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Long Term Follow-up Demonstrates Ongoing Efficacy Benefit of ^{131}I-apamistamab-led Allogeneic Hematopoietic Cell Transplantation in Older Patients with Active, R/R AML in the Phase 3 SIERRA Trial

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

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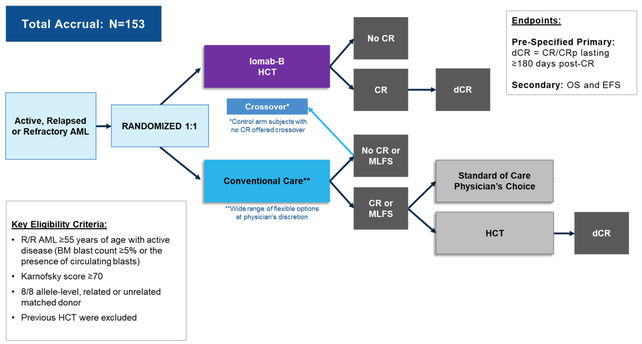
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Background

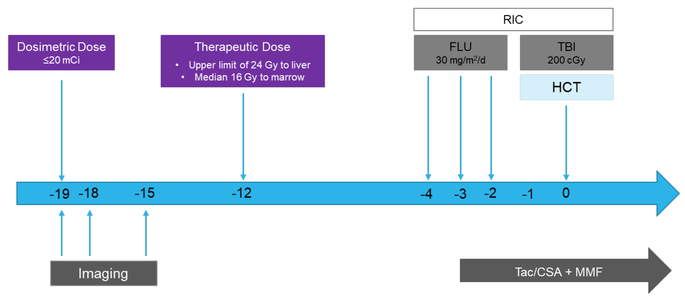
Most older patients with relapsed or refractory acute myeloid leukemia (R/R AML, either primary refractory, or with early relapse (<6 months), or >1 relapse) are ineligible for curative allogeneic hematopoietic cell transplant (HCT) due to intolerance to intensive therapies. Iomab-B (^{131}I-apamistamab) delivers high- dose targeted radiation to CD45-expressing cells, producing anti-leukemic effect and myeloablation while limiting off-target toxicity. With better disease control and safer access to HCT, Iomab-B conditioning can improve outcomes in pts with active R/R AML. In SIERRA, Iomab-B-led allogeneic HCT improved outcomes in active R/R AML patients (shown at June 2022 data cutoff). We report a subsequent analysis of efficacy after longer follow-up (as of January 2024).

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

Study Design: SIERRA was a controlled, optional one-way crossover study of Iomab-B versus Investigator's choice of salvage therapy in patients aged 55 years or older with active, R/R AML. Patients randomized to CC who achieve CR could proceed to allogeneic HCT or other standard treatment. Patients not achieving CR could crossover to Iomab-B.



SIERRA Iomab-B Treatment Schedule



Baseline 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/Poor: **43** (56.6)	Favorable: **2** (2.6) Intermediate: **31** (40.3) Adverse/Poor: **43** (55.8)	Favorable: **1** (2.3) Intermediate: **21** (47.7) Adverse/Poor: **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

Conditioning and 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

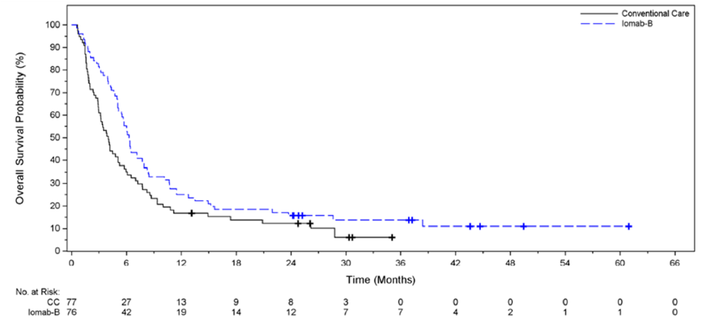
dCR and Engraftment Rates

- **The rate of dCR was higher in Iomab-B versus CC, with rates of 22% vs 0% (p<0.0001; 95% CI [12.29, 34.73]) in the per-protocol analysis.**
- Of the patients who underwent transplant and were evaluable for engraftment, 100% engrafted.

Improved Survival

Using a two-stage estimation model, median OS for Iomab-B-treated pts was 6.3 mos versus 4.0 mos in CC pts (p=0.0314; HR 0.69 [95% CI, 0.49-0.97]).

Figure 1. Overall Survival in the Intent-to-Treat Population with Extended Follow Up



Treatment Emergent Adverse Events (Grade ≥3)

Adverse Event	Iomab-B (N=66)	CC (N=14)
Sepsis[1] N (%)	**4** (6.1)	**4** (28.6)
Febrile Neutropenia N (%)	**29** (43.9)	**7** (50.0)
Mucositis[2] N (%)	**10** (15.2)	**3** (21.4)
Acute GVHD (Gr III-IV)[3] Cumulative Incidence % (95% CI)	**9.4** (3.8, 18.2)	**14.3** (2.1, 37.6)

1. "Sepsis" includes Preferred Terms of Sepsis, Septic Shock, Neutropenic Sepsis & Septic Embolus
2. "Mucositis" includes Preferred Terms of Stomatitis & Mucosal Inflammation
3. GVHD Prophylaxis: Iomab-B pts received cyclosporin and mycophenolate mofetil, CC pts received investigator's choice of therapy

Conclusions

- An Iomab-B-led regimen with HCT resulted in high initial CR/CRp rates and statistically significant improvement in the pre-specified primary endpoint of dCR in patients ≥55 years of age with R/R AML.
- Most patients who achieved dCR are long term survivors with median OS not reached.
- Iomab-B was well-tolerated in a vulnerable pt population traditionally considered ineligible for HCT.
- The improved outcomes in the Iomab-B treated patients persisted when analysis was performed with longer follow up.

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