
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.

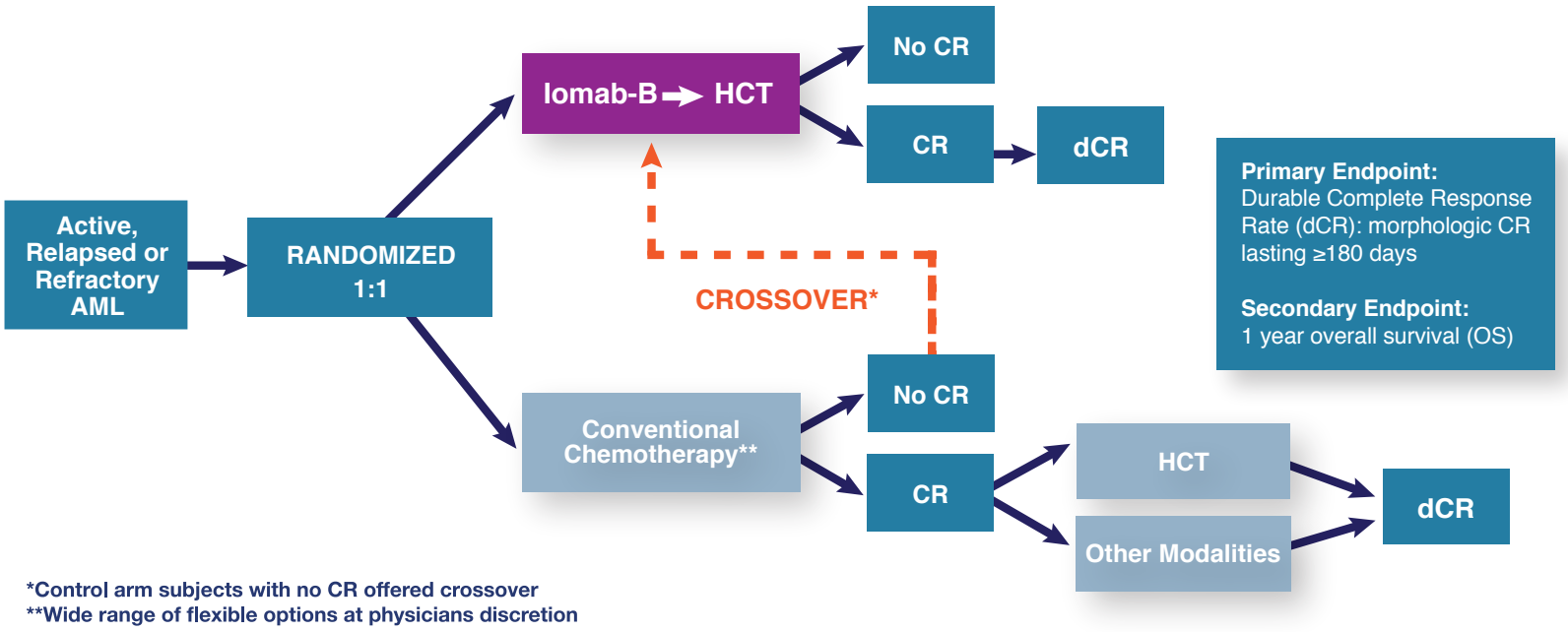
Transplant Can Be An Option for Patients with Active, Relapsed or Refractory Acute Myeloid Leukemia

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
STUDY OF IOMAB-B IN ELDERLY RELAPSED/REFRACTORY AML

The safety and efficacy of the investigational use of this product has not been determined. There is no guarantee that the investigational use listed will be filed with and/or approved for marketing by a regulatory agency.

For additional information, e-mail iomab@actiniumpharma.com or visit www.sierratrial.com.

Actinium Pharmaceuticals, Inc.

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
Ohio	**Ohio State University**	**Columbus, OH**	https://bit.ly/2D6Vqfm
	University Hospitals	**Cleveland, OH**	https://bit.ly/2Pk9Hez
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

SIERRA Trial Site List as of Nov 13th 2018

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

SIERRA
STUDY OF IOMAB-B IN ELDERLY 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

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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

ASH 2018 Abstract Number: 1017

Title: 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

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 Iomab-B, an ^{131}I-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 Iomab-B followed 12 days later by HCT with fludarabine 30 mg/m^2 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 Iomab-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 = Iomab-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 Iomab-B arm and 47% in the crossover arm prior to receiving Iomab-B (Table 1). Of the patients in the CC arm, 88% did not achieve a CR and 65% of those crossed-over to receive Iomab-B. The most common reason preventing crossover was declining performance status. Time to HCT was not increased in the crossover patients receiving Iomab-B compared to those that underwent a standard of care transplant after achieving CR (median 65 vs 75 days), while the Iomab-B arm patients were transplanted at a median of 27 days after randomization. Iomab-B therapy was well-tolerated with no grade 3 or 4 infusion-related reactions reported. The median activity of Iomab-B was 626 mCi (range: 397-1027). All patients randomized to Iomab-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 Iomab-B after crossover (N=9) also engrafted with time to engraftment similar to patients initially randomized to the Iomab-B arm (Table 1). Donor chimerism (≥95%), within 100 days after HCT, was found in 9 of 10 patients in the Iomab-B arm and 8 of 9 patients in those that crossed over to receive Iomab-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 Iomab-B-related deaths.

Interpretation: Preliminary safety analysis demonstrates the feasibility of delivering targeted conditioning with Iomab- 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 Iomab-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 Iomab-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)	Iomab-B	Conventional Care	Cross-Over to Iomab-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)
Iomab-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

Oral presentation on Dec 3, 6:45pm: Session 721. Clinical Allogeneic Transplantation: Conditioning Regimens, Engraftment, and Acute Transplant Toxicities