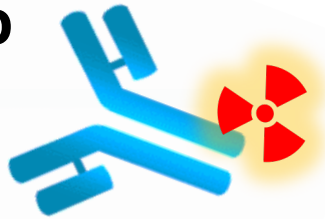
Myeloablative Targeted Conditioning with Anti-CD45 Iodine (131I) Apamistamab [Iomab-B] Spares the GI Tract and Has Low Incidence of Severe Mucositis, Febrile Neutropenia and Sepsis in the Prospective, Randomized Phase 3 Sierra Trial for Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML)

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

Rajneesh Nath, MD, Boglarka Gyurkocza, MD, Hannah Choe, MD, Stuart E. Seropian, MD, Patrick Stiff, MD, Edward Agura, MD, Sunil Abhyankar, MD, Mark R. Litzow, MD, Benjamin Tomlinson, MD, Camille Abboud,MD, George L Chen, MD, Parameswaran Hari, MD, MRCP, Johnnie J. Orozco, MD, PhD, Mitchell Sabloff, MD, Zaid Al-Kadhimi, MD, Koen Van Besien, MD, PhD, Margarida Silverman, MD, James Foran, MD, Michael W Schuster, MD, Partow Kebriaei, MD, Moshe Yair Levy, MD, Hillard M. Lazarus, MD, Sergio A Giralt, MD, Qing Liang, PhD, Mark S. Berger, MD, Vijay Reddy, MD, PhD and John M. Pagel, MD, PhD

