median, range)</td>
<td>62 (55-72)</td>
<td>64 (55-76)</td>
</tr>
<tr>
<td><strong>Disease Status</strong></td>
<td><strong>At Randomization</strong></td>
<td><strong>First Early Relapse (1)</strong>&lt;br&gt;<strong>Primary Induction Failure (10)</strong>&lt;br&gt;<strong>Relapsed / Refractory (4)</strong>&lt;br&gt;<strong>2nd / Subsequent Relapse (3)</strong>&lt;br&gt;<strong>1 patient not entered</strong></td>
</tr>
<tr>
<td><strong>% Bone Marrow Blasts at Randomization (median, range)</strong></td>
<td>30% (4*-74)</td>
<td>26% (6-97)</td>
</tr>
</tbody>
</table>

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*1 patient with 4% blasts in the marrow had circulating AML blasts.
Novel Re-induction and Targeted Conditioning Therapy Yields Encouraging Results in Active, Relapsed or Refractory AML

<table>
<thead>
<tr>
<th>Median (range)</th>
<th>Randomized to Iomab-B and transplanted (N=18/19)^</th>
<th>Randomized to Conventional Care (N=19)</th>
<th>Did not achieve CR Crossed over to Iomab-B arm and transplanted (N=10/15) ^^</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days to ANC Engraftment</td>
<td>13 (9-22)***</td>
<td>Not collected</td>
<td>13 (9-20)</td>
</tr>
<tr>
<td>Days to Platelet Engraftment</td>
<td>16 (13-26)***</td>
<td>Not collected</td>
<td>17 (10-20)**</td>
</tr>
<tr>
<td>Full Donor Chimerism (&gt;95% prior to day 100)</td>
<td>17/18 (1 patient 65% donor)</td>
<td>n/a</td>
<td>9/10 (1 patient 86% donor)</td>
</tr>
<tr>
<td>Days to HCT (Post Randomization)</td>
<td>28 (23-38)</td>
<td>67 (66-86)</td>
<td>66 (57-161)****</td>
</tr>
<tr>
<td>Dose Delivered to Bone Marrow</td>
<td>18 (8.2-32) Gy 616 (397-1027) mCi</td>
<td>n/a</td>
<td>16 (6.3-20) Gy 518 (313-1008) mCi</td>
</tr>
</tbody>
</table>

^ 1 patient had unfavorable dosimetry
^^ 5 patients ineligible for transplant

Key Data Highlights:

- Despite high blast count all patients receiving Iomab-B successfully engrafted
- 15/19 (79%) of patients in the control arm failed to achieve complete remission
- 10/15 (67%) of eligible patients in the control arm crossed-over to receive Iomab-B
- Faster time to transplant in patients randomized to Iomab-B (28 days) vs. conventional care (67 days)
- If on conventional care arm, no delay to HCT with crossover to Iomab-B

** N=2 patients, platelet engraftment data not available; *** ANC engraftment data not available (N=2), platelet engraftment data not available (N=3); ****1 patient at 161 days had delayed transplant due to infection & respiratory failure, received lomab & transplant when stable
Non–Heme Grade 3 or 4 AEs (>10% of patients)
Up to a 100-days post transplant or till crossover assessment*

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Randomized to Iomab-B Study Arm (N=19) (%)</th>
<th>Randomized to Conventional Care Arm (N=19) (%)</th>
<th>Total (N=38) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Febrile Neutropenia</td>
<td>4 (21.1)</td>
<td>9 (47.4)</td>
<td>13 (34.2)</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>3 (15.8)</td>
<td>3 (15.8)</td>
<td>6 (15.8)</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>2 (10.5)</td>
<td>3 (15.8)</td>
<td>5 (13.2)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>2 (10.5)</td>
<td>2 (10.5)</td>
<td>4 (10.5)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>0 (0)</td>
<td>4 (21.1)</td>
<td>4 (10.5)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>1 (5.3)</td>
<td>3 (15.8)</td>
<td>4 (10.5)</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>1 (5.3)</td>
<td>3 (15.8)</td>
<td>4 (10.5)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3 (15.8)</td>
<td>1 (5.3)</td>
<td>4 (10.5)</td>
</tr>
</tbody>
</table>

