Efficacy and Safety Results of the SIERRA Trial:
A Multicenter, Pivotal Phase 3 Study of Iomab-B Prior to Allogeneic Hematopoietic Cell Transplantation Versus Conventional Care in Older Patients with Active, Relapsed or Refractory Acute Myeloid Leukemia (R/R AML)

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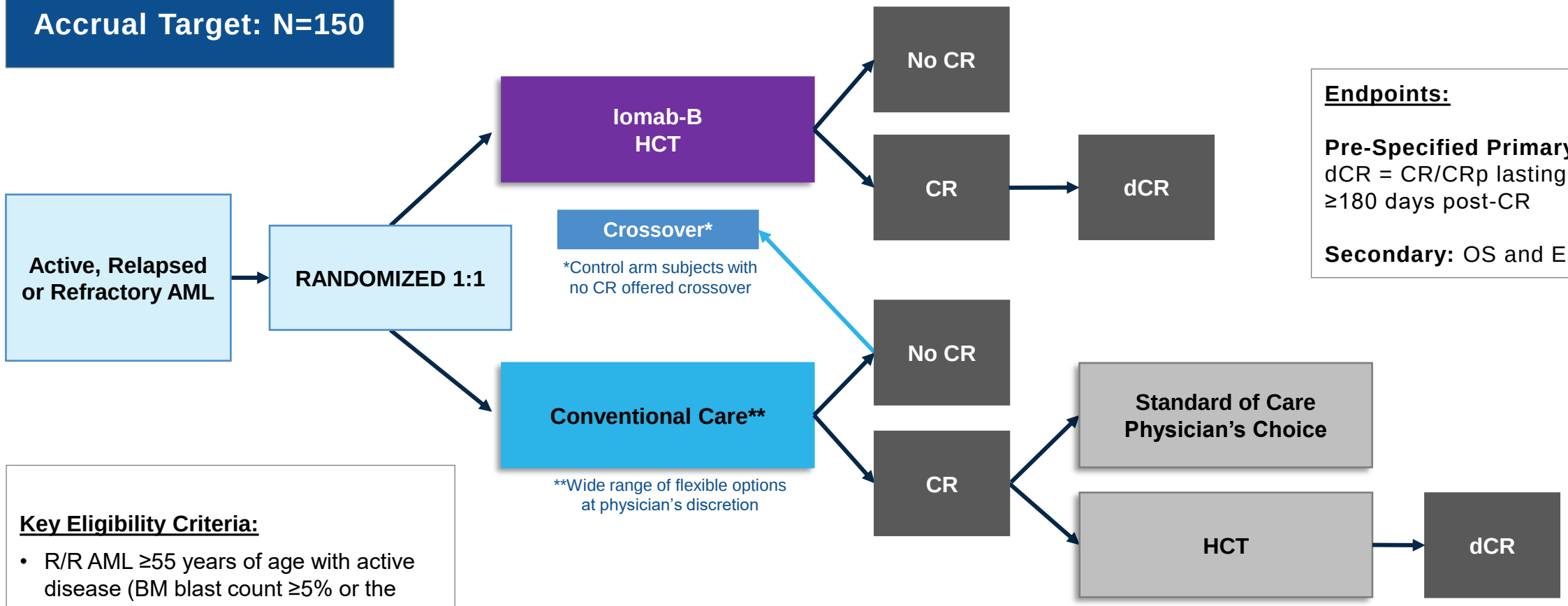
Background

- Patients with active, R/R AML have a dismal prognosis, particularly with increasing age, and typically are not offered allogeneic HCT due to failure to achieve remission, poor tolerance of conditioning, and substantial transplant-related mortality
- Iomab-B (Iodine (^{131}I) apamistamab), an anti-CD45 antibody conjugated to radioactive iodine (^{131}I), is designed to deliver targeted myeloablative radiation to hematopoietic cells along with reduced intensity conditioning prior to allogeneic HCT
- The SIERRA Trial is a prospective, randomized, controlled Phase 3 study in patients ≥ 55 years to compare rates of durable complete remission (dCR) ≥180 days following initial complete remission (CR/CRp) between two arms:
  - Iomab-B followed by HCT versus
  - Physician's choice conventional care (CC) followed by HCT
- Here we present the primary efficacy and safety results from the 153 patients enrolled to the SIERRA Trial