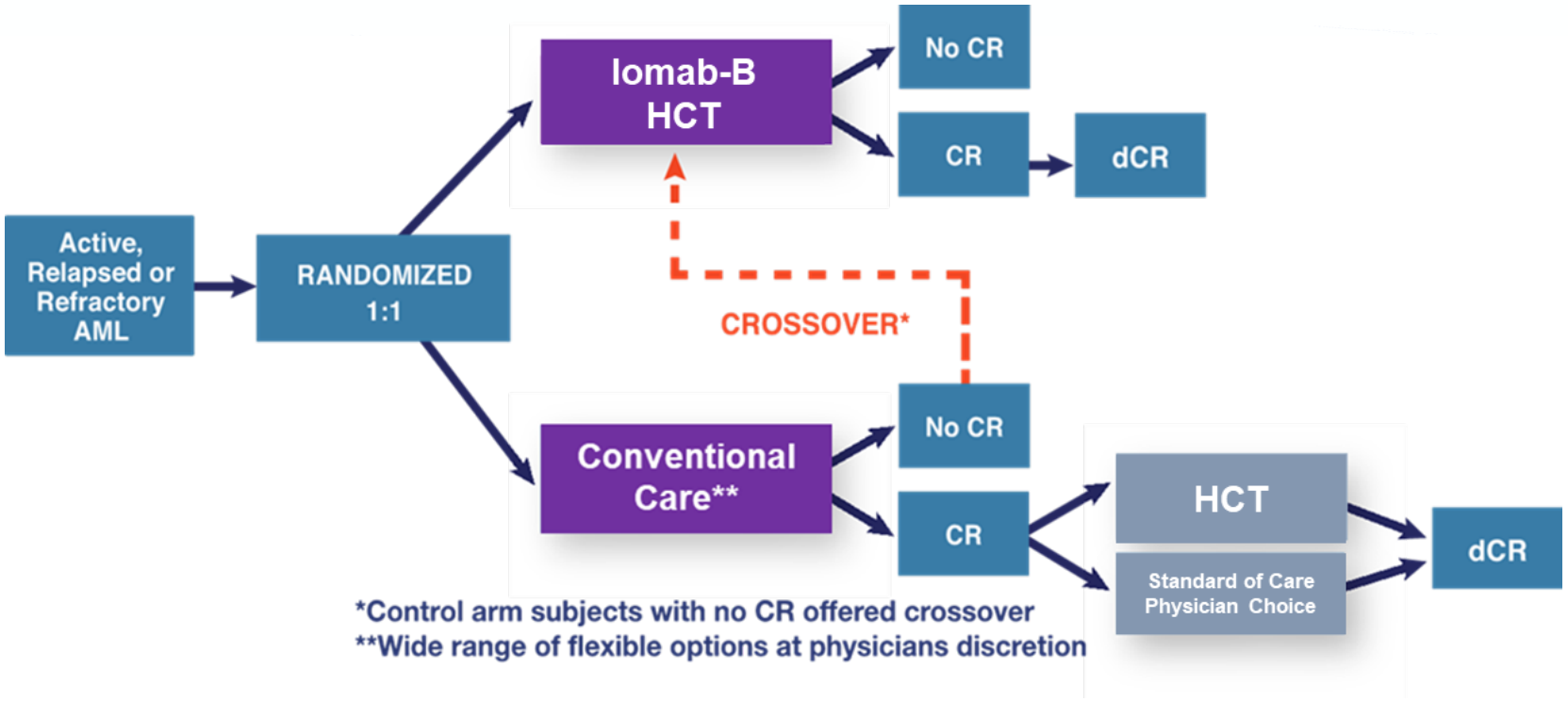
Iomab-B: Iodine (^{131}I) apamistamab



- Radioactive iodine (^{131}I) - labeled anti-CD45 antibody that was developed at the Fred Hutchinson Cancer Research Center
- CD45 is expressed on hematopoietic cells, including the majority of malignant myeloid and lymphoid cells
- Patient-specific dosimetry is used to generate individualized therapeutic dose to target marrow and spare non-hematopoietic organs
- Robust safety and long-term efficacy data in 271 patients treated on 9 different phase 1 and 2 clinical trials

SIERRA Phase 3 Trial Design

Accrual Target: N=150



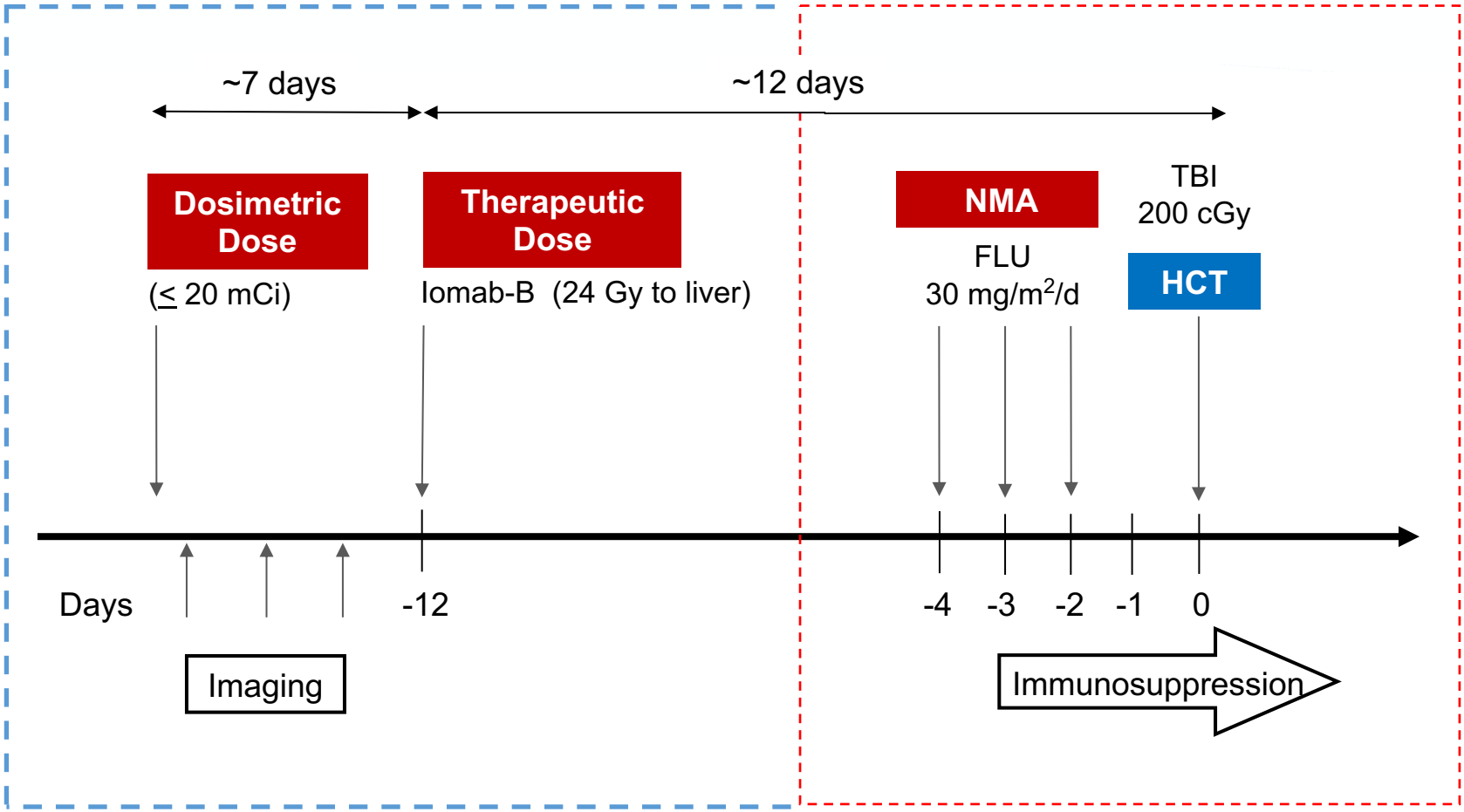
Primary End-point: Durable Complete Remission Rate (dCR): CR/CRp at 6 months post-CR

