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Mid-Point Analysis of Pivotal Phase 3 SIERRA Trial
Including Materials Presented at 2020 Transplantation &
Cellular Therapy Meetings of ASTCT and CIBMTR (TCT)

Targeted Conditioning with Anti-CD45 Iodine (¹³¹I) Apamistamab [Iomab-B] leads to High Rates of Allogeneic Transplantation and Successful Engraftment in Older Patients with Active, Relapsed or Refractory AML after Failure of Chemotherapy and Targeted Agents: Preliminary Midpoint Results from the Prospective, Randomized Phase 3 SIERRA Trial

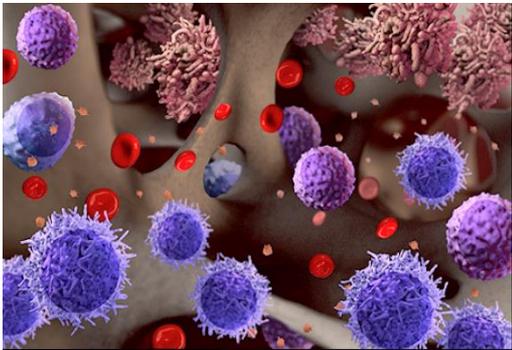
SIERRA: Study of Iomab-B in Elderly Relapsed/Refractory AML

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Iodine (131I) apamistamab [lomab-B] CD45 Targeted Conditioning

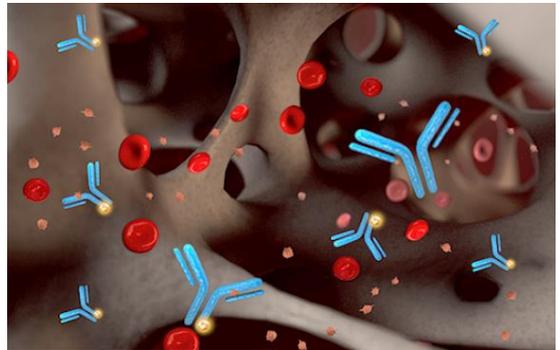
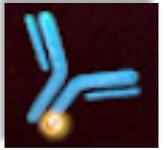
- Iodine (131I) apamistamab [lomab-B] is a murine anti-CD45 targeted therapy that was developed at the Fred Hutchinson Cancer Research Center
- CD45 is expressed on hematopoietic cells, including leukemia, lymphoma and immune cells
- High doses, such as in the SIERRA trial, deplete hematopoietic stem cells
- Targets radiation directly to leukemia cells and elicits a direct anti-tumor effect