SIERRA: Study of Iomab-B in Elderly R/R AML

Accrual Target: N=150



Endpoints:

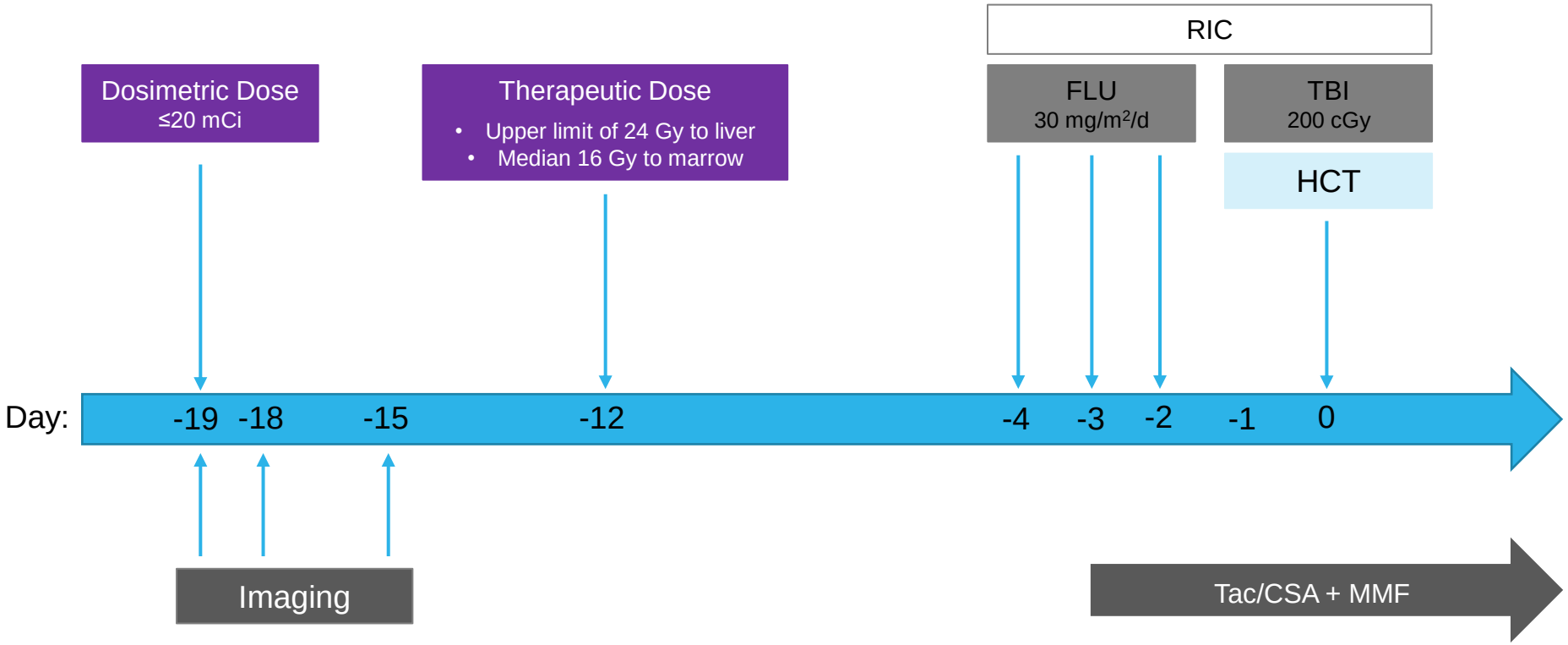
Pre-Specified Primary:
dCR = CR/CRp lasting ≥180 days post-CR

Secondary: OS and EFS

Key Eligibility Criteria:

