High Rates of Transplantation in the Phase III SIERRA Trial Utilizing Anti-CD45 Apamistamab with 131-Iodine (Iomab-B) Conditioning with Successful Engraftment and Tolerability in Relapsed/Refractory Acute Myeloid Leukemia Patients after Lack of Response to Conventional Care and Targeted Therapies

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

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Relevant Disclosures

- **Dr. Sunil Abhyankar**: Incyte, Therakos
- **Dr. George Chen**: Actinium
- **Dr. James Foran**: Pfizer, Novartis, Servier, BMS, Revolution Medicine, Taiho, Syros, Sanofi, Certara, Gamida, OncLive, AbbVie, Boehringer Ingelheim, Takeda, Xencor, Trillium, Aptose, Actinium, Kura, H3 Biomedicine, Aprea, Sella, Stemline
- **Dr. Sergio Giralt**: Actinium, Celgene, BMS, Sanofi, Amgen, Pfizer, Janssen, GSK, Jazz
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- **Dr. Michael Schuster**: Takeda, MorphoSys, Astellas Pharma, Intellisphere, AbbVie, Pharmacyclics, Janssen, Epizyme, BMS, BeiGene, Actinium, Rafael Pharmaceuticals, GSK, AlloVir, Incyte, Seattle Genetics, Novartis, Genentech, Amgen, Celgene
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Background & Objectives

- Patients 55 years and older with relapsed/refractory (R/R) acute myeloid leukemia (AML) with active disease are usually not considered candidates for potentially curative allogeneic hematopoietic cell transplantation (HCT).

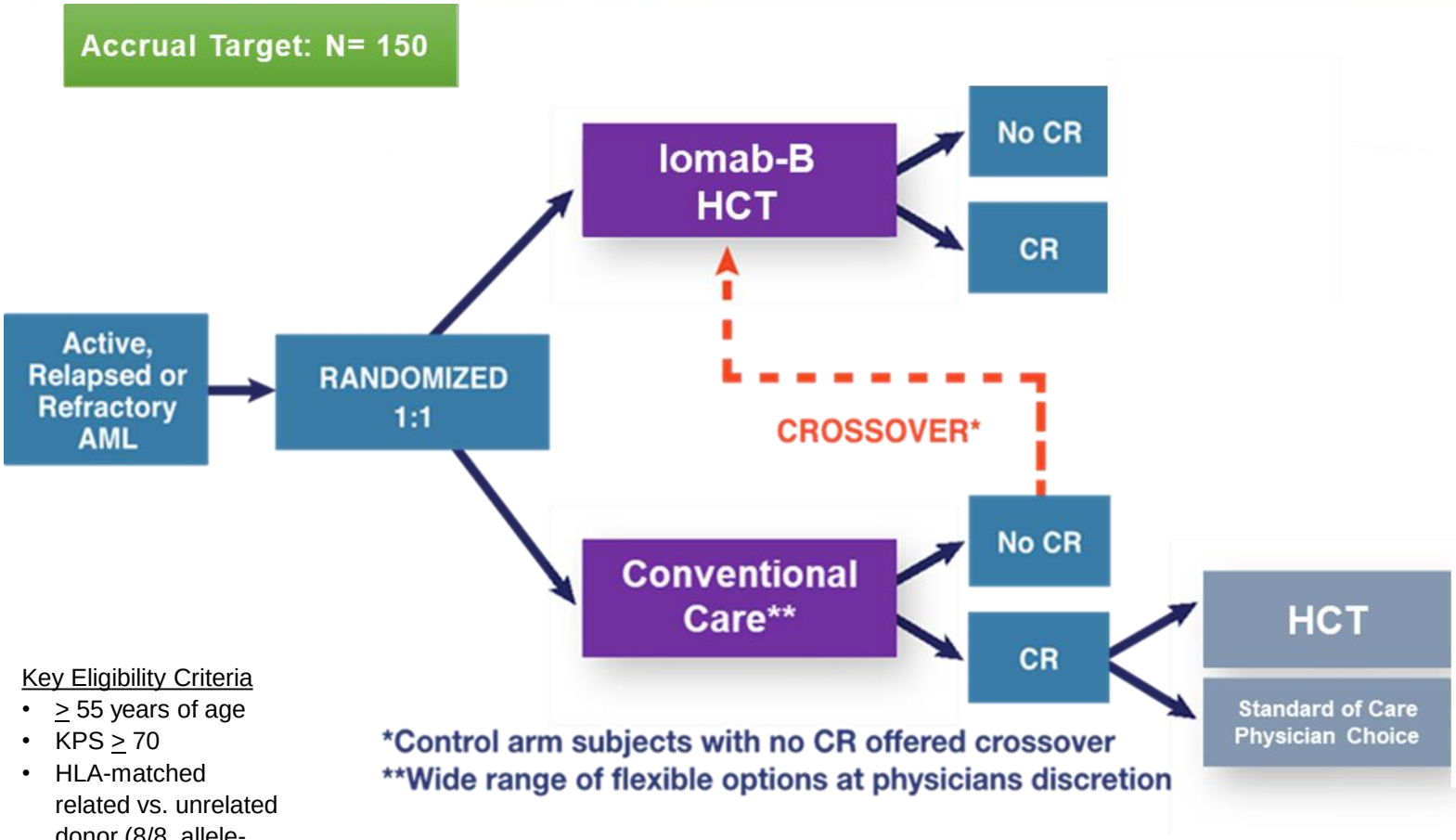
- Complete remission (CR) rates in R/R AML patients remain low despite recently approved targeted therapies (e.g., BCL-2, FLT-3, and IDH-1/IDH-2 inhibitors).

