
Please Share the Following Information with Your Doctor

Use this document to facilitate a discussion with your doctor
about participating in the SIERRA clinical trial.

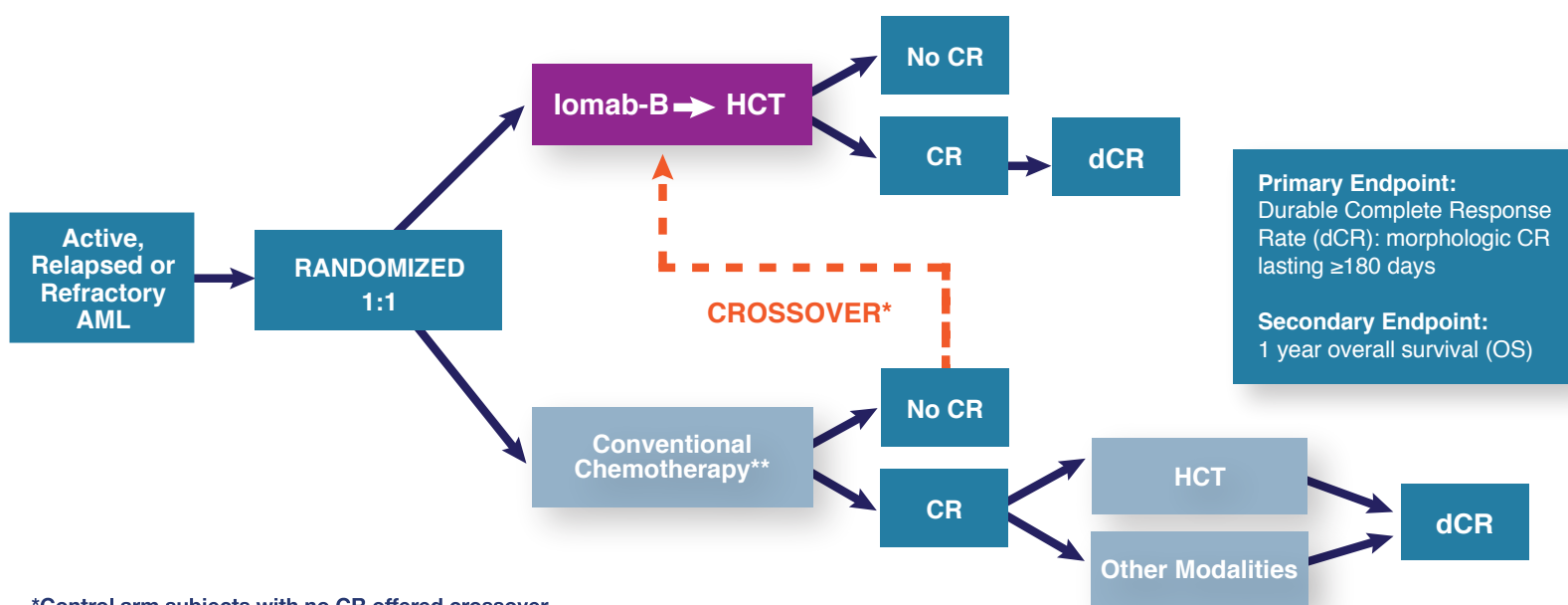
Transplant Can Be An Option for Patients with Active, Relapsed or Refractory Acute Myeloid Leukemia

SIERRA
PHASE 3 Trial
Now Enrolling
www.sierratrial.com

SIERRA (NCT02665065)

For patients ≥ 55 years with active, relapsed or refractory AML who might benefit from a transplant.
 Allogeneic HCT now (Iomab-B) or after further leukemic reduction (Conventional Care)

Study Design (N=150)



*Control arm subjects with no CR offered crossover
 **Wide range of flexible options at physicians discretion

Key Eligibility Criteria

Inclusion

- 55 years and older with active, relapsed or refractory AML as defined by:
 - Refractory AML: primary induction failure or Relapse after CR1 lasting <6 months or Second or higher relapse
 - or Relapse refractory to salvage attempt
- Matched related/unrelated donor
- Karnofsky Performance Status ≥ 70

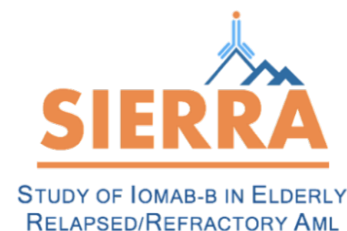
Exclusion

- Acute promyelocytic leukemia
- Active leukemic CNS involvement
- Have previously received hematopoietic cell transplant (HCT)
- Currently receiving any investigational agent