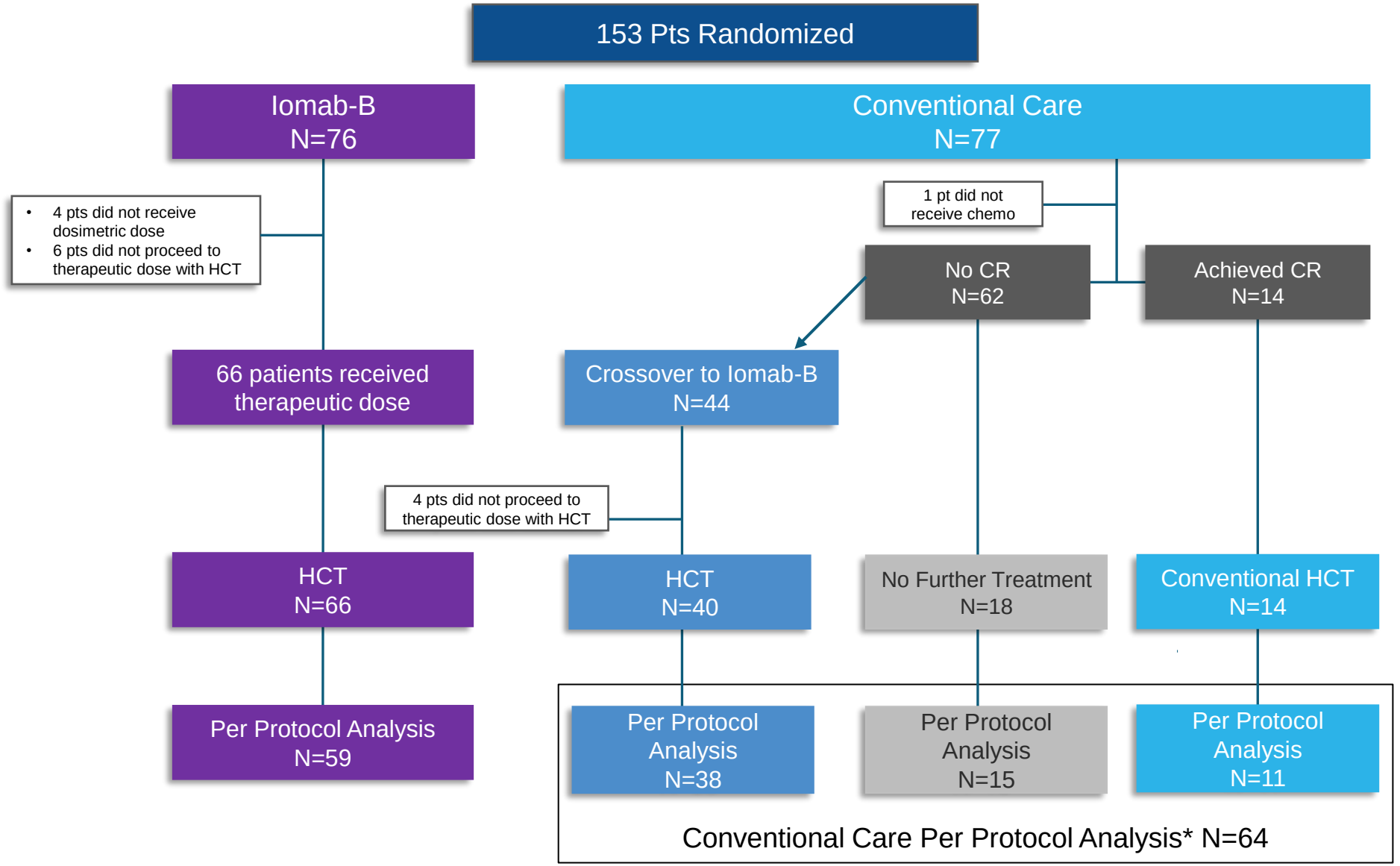
- R/R AML ≥55 years of age with active disease (BM blast count ≥5% or the presence of circulating blasts)
- Karnofsky score ≥70
- 8/8 allele-level, related or unrelated matched donor
- Previous HCT were excluded

Personalized Single Dose Combined Induction/Conditioning



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

CONSORT Chart



* Patients were excluded from the Per Protocol Analysis Set due to 1) major protocol deviations that impacted interpretation of the primary endpoint, 2) missed disease assessments, or 3) failure to complete primary therapy.