Secondary End-points Include: Overall Survival and Event-Free Survival

SIERRA Key Eligibility Criteria

- Marrow blast count ≥ 5% or the presence of peripheral blasts
- ≥ 55 years of age
- Karnofsky score ≥ 70
- Medically cleared related/unrelated donor, matching at HLA-A, HLA-B, HLA-C, and DRB-1 (8/8; allele-level)
- Secondary AML or treatment-related AML are eligible
- **Active, relapsed or refractory AML is defined as:**
  - Primary Induction Failure after 2 or more cycles of therapy that includes either chemotherapy or two or more cycles of venetoclax in combination with HMA or low-dose cytarabine
  - First early relapse after CR1 of < 6 months
  - Relapse refractory to salvage combination chemotherapy
  - Second or subsequent relapse

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

Iomab-B Provides Targeted Radiation

Hypothesis:

Iomab-B delivers myeloablative doses of radiation to the marrow and leukemia sites, while sparing other organs, like the GI tract

Reduced radiation exposure of the GI tract corresponds to improved toxicity profile, with lower rates of mucositis, neutropenic fever and sepsis

SIERRA Trial: Demographic Highlights of First 113 Patients
75% Enrollment

Patient Characteristics (N=113)			
	Iomab-B Arm (N=56)	**Conventional Care Arm (N=57)**	**Randomized to Conventional Care and Crossed Over to Iomab with HCT (N=30)[4]**
Age median, (range)	63 (55-77)	65 (55-77)	65 (55-77)
Cytogenetic and Molecular Risk[1,3]	Favorable: 4% Intermediate: 35% Adverse: 61%	Favorable: 5% Intermediate: 32% Adverse: 63%	Favorable: 7% Intermediate: 33% Adverse: 60%
% Marrow Blasts at Randomization median, (range)	29% (4-95)[2]	20% (5-97)	**At randomization:** 28% (6-87) **At crossover:** 22% (2-75)
Disease Status at Randomization N, (%)[5]	Primary Induction Failure: 31 (56) First Early Relapse: 9 (16) Relapse/Refractory: 8 (15) 2nd + Relapse: 7 (13)	Primary Induction Failure: 28 (49) First Early Relapse: 12 (21) Relapse/Refractory: 12 (21) 2nd + Relapse: 5 (8.8)	Primary Induction Failure: 14 (47) First Early Relapse: 8 (27) Relapse/Refractory: 7 (23) 2nd + Relapse: 1 (3)
# Prior Regimens at Randomization median, (range)	3 (1-7)	3 (1-6)	3 (1-5)

Randomized to Conventional Care and Received Std HCT (N=10)
FLU + Melphalan: 2
FLU + Melphalan + TBI: 1
FLU + Busulfan: 1
FLU + Cyclophosphamide + TBI: 2
No Data Available: 4

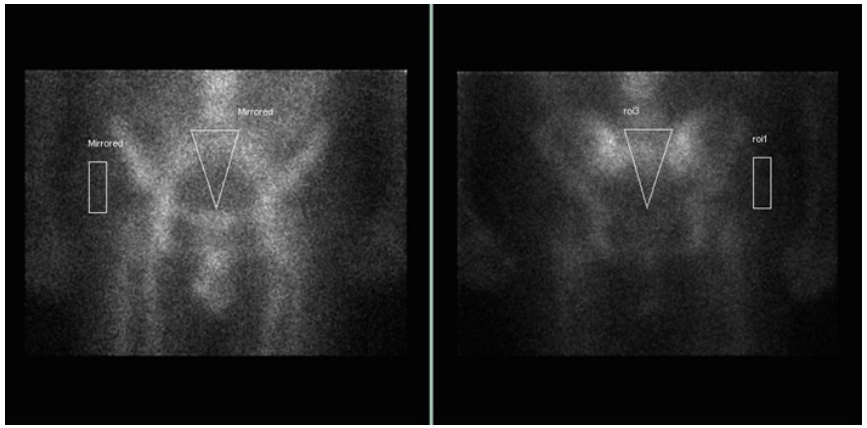
1) Iomab-B arm: data unavailable (4) and patient was excluded (1)
2) One patient with 4% blasts in the marrow had circulating AML blasts
3) Per NCCN guidelines version 3. 2020
4) Thirteen (13) patients ineligible for crossover due to: hospice care/progression (4), declined/ineligible for HCT (5), died pre-crossover (4). Four (4) patients were eligible for crossover and did not receive Iomab-B due to declining KPS
5) One pt was excluded in the Iomab-B group due to post-randomization eligibility