Leukemic Bone Marrow



Post-lomab-B Myeloablated Bone Marrow

Iomab-B



B-cell



cancer cell



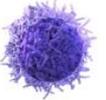
cytokines



platelets



RBC

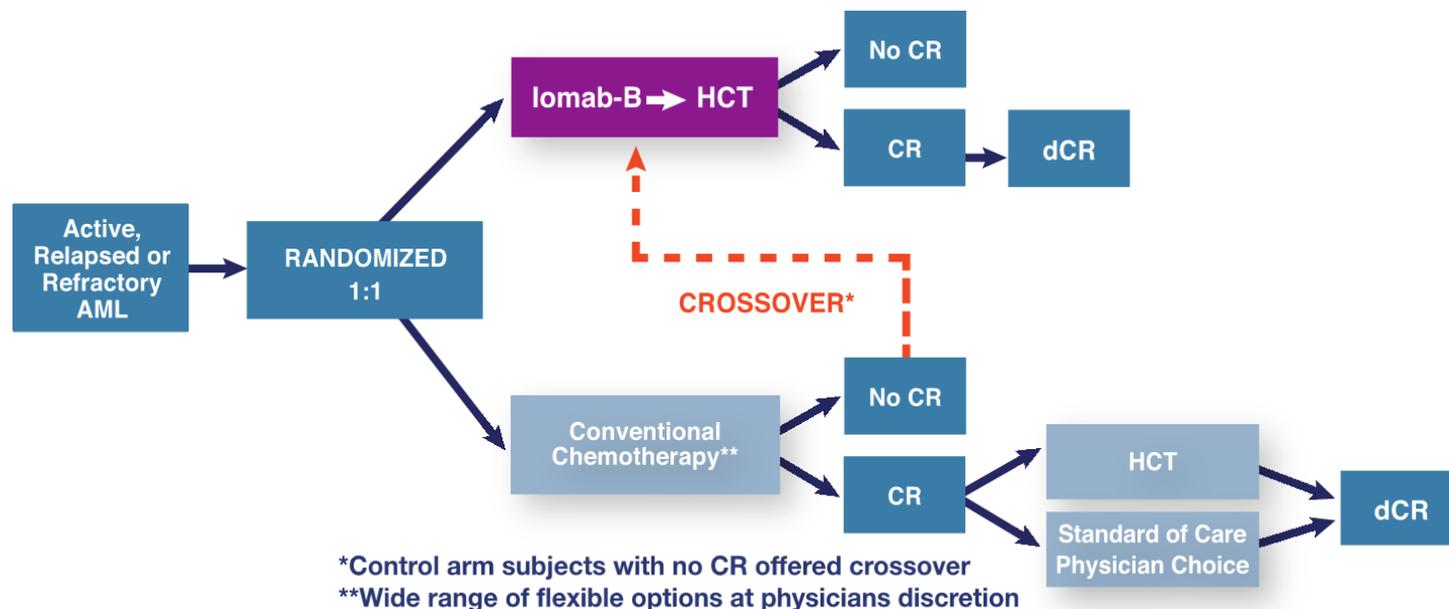


T-cell

- 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)

SIERRA Phase 3 Trial Design

Study Design (N=150)



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

SIERRA Key Eligibility Criteria

- Bone marrow blast count $\geq 5\%$ or the presence of peripheral blasts
- ≥ 55 years of age
- Karnofsky score ≥ 70
- Medically cleared donor related/unrelated, 8/8 allele-level, matching at HLA-A, HLA-B, HLA-C, and DRB-1
- Secondary AML or treatment-related AML are eligible
- **Active, relapsed or refractory AML is defined as either:**
 - (1) Primary Induction Failure (PIF) after 2 or more cycles of therapy that includes either chemotherapy OR
Two or more cycles of Venetoclax in combination with Azacitidine or Decitabine (newly added)
 - (2) First early relapse after a remission duration of fewer than 6 months, OR
 - (3) Relapse refractory to salvage combination chemotherapy containing high-dose Cytarabine, OR
 - (4) Second or subsequent relapse

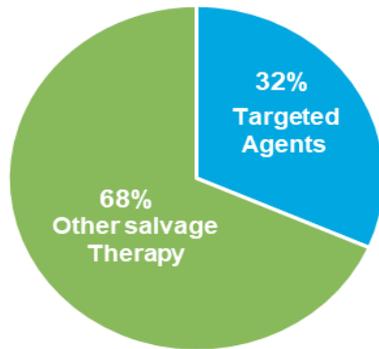
Analyzing the Inclusion of Targeted Agents in SIERRA

Therapies Prior to Enrollment into the Trial:

85% patients enrolled had failed ≥ 2 regimens (induction/re-induction)