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/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

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

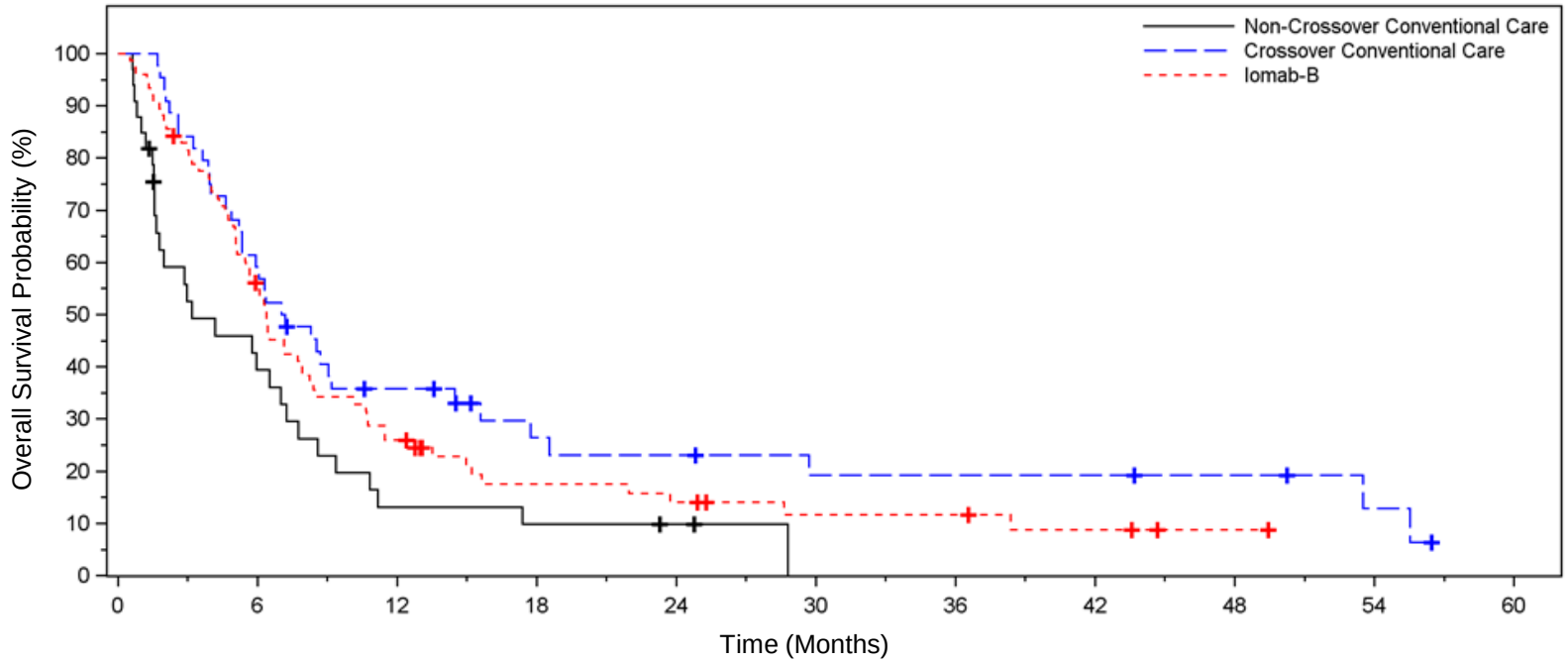
- In the crossover arm (N=44), 91% received transplant with 52.3% achieving CR/CRp
- Six crossover patients (13.6%) achieved dCR of ≥180 days (95% CI [5.17, 27.35])
- **Post-HCT maintenance with TKI allowed only for Iomab-B patients with FLT3 mutation, FLT3-ITD or BCR-ABL translocation at screening.**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

* Patients were excluded from the Per Protocol Analysis Set due to 1) major protocol deviations that impacted interpretation of the primary endpoint, 2) missed disease assessments, or 3) failure to complete primary therapy.

