soho2023
ELEVENTH ANNUAL MEETING

Poster: AML-521

The Randomized Phase III SIERRA (Study of Iomab-B in Elderly Relapsed or Refractory AML) Trial: Successful Allogeneic Hematopoietic Stem Cell Transplantation Using Treatment With Iomab-B Led Regimen for Patients With Active, Relapsed or Refractory AML With Failed Targeted Therapies

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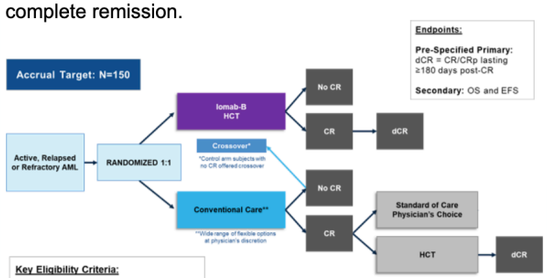
SIERRA
STUDY OF IOMAB-B IN ELDERLY RELAPSED/REFRACTORY AML

BACKGROUND

Patients with relapsed or refractory (R/R) acute myeloid leukemia (AML) have dismal outcomes, and <20% undergo allogeneic hematopoietic stem cell transplantation (alloHSCT). Those who failed venetoclax have worse outcomes (median survival of 2-3 months) without alloHSCT. SIERRA investigated the use of ^{131}I-apamistamab (Iomab-B), an ^{131}I-labelled anti-CD 45 monoclonal antibody, to enable alloHSCT in patients with active R/R AML; Iomab-B was compared to conventional care (CC).

METHODS

Patients ≥ 55 years of age with R/R AML were randomized 1:1 to receive Iomab-B followed by fludarabine, total body irradiation (2 Gy), and alloHSCT or CC (physician's choice of therapy, including targeted agents, and alloHSCT if leukemia free). Crossover to Iomab-B based alloHSCT was permitted for CC patients with progression or without complete remission.



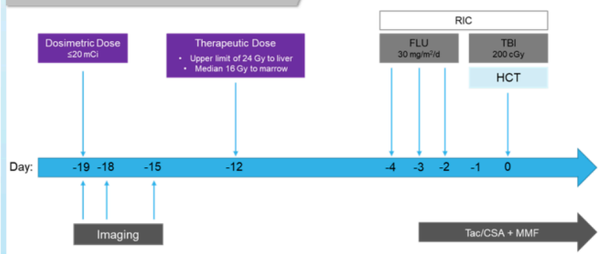
Key Eligibility Criteria:

- R/R AML ≥55 years of age with active disease (BM blast count ≥5% or the presence of circulating blasts)
- Karnofsky score ≥70
- 8/8 allele-level, related or unrelated matched donor
- Previous HCT were excluded

OBJECTIVES

Here we report outcomes from SIERRA patients who failed targeted therapies.

TREATMENT



RIC: reduced intensity conditioning; FLU: fludarabine; TBI: total body irradiation; HCT: hematopoietic cell transplant; Tac/CSA: tacrolimus/cyclosporine; MMF: mycophenolate mofetil

PATIENT CHARACTERISTICS

Complete Enrollment, N = 153

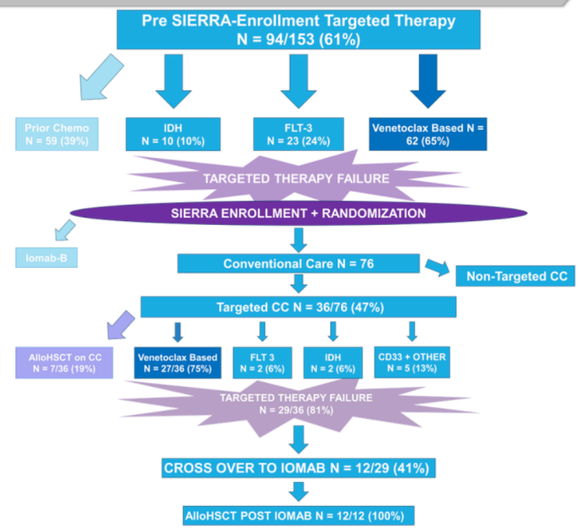
	Iomab-B Arm (N=76)	Conventional Care Arm (N=77)	Randomized to Conventional Care and Crossed Over to Iomab-B (N=44)
Age, years Median (Range)	64 (55-77) Pts ≥70 yrs: 14 (18.4%)	66 (55-76) Pts ≥70 yrs: 16 (20.8%)	64 (55-76) Pts ≥70 yrs: 12 (27.3%)
Cytogenetic and Molecular Risk[1] N (%)	Favorable: 5 (6.6) Intermediate: 27 (35.5) Adverse: 43 (56.6)	Favorable: 2 (2.6) Intermediate: 31 (40.3) Adverse: 43 (55.8)	Favorable: 1 (2.3) Intermediate: 21 (47.7) Adverse: 21 (47.7)
Disease Status at Randomization N (%)	Primary Induction Failure: 43 (56.6) First Early Relapse:16 (21.1) Relapse/Refractory: 10 (13.2) 2nd + Relapse: 7 (9.2)	Primary Induction Failure: 40 (51.9) First Early Relapse: 22 (28.6) Relapse/Refractory: 10 (13.0) 2nd + Relapse: 5 (6.5)	Primary Induction Failure: 24 (54.5) First Early Relapse: 11 (25.0) Relapse/Refractory: 7 (15.9) 2nd + Relapse: 2 (4.5)
Prior Lines of Treatment Median (Range)	3 (1-8)	3 (1-8)	3 (1-8)
Received Prior Targeted Therapy N (%)	47 (61.8)	47 (61.0)	26 (59.1)
Karnofsky Performance Status N (%)	≥90: 31 (40.8) <90: 45 (59.2)	≥90: 34 (44.2) <90: 43 (55.8)	≥90: 22 (50.0) <90: 22 (50.0)
% Marrow Blasts at Randomization Median (Range)	30% (2-97)[2]	20% (3-97)[2]	At Randomization: 24.5% (3-87)[2] At crossover: 35% (2-89)[2]

