65th ASH Annual Meeting & Exposition
San Diego, CA
Dec 9-12, 2023
PUBLICATION #2159

^{131}I-apamistamab Effectively Achieved Durable Responses in Patients with R/R AML Irrespective of the Presence of Multiple High-Risk Factors

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

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Background

Most older patients with relapsed/refractory (R/R) AML cannot tolerate intensive treatment and are not eligible for curative allogeneic hematopoietic cell transplant (HCT).

^{131}I-apamistamab delivers high dose targeted radiation to hematopoietic cells, allowing for myeloablation and eradication of leukemic cells while sparing toxicity to healthy organs.

^{131}I-apamistamab-based novel induction/conditioning can thus provide these high-risk patients with access to allogeneic HCT.

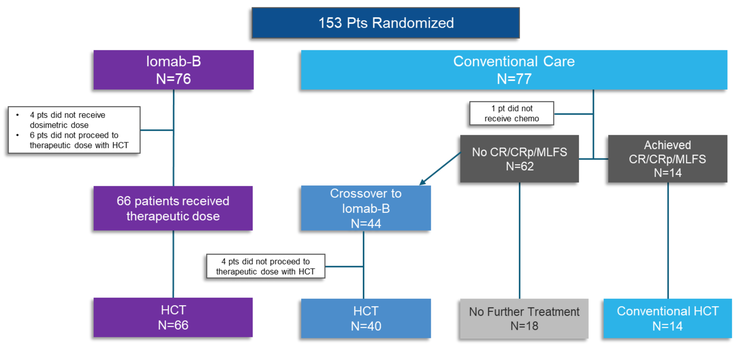
Objective

We analyzed the rate of durable complete response (dCR) in patients with high-risk factors, such as adverse risk cytogenetics, age >65, prior treatment failure with venetoclax, high HCT comorbidity index, or reduced KPS. We compared the rate of dCR across subgroups in the presence of one or more of these high-risk factors.

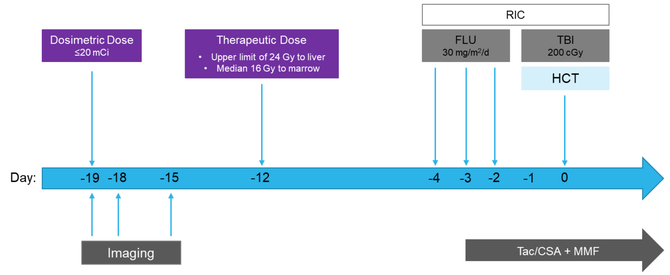
^{131}I-apamistamab (Iomab-B)

Iomab-B targets CD45, expressed on hematopoietic cells, including the majority of malignant myeloid and lymphoid cells. Iomab-B delivers targeted radiation directly to leukemic cells and avoids non-targeted tissue.

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 Conventional Care (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



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

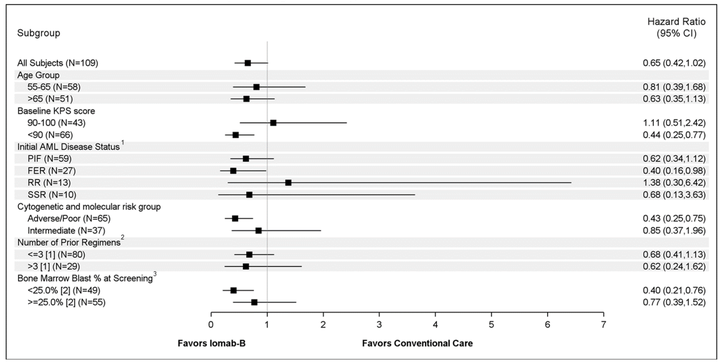
Patient Characteristics dCR vs. non-dCR

	Achieved dCR (N=19)	No dCR (N=134)
Age, years Median (Range) N (%)	62 (57-73) Pts >65 yrs: 6 (31.6%)	65 (55-77) Pts >65 yrs: 63 (47.0%)
Cytogenetic and Molecular Risk[1] N (%)	Favorable: 1 (5.3) Intermediate: 9 (47.4) Adverse/Poor: 9 (47.4)	Favorable: 6 (4.5) Intermediate: 49 (36.6) Adverse/Poor: 77 (57.5)
Disease Status at Randomization N (%)	Primary Induction Failure: 8 (42.1) First Early Relapse: 6 (31.6) Relapse/Refractory: 4 (21.1) 2nd + Relapse: 1 (5.3)	Primary Induction Failure: 75 (56.0) First Early Relapse: 32 (23.9) Relapse/Refractory: 16 (11.9) 2nd + Relapse: 11 (8.2)
Prior Lines of Treatment Median (Range)	3 (1-5)	3 (1-8)
Prior Venetoclax Treatment N (%)	7 (36.8)	55 (41.0)
Karnofsky Performance Status N (%)	≥90: 9 (47.4) <90: 10 (52.6)	≥90: 56 (41.8) <90: 78 (58.2)
HCT Co-Morbidity Index N (%)	0-2: 9 (47.4) ≥3: 10 (52.6)	0-2: 66 (49.3) ≥3: 68 (50.7)

1. Per NCCN Guidelines, Version 3, 2020

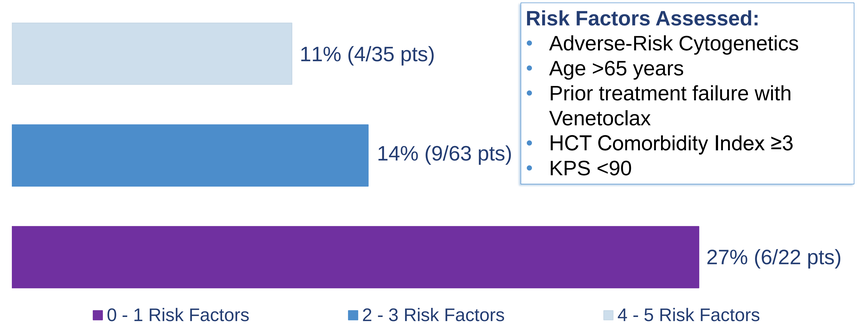
Overall Survival Favors Iomab-B Across Most Subgroups

Overall Survival: Iomab-B, N=76; CC (Excluding Crossover), N=33



1. PIF: Primary induction failure; FER: First early relapse; RR: Relapse refractory; SSR: Second or subsequent relapse.
2. Median 3 prior regimens across both treatment groups for the Intent-to-Treat Analysis set
3. Median 25% marrow blasts across both treatment groups for the Intent-to-Treat Analysis set

Rate of dCR Stratified by Number of Risk Factors



Risk Factors Assessed:
- Adverse-Risk Cytogenetics
- Age >65 years
- Prior treatment failure with Venetoclax
- HCT Comorbidity Index ≥3
- KPS <90

There was no difference between the dCR rates in patient groups across the risk factor categories (p=0.251).

Superior dCR Rate for Iomab-B versus CC

	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)	0 (0.0)
	p<0.0001; 95% CI [12.29, 34.73]	

- 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 FLT-3 mutation or BCR-ABL translocation at baseline.
- CC patients received investigator's choice post-HCT maintenance therapy.

Conclusions

- Patients with R/R AML who have multiple risk factors are typically not considered for allogeneic HCT due to high transplant-related mortality and post-transplant relapse rates.
- ^{131}I-apamistamab was effective in achieving durable responses in R/R AML patients irrespective of the presence of multiple high-risk factors such as adverse cytogenetics, age >65, venetoclax failure, high comorbidity index, or reduced KPS, due to its targeted mechanism of action.

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