Iomab-B Doubles Overall Survival Compared to CC

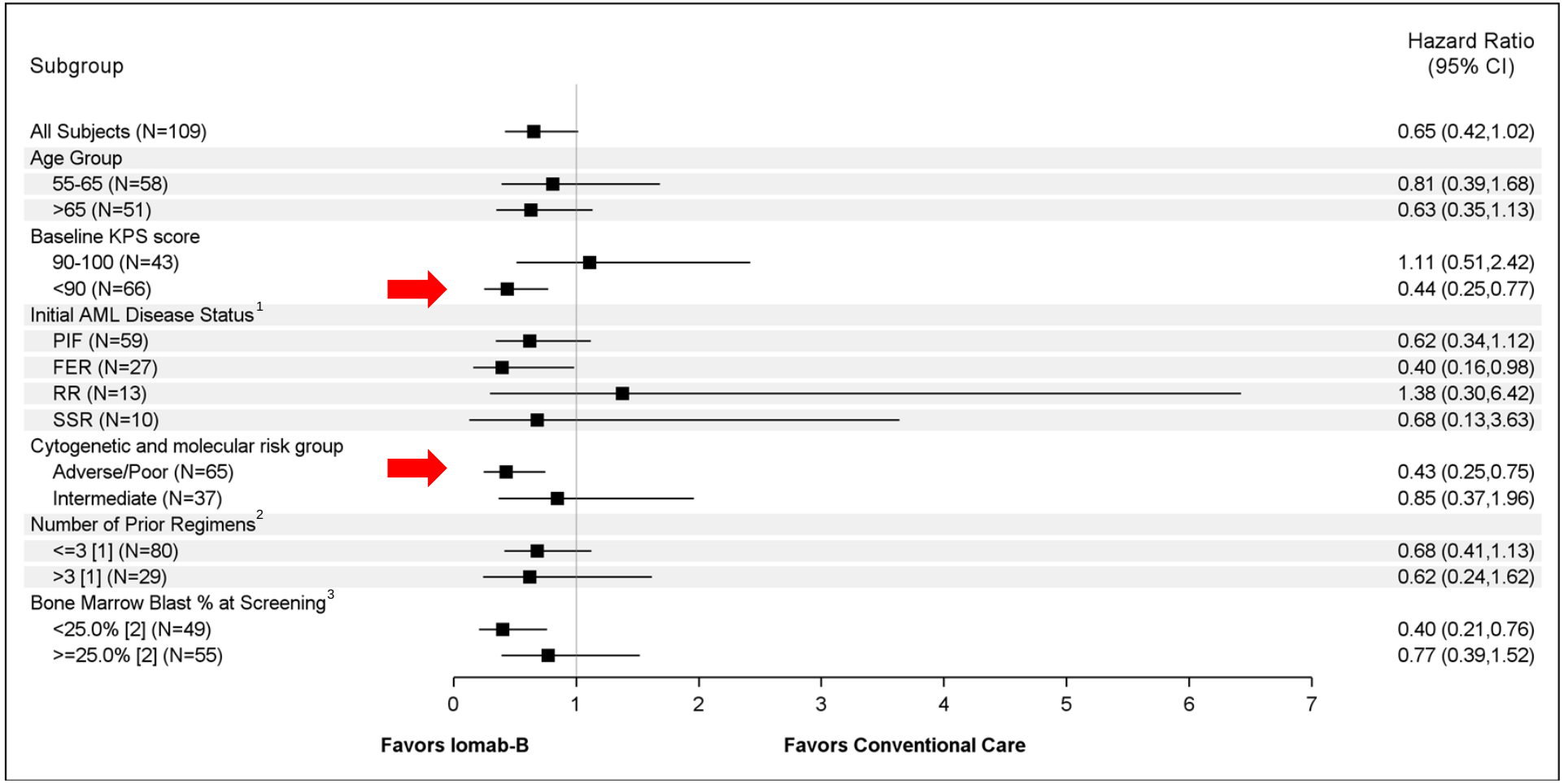
	Iomab-B (N=76)	CC Only (without Crossover) (N=33)
Overall Survival (mos) Median (95% CI)	**6.4** (5.1, 7.9)	**3.2** (1.6, 7.0)
One-Year Survival % (95% CI)	**26.0** (16.7, 36.4)	**13.1** (4.2, 27.4)
Duration of Follow-up (mos) Median (Range)	**6.3** (0.5-49.5)	**3** (0.6-28.8)

- Median OS in crossover cohort was **7.1 mos** (95% CI [5.2, 9.2])
- In crossover cohort, survival at 1 year was **35.8%** (95% CI [22.0, 49.8])
- Duration of follow-up (median, range) was **7.1 mos** (1.7-56.5)



Iomab-B Superior to CC Across Subgroups

- Forest Plot of Hazard Ratios for Overall Survival
  - Iomab-B, N=76; CC (without Crossover), N=33