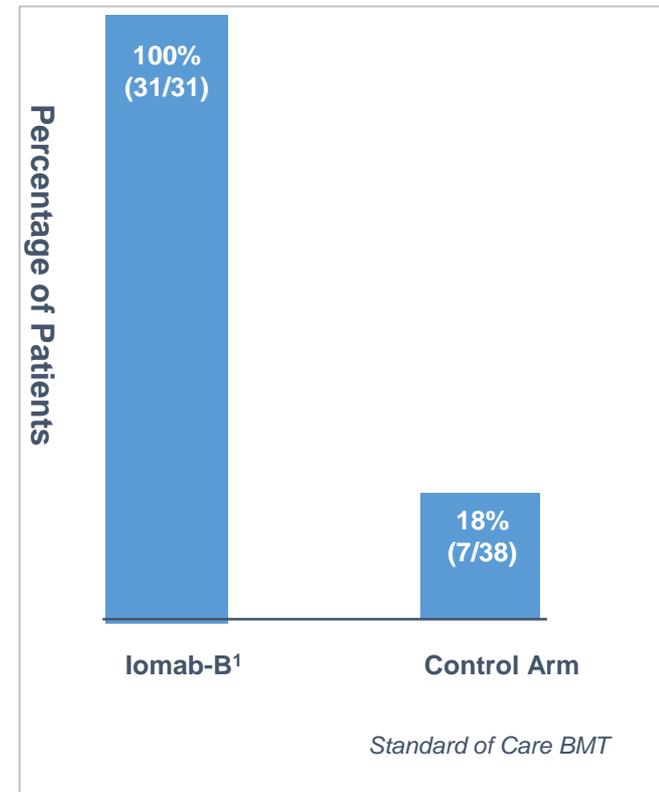
33% had failed targeted therapies

Therapies After Enrollment: Control Arm



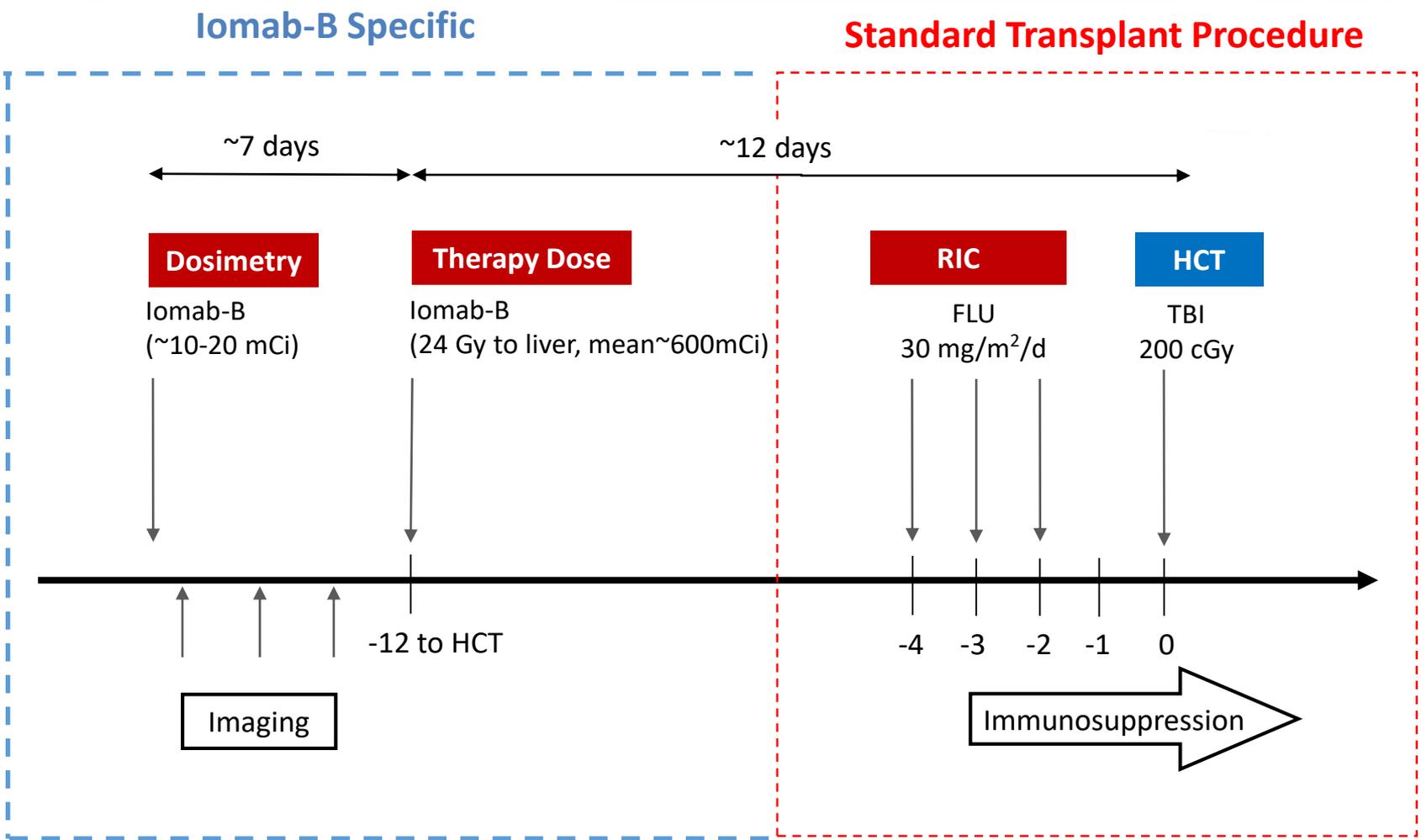
- 12/38 patients (32%) in the control arm received targeted therapies
- 11/12 patients (92%) received venetoclax + HMA or LDAC
- 3/11 patients (27%) of venetoclax patients went to std of care HCT

