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# High-Dose Targeted Radiation with $^{131}$I-apamistamab Prior to HCT Demonstrated a Dose-Response for Durable Complete Remission in Patients with R/R AML

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

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## Background

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

$^{131}$I-apamistamab, an anti-CD45 radioimmunoconjugate, delivers high dose targeted radiation to hematopoietic cells, allowing for myeloablation and eradication of leukemic cells.

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

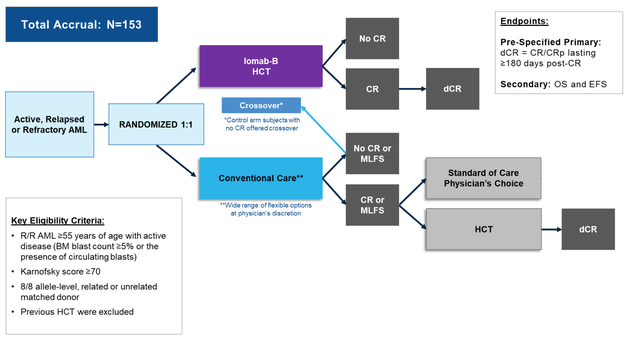
## Objective

Here we report on the rates and distributions of durable complete remission (dCR) in patients who received $^{131}$I-apamistamab at varying dose levels.

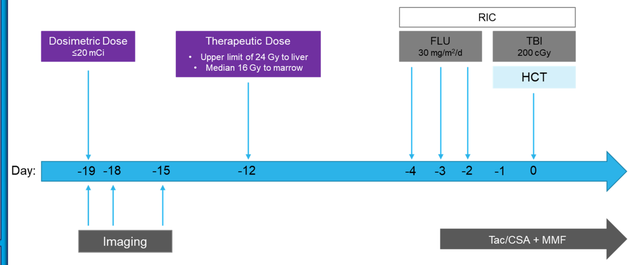
## Iomab-B: Iodine ($^{131}$I) Apamistamab

$^{131}$I-apamistamab, or Iomab-B, targets CD45, which is expressed on hematopoietic cells, including the majority of malignant myeloid and lymphoid cells. In this way, Iomab-B delivers targeted radiation directly to leukemic cells and avoids non-targeted tissue. Following a dosimetric dose and biodistribution assessment, patients receive a personalized therapeutic dose designed to deliver a maximum of 24 Gy to the liver or 48 Gy to the bone marrow, whichever results in a lower activity to be administered.

**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 achieved CR could proceed to allogeneic HCT or other standard treatment. Patients not achieving CR could crossover to receive 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

*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)<br>Pts ≥70 yrs: 14 (18.4%) | 66 (55-76)<br>Pts ≥70 yrs: 16 (20.8%) | 64 (55-76)<br>Pts ≥70 yrs: 12 (27.3%) |
| Cytogenetic and Molecular Risk[1] N (%) | Favorable: 5 (6.6)<br>Intermediate: 27 (35.5)<br>Adverse: 43 (56.6) | Favorable: 2 (2.6)<br>Intermediate: 31 (40.3)<br>Adverse: 43 (55.8) | Favorable: 1 (2.3)<br>Intermediate: 21 (47.7)<br>Adverse: 21 (47.7) |
| Disease Status at Randomization N (%) | Primary Induction Failure: 43 (56.6)<br>First Early Relapse:16 (21.1)<br>Relapse/Refractory: 10 (13.2)<br>2nd + Relapse: 7 (9.2) | Primary Induction Failure: 40 (51.9)<br>First Early Relapse: 22 (28.6)<br>Relapse/Refractory: 10 (13.0)<br>2nd + Relapse: 5 (6.5) | Primary Induction Failure: 24 (54.5)<br>First Early Relapse: 11 (25.0)<br>Relapse/Refractory: 7 (15.9)<br>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)<br><90: 45 (59.2) | ≥90: 34 (44.2)<br><90: 43 (55.8) | ≥90: 22 (50.0)<br><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]<br>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)<br>PLT: 19 Days (10-40) | ANC: 16 Days (1-83)<br>PLT: 14.5 Days (1-35) | ANC: 13 Days (10-35)<br>PLT: 18 Days (1-38) |
| HCT Comorbidity Index N (%) | 0-2: 30 (45.5)<br>≥3: 36 (54.5) | 0-2: 9 (64.3)<br>≥3: 5 (35.7) | 0-2: 20 (50.0)<br>≥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

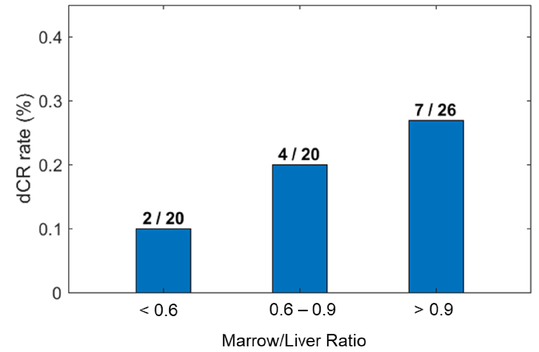
Of the evaluable patients treated with Iomab-B & HCT, 100% engrafted.