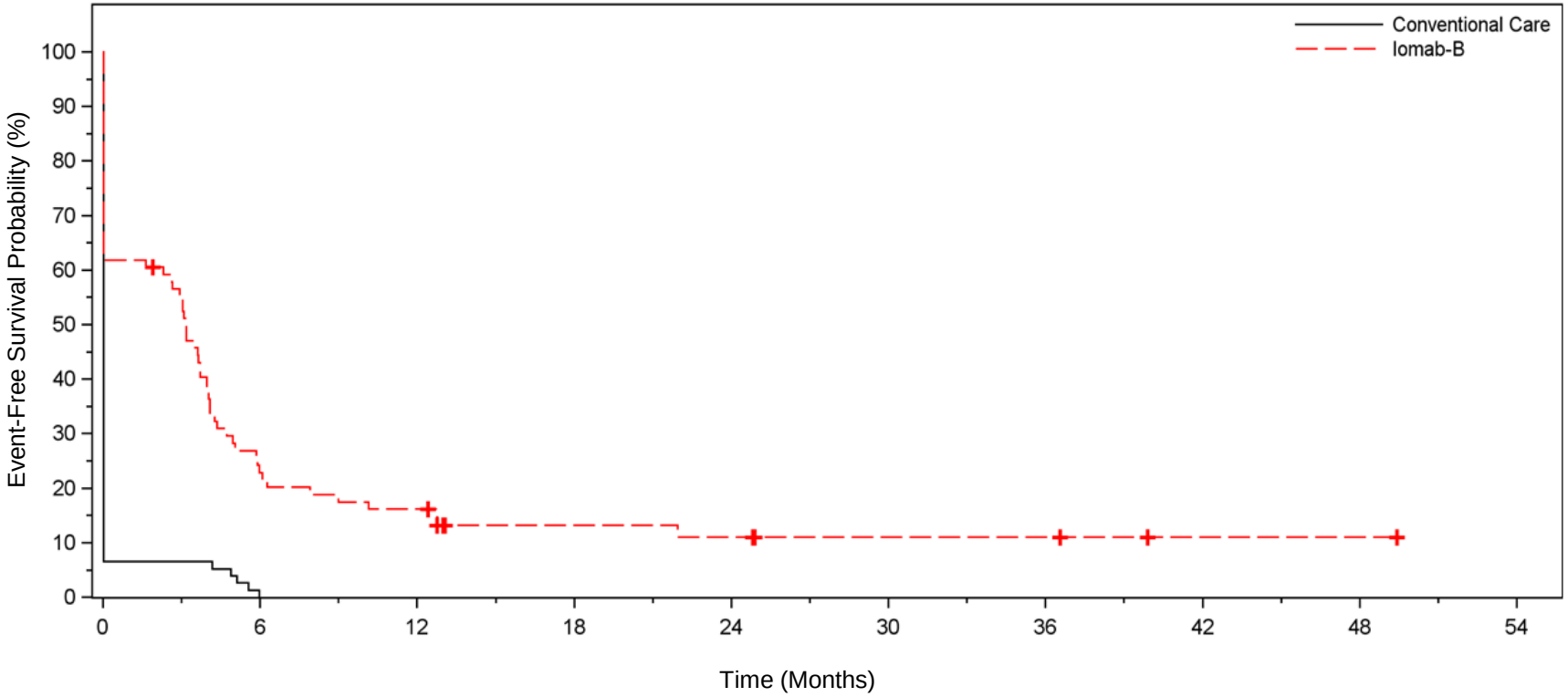
1. PIF: Primary induction failure; FER: First early relapse; RR: Relapse refractory; SSR: Second or subsequent relapse.
2. Median 3 prior regimens across both treatment groups for the Intent-to-Treat Analysis set
3. Median 25% marrow blasts across both treatment groups for the Intent-to-Treat Analysis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