HCT Rate After lomab-B vs Std of Care Control



1) Patients receiving a therapeutic dose of lomab-B

SIERRA Iomab-B Treatment Schedule



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 of first 75 patients (50% Enrollment)

Phase 3 SIERRA Trial Patient Characteristics (N=75)		
	Randomized to lomab-B (N=37)	Randomized to Conventional Care (N=38)
Age median, (range)	65 (55-77)	64 (55-76)
Molecular & Cytogenetic Risk^{1,3}	Favorable: 0% Intermediate: 34% Adverse: 66%	Favorable: 5% Intermediate: 29% Adverse: 66%
% Bone Marrow Blasts at Randomization median, (range)	29% (5-88) ²	26% (5-97)
Disease Status at Randomization N, (%)	Primary Induction Failure: 21 (57) First Early Relapse: 6 (16) Relapse/Refractory: 6 (16) 2 nd + Relapse: 3 (8)	Primary Induction Failure: 18 (47) First Early Relapse: 6 (16) Relapse/Refractory: 9 (24) 2 nd + Relapse: 5 (13)
# Prior Regimens at Randomization median, (range)	3 (1-5)	3 (1-5)

Randomized to Conventional Care and Crossed Over to lomab with HCT (N=20)
63 (56-72)
Favorable: 5% Intermediate: 30% Adverse: 65%
At randomization: 31% (6-87) At crossover: 35% (5-75)
Primary Induction Failure: 8 (40) First Early Relapse: 4 (20) Relapse/Refractory: 7 (35) 2 nd + Relapse: 1 (5)
3 (1-5)

- 1) Data unavailable for two patients in the lomab-B group
- 2) 1 patient with 4% blasts in the marrow had circulating AML blasts
- 3) Per NCCN guidelines version 3. 2020

Novel Re-induction and Targeted Conditioning Therapy Yields Encouraging Results in Active, Relapsed or Refractory AML

	Randomized to Study Arm (N=37)	Randomized to Conventional Care (N=38)	
	Received Therapeutic Dose of lomab-B, transplanted 100% (N=31/31) ¹	Achieved CR and received standard of care transplant 18% (N=7/38)	Did not Achieve CR (N=31/38)² Crossed over, lomab-B therapy and transplanted 100% (N=20/20) ²
Days to Absolute Neutrophil Count (ANC) Engraftment	15 (9-22) ³	18 (13-82) ⁴	14 (10-37) ⁵
Days to Platelet Engraftment	20 (4-39) ³	22 (9-35) ⁴	19 (13-38) ⁵
Days to HCT (Post Randomization)	30 (23-50)	67 (51-86)	64 (44-161) ⁶

Key Data Highlights:

- Despite high blast counts, 100% evaluable patients receiving therapeutic lomab-B successfully engrafted^{3,5}
- 7/38 (18%) of patients achieved a CR on the control arm and received a standard of care (SOC) HCT
- 31/38 (82%) of patients did not achieve a CR and 20/31 (65%) of patients crossed over to receive lomab-B + HCT
- If randomized to conventional care arm, time to HCT after cross over to lomab-B is consistent with SOC transplant

1) No therapy dose (6) due to: declining KPS (3), Infusion reaction (1), unfavorable biodistribution (1), post-randomization eligibility (1). 2/6 did not receive DI, 4/6 received DI without proceeding to TI.

2) 9 Ineligible for crossover due to: hospice care/progression (4), declined/ineligible for HCT (2), died pre-crossover (3),
2 eligible for crossover and did not receive lomab-B due to declining status, received DI without proceeding to TI

3) ANC engraftment data not available (1), platelet engraftment data not available (4)

4) ANC and platelet engraftment data not available (1), engraftment failure (1)

5) ANC engraftment data not available (1) out of 20, platelet engraftment data not available (3)

6) 1 patient at 161 days had delayed transplant due to infection and respiratory failure, received lomab-B and BMT when stable

100 Days Post-Transplant Non-Relapse Mortality

Favorable safety profile for lomab-B observed with low 100-day non-relapse transplant related mortality