## Delivered Dose vs. dCR Rate

| Patients randomized to $^{131}$I-apamistamab receiving the therapeutic infusion (N=66) | |
|---|---|
| Administered liver dose <=22 Gy | Administered liver dose >22 Gy |
| 5/37 (**13.5%** [95% CI: 4.5, 28.8%]) | 8/29 (**27.6%** [95% CI: 12.7, 47.2%]) |

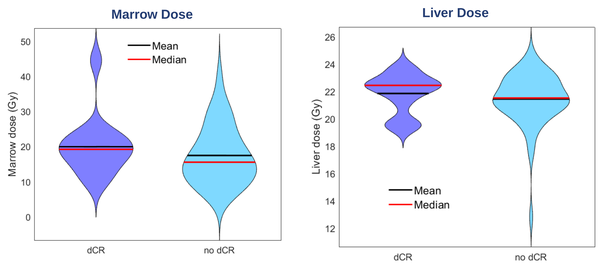
| Marrow/Liver ratio <0.6 | Marrow/Liver ratio 0.6 – 0.9 | Marrow/Liver ratio >0.9 |
|---|---|---|
| 2/20 (**10.0%** [95% CI: 1.2, 31.7%]) | 4/20 (**20.0%** [95% CI: 5.7, 43.7%]) | 7/6 (**26.9%** [95% CI: 11.6, 47.8%]) |

**Figure 1.** Distribution of pts with durable complete remission (dCR) stratified by the ratio of marrow/liver absorbed radiation dose, with higher ratio indicating more favorable biodistribution.




- In patients who received liver doses of >22 Gy the rate of dCR was 27.6% vs. 13.5% in patients with liver doses ≤22 Gy.

## Distribution of Marrow and Liver Dose by dCR




- The distribution of bone marrow and liver absorbed dose demonstrates a dose-response relationship with a higher dose to the liver and marrow observed in patients achieving dCR.
- In patients achieving dCR, median liver dose was 22.5 Gy vs. 21.5 Gy for patients not achieving dCR.
- In patients achieving dCR, median bone marrow dose was 19.2 Gy vs. 15.6 Gy for patients not achieving dCR.

## Organ-Specific Dosimetry with Iomab-B

| Organ | Absorbed dose per unit administered activity (cGy/mCi) | Total absorbed dose (Gy) |
|---|---|---|
| Bone marrow | 2.60 (0.9 – 9.6) | 16.0 (4.6 – 44.6) |
| Spleen | 14.1 (2.7 – 34.5) | 91.5 (30.3 – 159.2) |
| Liver | 3.34 (1.4 – 6.1) | 21.6 (12.8 – 24.5) |
| Heart | 0.42 (0.2 – 1.0) | 2.6 (1.5 – 6.5) |
| Lungs | 0.40 (0.2 – 1.0) | 2.5 (1.5 – 6.1) |
| Small intestine | 0.39 (0.2 – 1.0) | 2.4 (1.1 – 6.8) |
| Stomach wall | 0.58 (0.3 – 1.1) | 3.6 (2.0 – 8.2) |
| Kidneys | 0.67 (0.4 – 1.2) | 4.1 (2.5 – 8.2) |
| Whole body | 0.52 (0.3 – 1.1) | 3.3 (2.0 – 10.0) |

## Grade ≥3 Treatment Emergent Adverse Events

| Adverse Event | Administered Liver Dose ≤ 22 Gy (N=37) N (%) | Administered Liver Dose > 22 Gy (N=29) N (%) |
|---|---|---|
| Febrile Neutropenia (FN) | 17 (45.9) | 10 (34.5) |
| Sepsis | 2 (5.4) | 2 (6.9) |
| Mucositis[1] | 5 (13.5) | 5 (17.2) |
| Acute Kidney Injury | 2 (3.4) | 1 (2.1) |
| aGVHD | 3 (8.1) | 3 (10.3) |
| Venoocclusive liver disease | 1 (2.7) | 0 (0.0) |

1."Mucositis" includes the Preferred Terms "Mucosal Inflammation" and "Stomatitis"

## Conclusions

- $^{131}$I-apamistamab led induction/conditioning followed by HCT resulted in statistically significant improvement in dCR at 6 months vs. conventional care.
- A dose response was demonstrated for patients receiving $^{131}$I-apamistamab, with those receiving a liver dose closer to the MTD of 24 Gy having about twice the dCR rate compared to patients receiving 22 Gy (MTD -1) or less.
- Patients with higher marrow/liver ratio experienced considerably higher rate of dCR, highlighting the importance of maximizing the dose to target tissues within the limits of established risk organ dose tolerances.

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