Day +100 Non-Relapse Mortality (NRM) & Delivered Dose

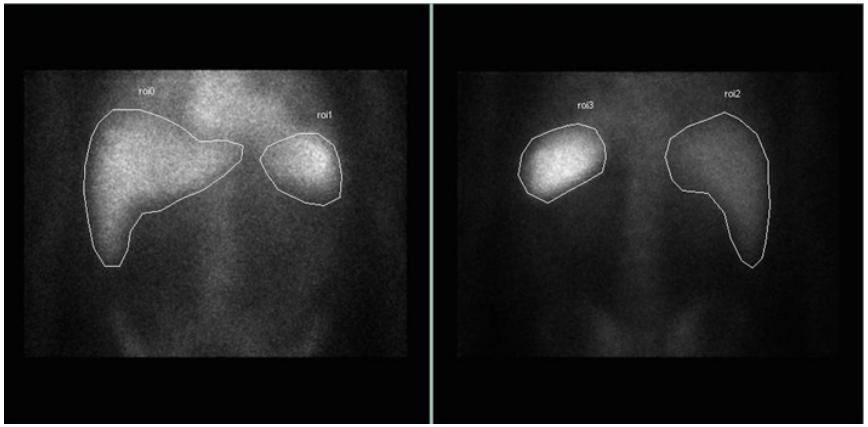
	Iomab-B Arm (N=56)[1]	Conventional Care Arm (N=57)[2]	
	Received Iomab-B/HCT (N=49)	**Achieved CR and received standard of care HCT (N=10)**	**Did not Achieve CR Crossed over to Iomab-B/HCT (N=30/47)**
Total Iomab-B Infused	**646** (354-1027) mCi	N/A	**592** (313-1013) mCi
Dose to Marrow	**14.7** (4.6-32)[3] Gy	N/A	**15.5** (6.3-42)[3] Gy
CD34+ Cells x10^6 /Kg	**5.6** (1.8-208)	**5.02** (0.68-9.8)	**5.1** (1.8-16.1)
Type of Graft	Marrow: 3, PBSC: 45 Related: 17, Unrelated: 31	Marrow: 2[4], PBSC: 8 Related: 3, Unrelated: 6 Not Reported: 1	Marrow: 2, PBSC: 28 Related: 10, Unrelated: 20
Day +100 NRM	**2/45 (4.4%)**	**2/10 (20%)**	**3/28 (10.7%)**

1) No therapy dose (7) due to: declining KPS (4), Infusion reaction (1), unfavorable biodistribution (1), post-randomization eligibility (1). 2/7 did not receive DI, 5/7 received DI without proceeding to TI.
2) 13 Ineligible for crossover due to: hospice care/progression (4), declined/ineligible for HCT (5), died pre-crossover (4); 1 patient pending crossover. 4 patients were eligible for crossover and did not receive Iomab-B due to declining KPS
3) Iomab-B arm: pt unevaluable (1); conventional care arm: pt unevaluable (1)
4) One patient had 2 HCTs

Dosimetric Imaging & Personalized Dose Calculation



Uptake in marrow[1]



Uptake in liver and spleen

- Post-dosimetry gamma camera imaging showed organ-specific uptake of Iomab-B to calculate total dose delivered to organs
  - Hematopoietic organs: marrow, spleen
  - Non-hematopoietic organs: liver, small & large bowel, stomach wall, lungs, kidneys, bladder, etc.
- Dosimetry calculations are performed using Olinda/EXM program (Version 2.1.1) using initial uptake & clearance of liver, spleen, bone marrow and total body, in addition to spleen & liver volume and patient body weight
- Radiation doses to specific organs are reported as cGy/mCi of Iomab-B infused
- Therapeutic dose was calculated to administer a maximum of 24 Gy to the liver, the dose-limiting organ