	Randomized to lomab-B (N=37)	Randomized to Conventional Care (N=38)	
	Received lomab-B therapeutic dose, transplanted (N=31)	Achieved CR and received standard of care transplant (N=7)	Did not Achieve CR Crossed over to lomab-B arm and transplanted (N=20)
100-Day Non-Relapse Transplant Related Mortality	2/31 (6%)	2/7 (29%)	2/20 (10%)
Dose Delivered to Bone Marrow	15.5 (4.6-32) Gy 616 (366-1027) mCi	n/a	14.4 (6.3-30) Gy 560 (313-1008) mCi

Key Data Highlights:

- Lower 100-day non-relapse transplant related mortality rates observed in lomab-B arm and cross over than control patients
- lomab-B delivers high amounts of radiation to the site of disease but is well tolerated with minimal extramedullary toxicities due to its targeted mechanism of action

Non-Heme Grade 3 or 4 AEs (>10% of all patients)

Up to a 100-days post transplant or till crossover assessment*

Adverse Event	Randomized to lomab-B Study Arm (N=35) (%)	Randomized to Conventional Care Arm (N=37) (%)
Febrile Neutropenia	8 (22.9)	17 (45.9)
Sepsis/Septic Shock	1 (2.9)	8 (21.6)
Pneumonia/Lung Infection	6 (17.1)	7 (18.9)
Device related infection	3 (8.6)	5 (13.5)
Stomatitis (mucositis)	4 (11.4)	4 (10.8)
Hypertension	6 (17.1)	3 (8.1)

Key Data Highlights from lomab-B study group

- Reduced incidence of febrile neutropenia, low rate of sepsis
- Within expected range of transplant related AEs
 - Acute GVHD: Grades 2-4 9/31 (29%), Grade 2 (n=6) Grade 3 (n=2) Grade 4 (n=1)
 - Chronic GVHD: Mild (n=1) Moderate (n=1)
 - VOD: Grade 1 (N=1). Day 13 to 103 post transplant, Grade 2 (N=1). Day 9 to 17 post transplant. Both Resolved

* Nine subjects on conventional care arm did not achieve CR and did not proceed to crossover. AE profile not collected post cross-over assessment as per protocol

^ Data reported on 72 of 75 Patients in the Intent-to-Treat Analysis Group – 3 subjects with data unavailable at the time of data cut

All AEs reported irrespective of attribution to protocol-directed procedures

Iomab-B vs Standard of Care HCT group

Non-Heme Grade 3 or 4 AEs in Transplanted Patients (Up to 100-days post transplant)

Adverse Event	Randomized to Iomab-B Arm and transplanted N=31 (%)	Randomized to Conventional Care with CR and transplanted N=7 (%)
Febrile neutropenia	8 (25.8)	3 (42.8)
Sepsis/Septic Shock	1 (3.2)	3 (42.8)
Stomatitis (mucositis)	3 (9.7)	2 (28.6)
Pneumonia/Lung Infection	4 (12.9)	1 (14.3)
Hypertension	6 (19.4) ¹	1 (14.3)
Decreased appetite	5 (16.1)	0 (0.0)
Device related infection	2 (6.5)	1 (14.3)
Hypophosphatemia	2 (6.5)	1 (14.3)

Key Data Highlights:

- Lower incidence of febrile neutropenia, and sepsis in the Iomab-B group
- Reduced incidence of mucositis/stomatitis with Iomab-B compared to standard of care transplant

1) Hypertension considered Unrelated to Iomab-B (5), Possibly related to Iomab-B (1)

All AEs reported irrespective of attribution to protocol-directed procedures

Conclusions from first 50% of Patients Enrolled in SIERRA

- ✓ **SIERRA is the only randomized Phase 3 trial to offer allogeneic HCT to patients with active rel/ref AML**
- ✓ **77% of all enrolled patients were able to receive transplant**
Only 18% in the control arm achieved remission and were transplanted conventionally
- ✓ **100% engraftment and low Transplant Related Mortality after Iomab-B/HCT**
Despite high pre-transplant median blast count of ~30%
- ✓ **Low rate of mucositis, febrile neutropenia, and sepsis with Iomab-B**
- ✓ **In addition to patients not responding to chemotherapy, patients not responding to venetoclax/HMA are now eligible for SIERRA**

1) Agura et al. 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 AML (R/R AML): Safety & Feasibility Data from the Prospective Randomized Phase III Sierra Trial. TCT 2019 Abstract # LBA3

Acknowledgements and Currently Active Sites

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AD MAJOREM DEI GLORIAM
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