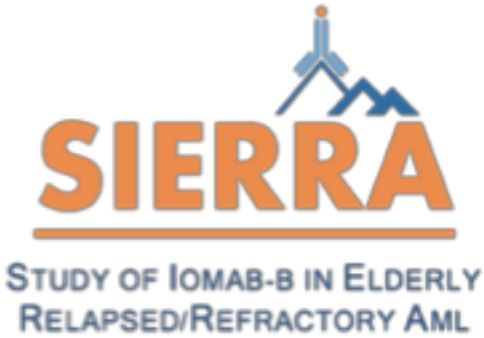
Targeted Conditioning of Iomab-B (^{131}I-anti-CD45) Prior to Allogeneic Hematopoietic Cell Transplantation Versus Conventional Care in Relapsed or Refractory Acute Myeloid Leukemia (AML): Preliminary Feasibility and Safety Results from the Prospective, Randomized Phase 3 Sierra Trial



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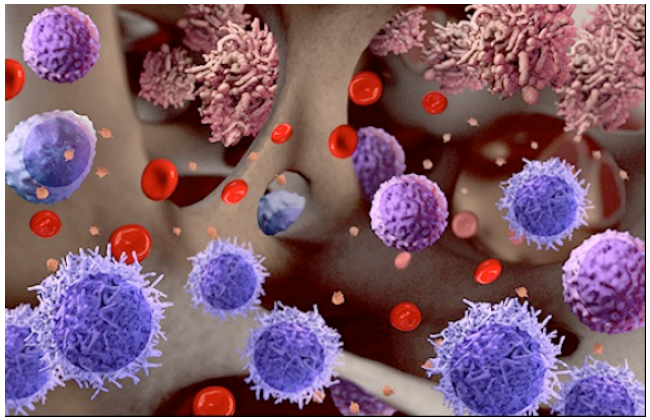
Iodine (^{131}I) apamistamab [Iomab-B] CD45 Targeted Conditioning

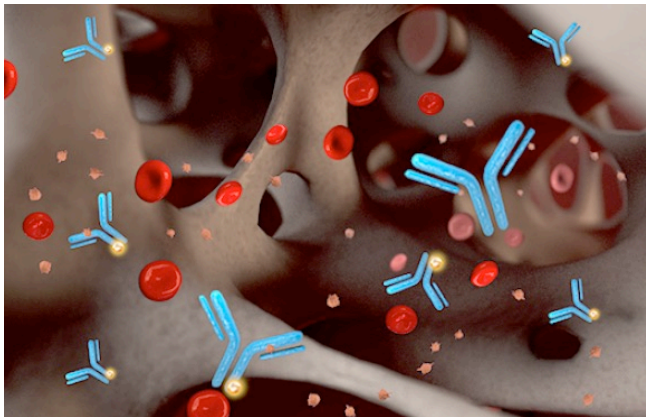
- Iodine (^{131}I) apamistamab [Iomab-B] is a murine anti-CD45 targeted therapy that was developed at the Fred Hutchinson Cancer Research Center
- Encouraging Phase II data led to the ongoing SIERRA Phase III trial
- CD45 is expressed on hematopoietic cells, including leukemia cells, lymphoma cells and 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