- We report on the rates of transplant in patients with R/R AML with Iomab-B-based conditioning in the SIERRA trial, along with engraftment and tolerability.

Iomab-B: Iodine (^{131}I) apamistamab

- Radioactive iodine (^{131}I) - labeled anti-CD45 antibody was developed at Fred Hutchinson Cancer Research Center.
- CD45 is expressed on hematopoietic cells, including majority of malignant myeloid, lymphoid and immune cells.
- Targeted hematopoietic irradiation delivering higher estimated radiation dose to red marrow and spleen than to liver, the normal organ receiving the highest dose
- Robust safety and long-term efficacy data in approximately 350 patients treated on multiple clinical trials.

SIERRA Phase III Study Design



Key Eligibility Criteria

- ≥ 55 years of age
- KPS ≥ 70
- HLA-matched related vs. unrelated donor (8/8, allele-level)

- Primary Induction Failure
- First Early Relapse
- Relapse/Refractory to Salvage
- 2nd + Relapse

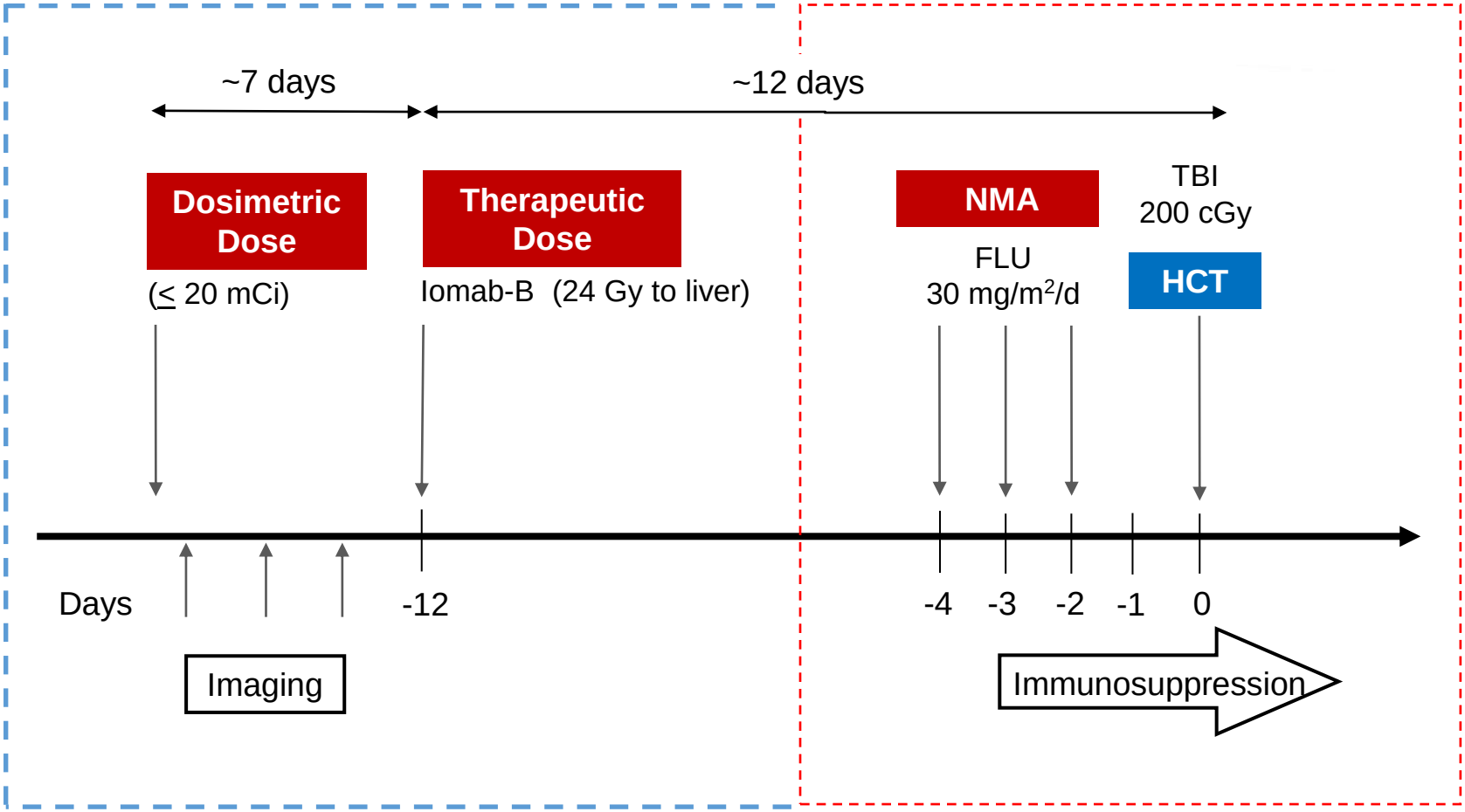
Primary Endpoint

6-month dCR

Secondary Endpoint

Overall Survival

SIERRA Iomab-B Treatment Schedule



NMA: nonmyeloablative conditioning; FLU: fludarabine; TBI: total body irradiation; HCT: hematopoietic cell transplant