Significantly Improved Event-Free Survival with Iomab-B Versus CC

EFS in Intent-to-Treat Groups

	Iomab-B (N=76)	CC (N=77)
EFS at 180 days	28%	0.2%

HR 0.22 (95% CI [0.15, 0.34])
p<0.0001

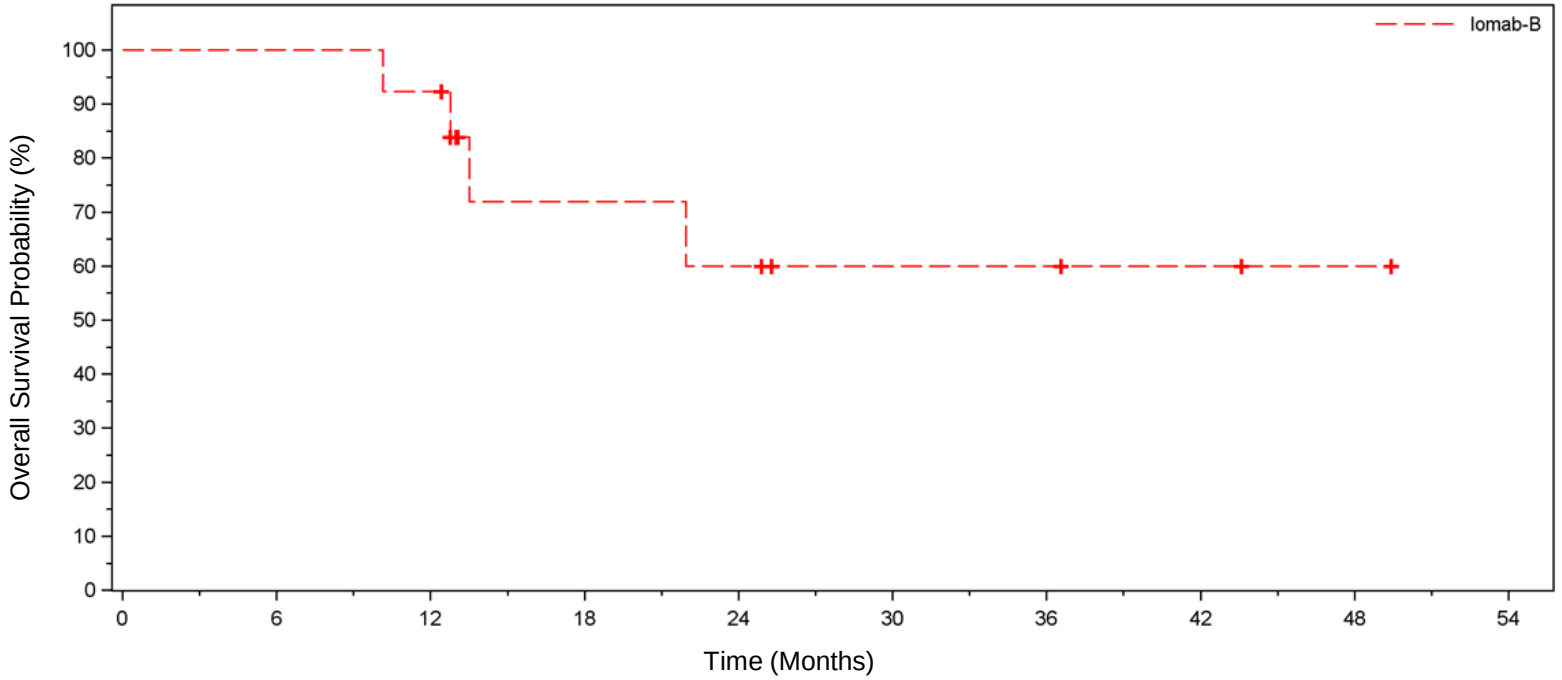


Events defined as:

- Induction treatment failure (ITF), defined as day of randomization
- Crossover following ITF
- Iomab-B patients who do not receive HCT
- Relapse after induction treatment success
- Death

Long-Term Survival in Patients with dCR

Rate of OS at:	Iomab-B (N=13)	CC (N=0)
6 months	100%	NA
12 months	92.3%	
18 months	71.9%	
24 months	59.9%	



Favorable Safety Profile for Iomab-B Compared to CC

Grade ≥3 Treatment-Emergent Adverse Events in Transplanted Patients Through Day 100 Post-HCT

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

- In pts ≥55yrs with active R/R AML, Iomab-B followed immediately by RIC conditioning with fludarabine and low-dose TBI enabled allogeneic HCT in a population not typically eligible for transplant
- Iomab-B was well-tolerated and resulted in engraftment in all treated patients, a high rate of dCR lasting ≥180 days, and a low rate of serious adverse events
- A significant proportion of patients who achieve dCR with Iomab-B are long-term survivors (~60%)
- Iomab-B offers a novel solution to increase access to HCT and improve outcomes in pts with R/R AML and establishes a potential new standard of care for patients failing to achieve remission
- Further exploration of Iomab-B in other indications and with different conditioning regimens and donor types is warranted and planned

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