Absorbed Radiation Exposure to Specific Organs

Organ	Iomab-B Gy, Median (Range)	Iomab-B w/ Crossover Gy, Median (Range)
Stomach Wall	4.0 (2.0-8.2)	4.1 (2.1-9.3)
Small Intestine	2.6 (1.1-6.8)	3.0 (1.6-8.8)
Upper Large Intestine Wall	2.7 (1.3-6.6)	3.1 (1.7-8.6)
Lower Large Intestine Wall	2.2 (0.4-6.4)	2.5 (1.1-8.3)
Heart Wall	2.7 (1.7-6.5)	3.1 (1.7-8.4)
Lungs	2.5 (1.6-6.1)	2.9 (1.7-8.0)
Kidneys	4.3 (2.5-8.2)	4.5 (2.5-10.3)
Liver	21.6 (17.5-24.0)	21.3 (12.1-24.0)
Spleen	93.0 (36.1-158.3)	83.7 (46.1-183.6)
Red Marrow	14.6 (4.6-32.0)	15.5 (6.3-42)
Total Body	3.4 (2.0-7.0)	3.4 (2.2-10.5)

Common Non–Hematologic Grade 3 or 4 AEs

Intent-to-Treat, Regardless of Attribution to Iomab-B

Iomab-B arm: Post randomization through Day100 post HCT
CC arm (CC with standard HCT & CC with crossover): Post randomization through Day 100 post HCT
(CC no HCT): Post randomization through Day 28-42 following the salvage chemo

Adverse Event	Iomab-B Arm (N=56)[1] 49 Received Drug & HCT % (N)	Conventional Care Arm (N=57)[1] % (N)
Febrile Neutropenia	40.7 (22)	48.2 (27)
Sepsis/Septic Shock	5.6 (3)	23.2 (13)
Mucositis[2]	11.1 (6)	14.3 (8)
Pneumonia	9.3 (5)	17.9 (10)
Hypertension	16.7 (9)	12.5 (7)
Respiratory Failure[3]	7.4 (4)	14.3 (8)
Hypoxia	7.4 (4)	14.3 (8)
Catheter-related infection	7.4 (4)	10.7 (6)
Hypotension	7.4 (4)	12.5 (7)
Acute Kidney Injury	5.6 (3)	1.8 (1)
SOS/VOD (Gr 1-2)	1.9 (1)	0.0

1) Iomab-B arm: Safety data unavailable (2); conventional care arm: withdrawal prior to chemo (1)
2) Mucositis includes AE Preferred Terms: Stomatitis and Mucosal Inflammation
3) Respiratory Failure includes AE Preferred Terms: Respiratory Failure and Acute Respiratory Failure
4) Iomab-B Acute GVHD (Gr III-IV): 4/48 evaluable pts

AEs of Interest in Day +100 Post-HCT

Safety data available for first 113 patients enrolled

Adverse Event	Iomab-B Arm (N=56)[1]	Conventional Care Arm (N=57)[2]		P-value: Iomab-B vs. Std HCT
	Received Iomab-B/HCT (N=49)[3]	Achieved CR and received Std HCT (N=10)	No CR Crossed over to Iomab-B/HCT (N=30)	
Sepsis % (n)	4.2 (2)	30.0 (3)	23.3 (7)	0.03
FN Gr 3-4 % (n)	41.7 (20)	50.0 (5)	40.0 (12)	ns
Mucositis Gr 3-4 % (n)	10.4 (5)	30.0 (3)	16.7 (5)	ns

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2) 13 Ineligible for crossover due to: hospice care/progression (4), declined/ineligible for HCT (5), died pre-crossover (4); 1 patient pending crossover. 4 patients were eligible for crossover and did not receive Iomab-B due to declining KPS
3) Adverse Event data available for 48 of 49 evaluable patients

Conclusions

- Conditioning regimen including targeted radiation with Iomab-B had lower incidence* of sepsis, and trends towards reduced rates of severe mucositis, febrile neutropenia, when compared to conventional care and standard conditioning regimens

- Adverse events were not correlated to the overall radiation dose

- Targeted radiation with Iomab-B led to relatively low radiation exposure of the GI tract and a higher radiation exposure of marrow, resulting in a favorable toxicity and safety profile in older patients with relapsed/refractory AML

Acknowledgements and Currently Active Sites