1. Per NCCN Guidelines, Version 3, 2020
2. Pts with <5% marrow blasts had circulating leukemic blasts

TARGETED THERAPY DATA

- Randomized patients received a median of 3 prior therapy regimens, with 93% failing at least 2 regimens prior to enrollment.
- A majority of enrolled patients (61%) had received and failed prior targeted agents, of which 65% were venetoclax-based.

TARGETED THERAPY DATA



CONDITIONING & TRANSPLANT CHARACTERISTICS

	Iomab-B (N=66)[1]	Standard HCT (N=14)	Crossover (N=40)[2]
Infused Activity Median (Range)	664.4 mCi (354-1027)	N/A	613.3 mCi (313-1008)
Dose to the Marrow Median (Range)	16 Gy (4.6-44.6)	N/A	16 Gy (6.3-39.8)
Time to HCT From Randomization Median (Range)	29 Days (23-60)	66.5 Days (35-104)	61.5 Days (36-161)
Engraftment Median (Range)	ANC: 14 Days (9-31) PLT: 19 Days (10-40)	ANC: 16 Days (1-83) PLT: 14.5 Days (1-35)	ANC: 13 Days (10-35) PLT: 18 Days (1-38)
HCT Comorbidity Index N (%)	0-2: 30 (45.5) ≥3: 36 (54.5)	0-2: 9 (64.3) ≥3: 5 (35.7)	0-2: 20 (50.0) ≥3: 20 (50.0)

1. Ten (10) pts randomized to Iomab-B did not receive therapeutic dose or undergo HCT
2. Four (4) pts crossed over but did not receive therapeutic dose or undergo HCT

Of the evaluable patients treated with Iomab-B/HCT, 100% engrafted.

RESULTS

Outcomes of Targeted Therapy Failure, Patients Who Achieved dCR

dCR assessed by Independent Endpoint Adjudication Committee

	Iomab-B N (%)	CC N (%)
Evaluable Per-Protocol*	59	64
Maintained dCR of ≥180 days	13 (22.0)	0 (0.0)
dCR Patients with Prior Targeted Therapy Failure	10 (76.9) *7/13 (53.8)	0 (0.0)

*Venetoclax Failure

- One year survival was 90% (9/10) in prior targeted therapy failure patients who achieved dCR.
- One year survival was 85% (6/7) in prior venetoclax failed patients who achieved dCR.

Superior dCR Rate for Iomab-B versus CC

dCR assessed by Independent Endpoint Adjudication Committee

	Iomab-B N (%)	CC N (%)
Evaluable Per-Protocol*	59	64
Achieved CR/CRp	44 (74.6)	4 (6.3)
Maintained dCR of ≥180 days	13 (22.0) *p<0.0001; 95% CI [12.29, 34.73]*	0 (0.0)

- In the crossover arm (N=44), 91% received transplant with 52.3% achieving CR/CRp
- Six crossover patients (13.6%) achieved dCR of ≥180 days (95% CI [5.17, 27.35])
- **Post-HCT maintenance with TKI allowed only for Iomab-B patients with FLT3 mutation, FLT3-ITD or BCR-ABL translocation at baseline.**
- **CC pts received investigator's choice of post-HCT maintenance therapy.**

CONCLUSIONS

- Patients with failure of targeted therapies, including venetoclax, were able to undergo alloHSCT with the Iomab-B led regimen.
- Of those patients who achieved dCR with Iomab-B, >70% had previous targeted therapy failure, including >50% with previous venetoclax failures.
- The majority of dCR patients were long-term survivors.
- Iomab-B significantly improves outcomes in patients with prior targeted therapy failure.

The SIERRA trial has completed enrollment (www.sierratrial.com or clinicaltrials.gov, NCT02665065)