Therapeutic dose individualized based on upper limit of 24 Gy liver exposure

Patient Characteristics

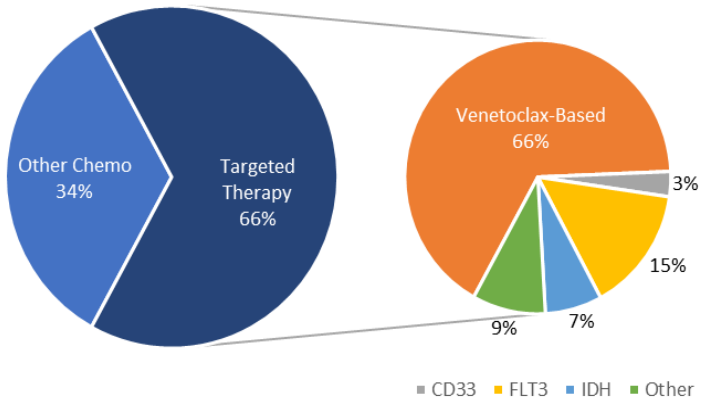
Complete Enrollment, N = 153			
	Iomab-B Arm (76)	**Conventional Care Arm (77)**	**Crossed Over to Iomab-B with HCT (40)**
Age median, (range)	**65.0** (55.1-77.3)	**66.1** (55.1-76.8)	**64.6** (55.3-76.8)
Cytogenetic and Molecular Risk	Favorable: 5.3% Intermediate: 32.9% Adverse: 60.5%	Favorable: 3.9% Intermediate: 33.8% Adverse: 62.3%	Favorable: 5% Intermediate: 35% Adverse: 60%
Disease Status at Randomization N, (%)	Primary Induction Failure: **43** (56.6) First Early Relapse: **17** (22.4) Relapse/Refractory: **11** (14.5) 2nd + Relapse: **5** (6.6)	Primary Induction Failure: **39** (50.6) First Early Relapse: **21** (27.3) Relapse/Refractory: **12** (15.6) 2nd + Relapse: **5** (6.5)	Primary Induction Failure: **20** (50.0) First Early Relapse: **11** (27.5) Relapse/Refractory: **7** (17.5) 2nd + Relapse: **2** (5.0)
% Marrow Blasts at Randomization median, (range)	**30%** (4-97)	**19.5%** (2.8-97.4)	**35%** (2-78) at crossover

Targeted Therapy Pre & Post Enrollment

66% patients received targeted therapies prior to SIERRA enrollment

- Of those, 66% received Venetoclax-based therapy
- Median of 3 prior regimens (range 1-7)