Leukemic Bone Marrow

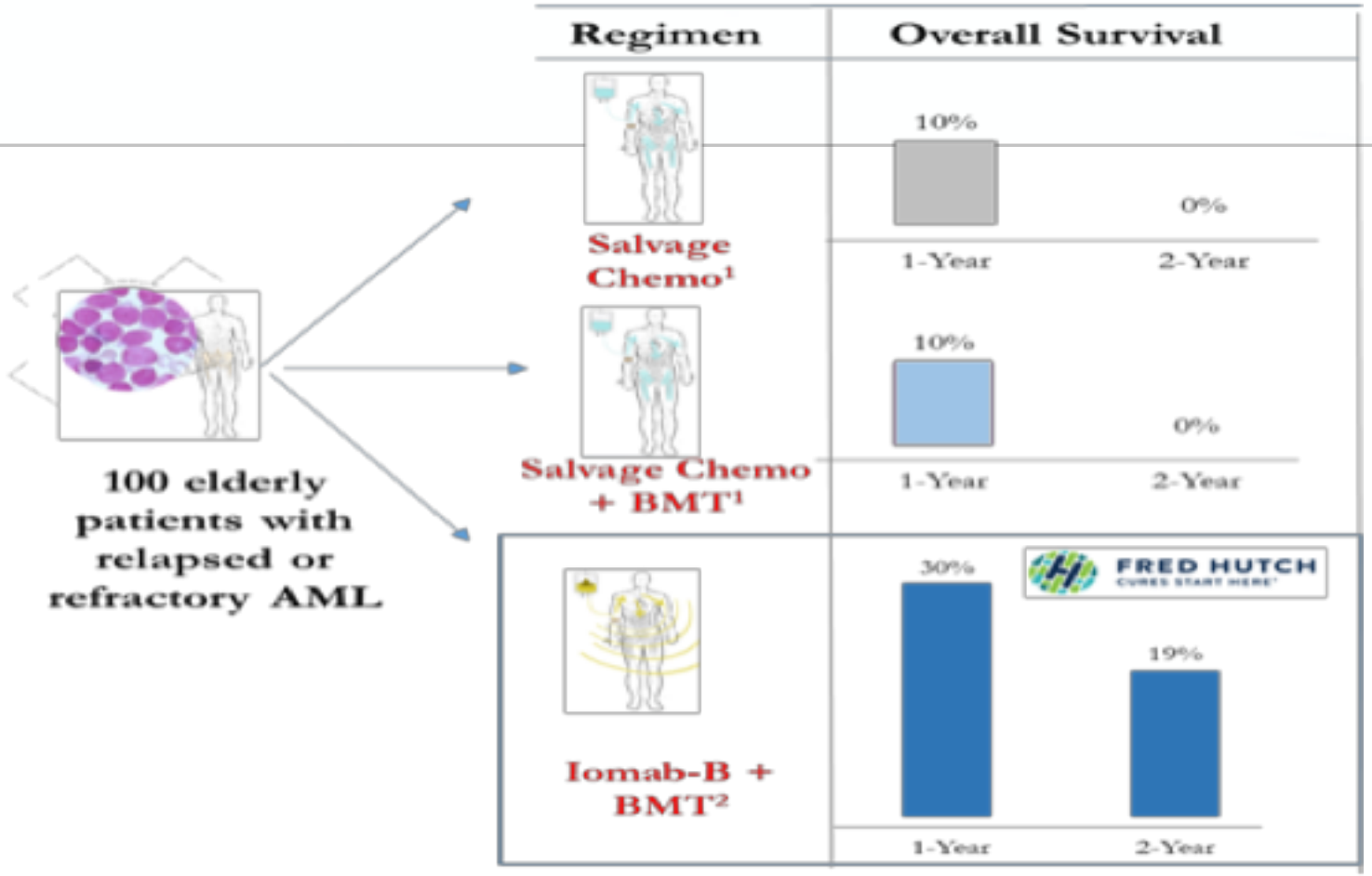


Iomab-B

Post-Iomab-B Myeloablated Bone Marrow



Iomab-B Potential – Background and Rationale

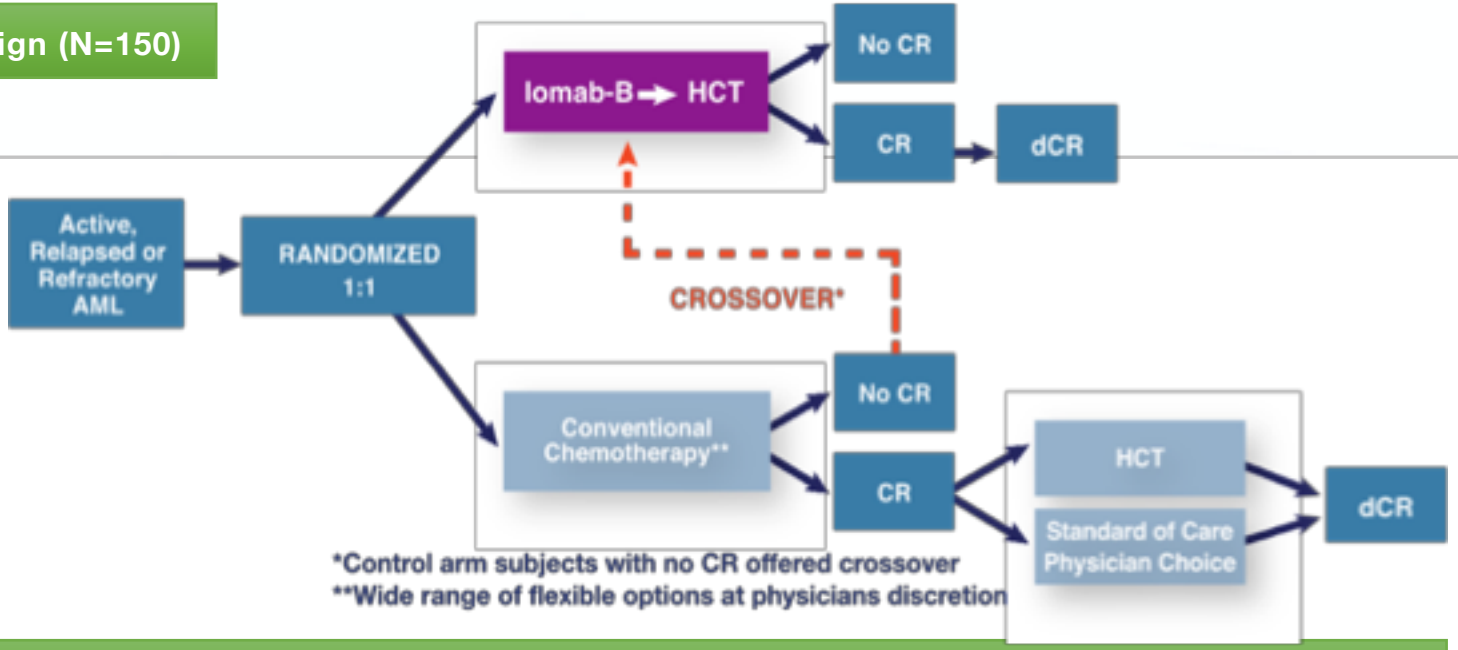


1) Biol Blood Marrow Transplant 15 :1431-1438 (2009), MD Anderson outcomes analysis. (Chemo + BMT n=19) (Salvage Chemo n = 95)
2) Iomab-B BMT: *Blood* 114:5444-5453 (2009) and additional data on file Pagel et. al. (n=36)

- 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): morphologic CR lasting ≥180 days
Secondary End-point: 1-year Overall Survival