* Note: Five patients on conventional care arm did not achieve CR and did not proceed to transplant. AE profile not collected post cross-over assessment as per protocol
Non-Heme Grade 3 or 4 AEs in Transplanted Patients
Up to a 100-days post transplant

<table>
<thead>
<tr>
<th>Adverse Event (&gt;10% of total patients)</th>
<th>Randomized to Iomab-B Study Arm N=19 (%)</th>
<th>Crossed over to Iomab-B arm and transplanted N=10 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Febrile Neutropenia</td>
<td>4 (21)</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>3 (16)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>2 (11)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>2 (11)</td>
<td>2 (20)</td>
</tr>
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</tr>
<tr>
<td>Fatigue</td>
<td>3 (16)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

- **No Grade 3 or 4 Iomab-B Infusion Related Reactions** (all infusions completed)
- **Acute GVHD**
  - Iomab-B: Grade 3 (N=1), Grade 4 (N=0)
  - Cross-over Iomab-B: Grade 3 (N=1), Grade 4 (N=1)
- **Chronic GVHD**
  - Iomab B: N=2 (mild)
  - Crossover Iomab-B: N=2 (mild)
- **VOD**
  - Iomab-B: Grade 2 (N=1). Day 9 to 17 post transplant. Resolved
## 100 Days Non-Relapse Mortality in Transplanted Patients

<table>
<thead>
<tr>
<th>Randomized to Iomab-B and transplanted (N=18)</th>
<th>Randomized to Conventional Care (N=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achieved CR and received standard of care transplant (N=4)</td>
<td>Did not achieve CR Crossed over to Iomab-B arm and transplanted (N=10)</td>
</tr>
<tr>
<td>0/18 (0%)</td>
<td>1/4 (25%)</td>
</tr>
<tr>
<td>1 patient: septic shock</td>
<td>1/10 (10%)</td>
</tr>
<tr>
<td>1 patient: diffuse alveolar hge</td>
<td></td>
</tr>
</tbody>
</table>

- No Non-Relapse mortality in Iomab-B arm
- Non-Relapse mortality increases with additional salvage therapy followed by transplant
- Based on investigator feedback, protocol recently amended for earlier cross over at day 14 for progression to potentially reduce this mortality and offer earlier transplant
Conclusions

♦ SIERRA is the only randomized, on-going Phase III clinical trial that offers transplant option to patients **55 years or older with active, relapsed or refractory AML**
  - Historically under-served population
  - Dismal survival prognosis
  - Limited options for patients with active disease

♦ Encouraging results with potential to broaden transplant eligibility and improve outcomes
  - Validated proof of concept of re-induction and targeted conditioning with Iomab-B
  - All patients receiving Iomab-B engrafted despite active disease with high blast count (median 30%, or median 45% for crossover patients)
  - 15/19 (79%) of patients in the control arm failed to achieve a complete remission
  - 10/15 (67%) of patients eligible for crossover successfully transplanted with Iomab-B
  - Faster time to transplant in patients receiving Iomab-B (28 days) vs. conventional care (67 days) and no delay to HCT with crossover to Iomab-B
  - No non-relapse mortality in patients randomized to Iomab-B arm
Acknowledgements and Currently Active Sites

- Memorial Sloan Kettering Cancer Center
- Baylor Scott & White Health
- Loyola Medicine
- Roswell Park Comprehensive Cancer Center
- University Hospitals Cleveland Medical Center
- The Ottawa Hospital
- University of Nebraska Medical Center
- Washington University in St. Louis School of Medicine
- Yale Cancer Center
- MD Anderson Cancer Center
- Mayo Clinic
- KU Medical Center
- Cornell University
- Stony Brook Cancer Center
- The Ohio State University Comprehensive Cancer Center
- Nationwide Children's Hospital
- Fred Hutch Cancer Center