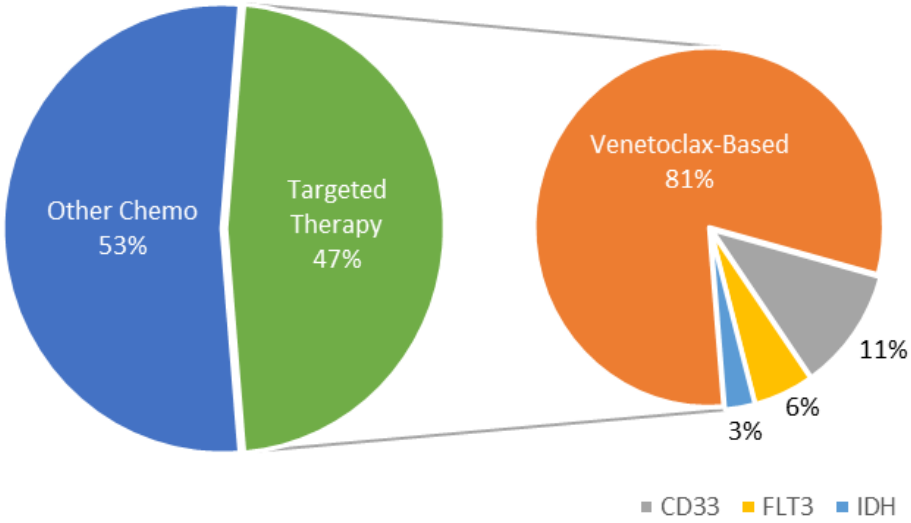
Targeted Therapy Pre-Enrollment



47% of patients enrolled to the CC arm received targeted agents

- Of those, 81% received Venetoclax-based therapy
  - Approximately 50% of whom failed and were rescued with Iomab-B

Use of Targeted Therapy in CC Group



Transplant Characteristics & Engraftment

Patients who received Iomab-B and are evaluable demonstrated **100% engraftment.**

Transplant Characteristics	Iomab-B Arm (76)	Conventional Care (77)	
	Received Iomab-B/HCT (66)	Did not Achieve CR Crossed over to Iomab-B/HCT (40)	Achieved CR and received standard of care HCT (14)
Total Iomab-B Activity median (range)	**649.5** (354-1027) mCi	**606.5** (313-1013) mCi	N/A
Dose to Marrow median (range)	**15.9** (4.6-44.6) Gy	**16.1** (6.3-41.8) Gy	N/A
CD34+ Cells x10^6 /Kg Median (range)	**5.5** (1.8 – 207.9)	**5.4** (1.8-16.1)	**5.0** (0.7-25.1)
Type of Graft	Marrow: 4, PBSC: 62	Marrow: 2, PBSC: 38	Marrow: 2, PBSC: 12
	Related: 25, Unrelated: 41	Related: 13, Unrelated: 27	Related: 5, Unrelated: 9
ANC Engraftment **PLT Engraftment** Median days (range)	ANC 14 (9-31) PLT 17 (4-40) **0/66 engraftment failure**	ANC 13 (10-35) PLT 17 (1-38) **0/40 engraftment failure**	ANC 16 (1-83) PLT 14 (8-35) **1/14 engraftment failure**

Day +100 Non-Relapse Mortality (NRM)

	Received Iomab-B/HCT (66)*	Crossed over to Iomab-B/HCT (40)	Standard of Care HCT (14)
Day +100 NRM Out of Evaluable Patients	**6/65**	**2/40**	**2/14**

* One patient not evaluable due to withdrawal of consent

Grade ≥3 Adverse Events (AEs) in ≥10% of All Patients

Adverse Event	Iomab-B Arm (N=76) % (N)	Conventional Care Arm (N= 77) % (N)
Febrile Neutropenia (FN)	27 (35.5)	35 (45.4)
Sepsis[1] *p = 0.002*	4 (5.3)	18 (23.4)
Mucositis[2]	10 (13.2)	9 (11.7)
Hypertension	9 (11.8)	11 (14.3)
Pneumonia	6 (7.9)	10 (13.0)
Hypoxia	6 (7.9)	10 (13.0)
Hypophosphataemia	6 (7.9)	8 (10.4)
Device-related infection	4 (5.3)	8 (10.4)
Acute Respiratory Failure	2 (2.6)	8 (10.4)
Acute Kidney Injury	3 (3.9)	2 (2.6)
Venoocclusive liver disease	1 (1.3)	0 (0)

1. "Sepsis" includes Preferred Terms of Sepsis, Septic Shock & Neutropenic Sepsis
2. "Mucositis" includes Preferred Terms of Stomatitis & Mucosal Inflammation

Conclusions

- **High rate of allogeneic HCT with Iomab-B-based** conditioning in patients with R/R AML
  - *Majority of study patients were able to undergo allogeneic HCT despite not achieving CR after standard chemotherapy and targeted agents.*

- **100% neutrophil and platelet engraftment**
  - *All evaluable study patients receiving Iomab-B-based conditioning followed by allogeneic HCT engrafted.*

- **Lower incidence of sepsis**
  - *Iomab-B-based conditioning was well tolerated, with a lower incidence of sepsis compared to the CC group.*

Clinical Sites