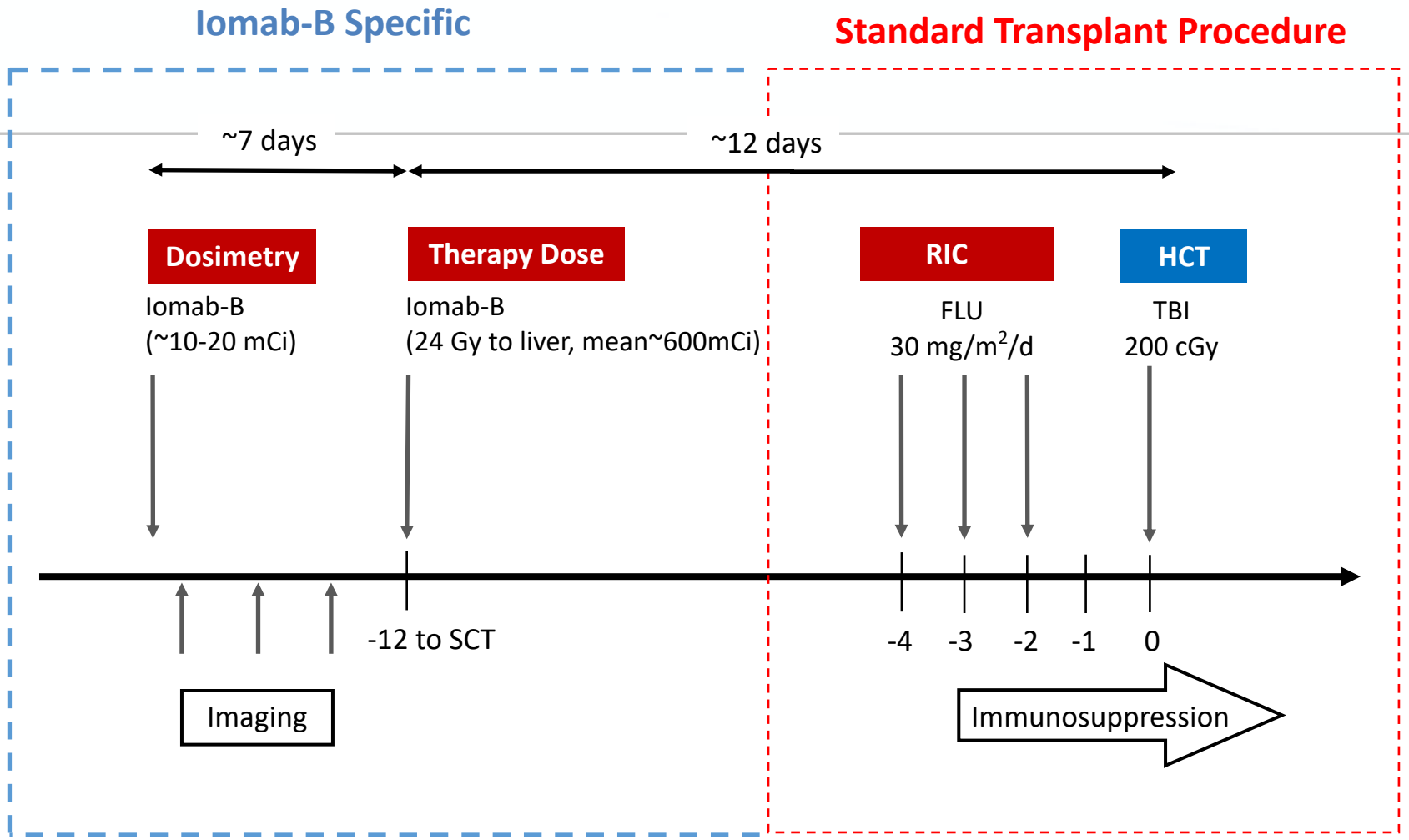
Key Eligibility Criteria:

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



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)			
	Randomized to Iomab-B Study Arm (N=19)	**Randomized to Conventional Care (N=19)**	**Randomized to Conventional Care and Crossed Over (N=10)**
Age (median, range)	62 (55-72)	64 (55-76)	63 (58-72)
Disease Status At Randomization	Primary Induction Failure (10) First Early Relapse (1) Relapsed / Refractory (4) 2nd / Subsequent Relapse (3) ***1 patient not entered*	Primary Induction Failure (6) First Early Relapse (1) Relapsed / Refractory (8) 2nd / Subsequent Relapse (4)	Primary Induction Failure (3) First Early Relapse (0) Relapsed / Refractory (6) 2nd / Subsequent Relapse (1)
% Bone Marrow Blasts at Randomization (median, range)	**30%** (4*-74)	**26%** (6-97)	**At randomization: 24% (6-70)** **At crossover: 45% (10-70)**

*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

Median (range)	Randomized to Iomab-B and transplanted (N=18/19)^	Randomized to Conventional Care (N=19)	
		Achieved CR and received standard of care transplant (N=4)	Did not achieve CR Crossed over to Iomab-B arm and transplanted (N=10/15) ^^
Days to ANC Engraftment	**13** (9-22)***	Not collected	**13** (9-20)
Days to Platelet Engraftment	**16** (13-26)***	Not collected	**17** (10-20)**
Days to HCT (Post Randomization)	**28** (23-38)	**67** (66-86)	**66** (57-161)****
Dose Delivered to Bone Marrow	**18** (8.2-32) Gy 616 (397-1027) mCi	n/a	**16** (6.3-20) Gy 518 (313-1008) mCi

^ 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 Iomab & transplant when stable

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

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

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

* **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

Adverse Event (>10% of total patients)	Randomized to Iomab-B Study Arm N=19 (%)	Crossed over to Iomab-B arm and transplanted N=10 (%)
Febrile Neutropenia	4 (21)	4 (40)
Stomatitis	3 (16)	2 (20)
Malnutrition	2 (11)	2 (20)
Epistaxis	2 (11)	2 (20)
Sepsis	0 (0)	3 (30)
Hypotension	1 (5)	2 (20)
Hyperbilirubinemia	1 (5)	1 (10)
Fatigue	3 (16)	0 (0)

- **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

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

- 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