SIERRA Clinical Trial Sites

Arizona	Banner MD Anderson	Gilbert, AZ	https://bit.ly/2RgTB2w
Connecticut	Yale Cancer Center	New Haven, CT	https://bit.ly/2z5XPCG
Florida	Mayo Clinic	Jacksonville, FL	https://mayocl.in/2EOHVmp
Illinois	Loyola University	Maywood, IL	https://bit.ly/2yA4iq7
Kansas	University of Kansas	Kansas City, KS	https://bit.ly/2Pmlgls
Minnesota	Mayo Clinic	Rochester, MN	https://mayocl.in/2EOHVmp
Missouri	Washington University	St. Louis, MO	https://bit.ly/2Jkvdu6
Nebraska	University of Nebraska	Omaha, NE	https://bit.ly/2DmDi17
New York	Memorial Sloan Kettering	New York, NY	https://bit.ly/2qb5A6c
	Stony Brook University	Stony Brook, NY	https://bit.ly/2ENMbm5
	Roswell Park	Buffalo, NY	https://bit.ly/2z5qWpv
	Weill Cornell Medicine	New York, NY	https://bit.ly/2ZtyFdx
Ohio	Ohio State University	Columbus, OH	https://bit.ly/2D6Vqfm
	University Hospitals	Cleveland, OH	https://bit.ly/2Pk9Hez
Ontario	The Ottawa Hospital	Ottawa, ON	Canada
Texas	Baylor University	Dallas, TX	https://bit.ly/2OSSdWW
	MD Anderson Cancer Center	Houston, TX	https://bit.ly/2Au2hwU
Washington	Fred Hutch	Seattle, WA	https://bit.ly/2yAlZWe
Wisconsin	Medical College of Wisconsin	Milwaukee, WI	https://bit.ly/2Prbxu1

Only Phase 3 Trial With Targeting Conditioning for Active, Relapsed/Refractory AML



This abstract was published online on November 1, 2018 for the American Society of Hematology (ASH) Annual Meeting, and is the latest update on the SIERRA Trial.

Investigational Drug: Iodine (^{131}I) apamistamab [Iomab-B]
Oral Presentation December 3rd, 6:45pm

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

Edward Agura, MD¹, Boglarka Gyurkocza, MD², Rajneesh Nath, MD³, Mark R. Litzow, M.D.⁴, Benjamin K. Tomlinson, MD⁵, Sunil Abhyankar, MD⁶, Stuart Seropian, MD^{7*}, Patrick J. Stiff, MD⁸, Hannah K. Choe, MD⁹, Partow Kebriaei, MD¹⁰, James M. Foran, MD¹¹, George Chen, MD¹², Moshe Yair Levy, MD¹, Hillard M Lazarus, MD⁵, Sergio A. Giralt, MD², Mark S. Berger, MD¹³, Vijay Reddy, MD, PhD¹³ and John M. Pagel, MD, PhD¹⁴

¹Baylor University Medical Center at Dallas, Dallas, TX; ²Adult Bone Marrow Transplant Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; ³Banner MD Anderson Cancer Center, Gilbert, AZ; ⁴Mayo Clinic, Department of Internal Medicine, Division of Hematology, Rochester, MN; ⁵University Hospitals Seidman Cancer Center, Cleveland, OH; ⁶University of Kansas Medical Center, Westwood, KS; ⁷Yale University School of Medicine, New Haven, CT; ⁸Loyola Univ. Med. Ctr., Maywood, IL; ⁹The Ohio State University Comprehensive Cancer Center, Columbus; ¹⁰Department of Stem Cell Transplantation and Cellular Therapy, MD Anderson Cancer Center, Houston, TX; ¹¹Division of Hematology and Medical Oncology, Department of Medicine, Mayo Clinic, Jacksonville, FL; ¹²Medicine, Roswell Park Cancer Institute, Buffalo, NY; ¹³Actinium Pharmaceuticals, New York, NY; ¹⁴Swedish Cancer Institute, Seattle, WA

Targeted Conditioning Engraftment Results in Active, Relapsed/Refractory AML

Ongoing Phase 3 SIERRA Trial (N=38) – Demographics*			
	Randomized to Iomab-B Study Arm (N=19)	Randomized to Conventional Care (N=19)**	Randomized to Conventional Care and Subsequently Crossed Over (N=9)
Age (median, range)	63.5 (56-72)	63 (55-76)	62.5 (55-64)
% Blasts prior to treatment	30% (4-74)	26% (6-97)	46.5% (10-89)
Engraftment Results			
Days to ANC Engraftment	13 (9-22)	n/a**	13 (9-15)
Days to Platelet Engraftment	17 (13-26)	n/a**	16 (10-19)
Median days to HCT (post randomization)	27 (N=18)	75 (N=2)	65 (N=9)

- Despite high blast count (median of 30%) all Iomab-B patients engrafted
- 88% of patients in the control arm failed to achieve a complete response. Only two proceeded to SoC transplant after CR
- 65% of eligible patients (11/17) in the control arm crossed-over to receive Iomab-B; All those that crossed over and received Iomab-B achieved engraftment following bone marrow transplant despite high bone marrow blast counts (46.5% median blast count baseline)
- No Iomab-B related deaths; Observed toxicity largely limited to myeloablation

*As of July 5, 2018

**Two patients transplanted in CR; engraftment data not available

Title: Targeted Conditioning of lomab-B (¹³¹I-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

Background: Patients ≥55 years of age with active, relapsed or refractory acute myeloid leukemia (R/R AML) who have failed standard induction therapies most often receive salvage therapy with a wide variety of agents, but very few achieve remission. These patients do not routinely undergo allogeneic hematopoietic cell transplantation (HCT) due to lack of efficacy using a standard HCT approach. The SIERRA trial is a prospective, randomized, phase 3, open-label, ongoing multicenter trial designed to address this significant unmet need in R/R AML. This trial compares lomab-B, an ¹³¹I-radiolabeled anti-CD45 antibody as targeted conditioning prior to HCT against standard conventional care therapies with an accrual goal of 150 patients. We have performed a preliminary safety analysis, validating the initial feasibility of this multi-center trial.

Methods: Eligible patients are ≥ 55 years of age with active, R/R AML, adequate organ function, and related/unrelated matched donor. Patients are randomized (1:1 ratio) to receive dosimetry directed lomab-B followed 12 days later by HCT with fludarabine 30 mg/m² x 3 days and 2 Gy of total body irradiation as transplant conditioning, or to a Conventional Care (CC) arm. Patients randomized to CC, may receive investigator’s choice of salvage induction chemotherapy including approved targeted agents as well as Venetoclax (in combination with a hypomethylating agent) and proceed to standard HCT if they achieve complete remission (CR). If patients do not achieve CR, the study allows optional cross-over to the lomab-B arm, evaluated between days 28-42 after CC therapy. The primary efficacy endpoint for the study is durable complete remission (dCR) of 6 months. The secondary efficacy objective is to evaluate overall survival at 1 year.

Results: Forty patients have been enrolled to date and data are available for 38 patients (19 = lomab-B, 19 = CC) as of July 5th, 2018. The median age was 63 years (range: 55-76). All patients had active disease at the time of enrollment with median bone marrow (BM) blasts of 30% in the lomab-B arm and 47% in the crossover arm prior to receiving lomab-B (Table 1). Of the patients in the CC arm, 88% did not achieve a CR and 65% of those crossed-over to receive lomab-B. The most common reason preventing crossover was declining performance status. Time to HCT was not increased in the crossover patients receiving lomab-B compared to those that underwent a standard of care transplant after achieving CR (median 65 vs 75 days), while the lomab-B arm patients were transplanted at a median of 27 days after randomization. lomab-B therapy was well-tolerated with no grade 3 or 4 infusion-related reactions reported. The median activity of lomab-B was 626 mCi (range: 397-1027). All patients randomized to lomab-B (N=13) engrafted, with median days to engraftment of ANC at 13 (range: 9-22) and platelets at 17 (range: 13-26). All patients who received lomab-B after crossover (N=9) also engrafted with time to engraftment similar to patients initially randomized to the lomab-B arm (Table 1). Donor chimerism (≥95%), within 100 days after HCT, was found in 9 of 10 patients in the lomab-B arm and 8 of 9 patients in those that crossed over to receive lomab-B, with two patient exceptions having mixed donor chimerism at day 28. A preliminary safety analysis for all randomized patients on either study arm showed the most frequent non-hematologic adverse events ≥ grade 3 occurring in >10% patients were febrile neutropenia (34.2%), stomatitis (15.8%), malnutrition (13.2%), epistaxis, sepsis, hypotension, hypobilirubinemia and fatigue (all 10.5%). There were no lomab-B-related deaths.

Interpretation: Preliminary safety analysis demonstrates the feasibility of delivering targeted conditioning with lomab-B for HCT in R/R AML patients who have active disease and a high BM blast burden (median: ≥ 30%) prior to transplantation. All patients who received lomab-B, including those crossed over after failing to achieve CR on CC salvage therapy, engrafted ANC within 13 days, despite active disease prior to transplant. In addition, the time to HCT from randomization was not increased in patients receiving lomab-B after cross-over compared to those who underwent standard of care HCT after achieving CR on the CC arm. This study is currently enrolling and for full study details see www.sierratrial.com or clinicaltrials.gov (NCT02665065)

Table 1.

Patient Data (Median & Range)	lomab-B	Conventional Care	Cross-Over to lomab-B
Age (years)	63.5 (56-72)	63 (55-76)	62.5 (55-64)
Bone Marrow Blasts (% prior to treatment)	30 (4*-74)	26 (6-97)	46.5 (10-89)
lomab-B Activity Administered (mCi)	626 (397-1027)	NA	531 (313-1008)
Neutrophil Engraftment [ANC] (days)	13 (9-22)	NA	13 (9-15)
Platelet Engraftment (days)	17 (13-26)	NA	16 (10-19)

*Subject with 4% BM blasts eligible due to circulating peripheral blasts