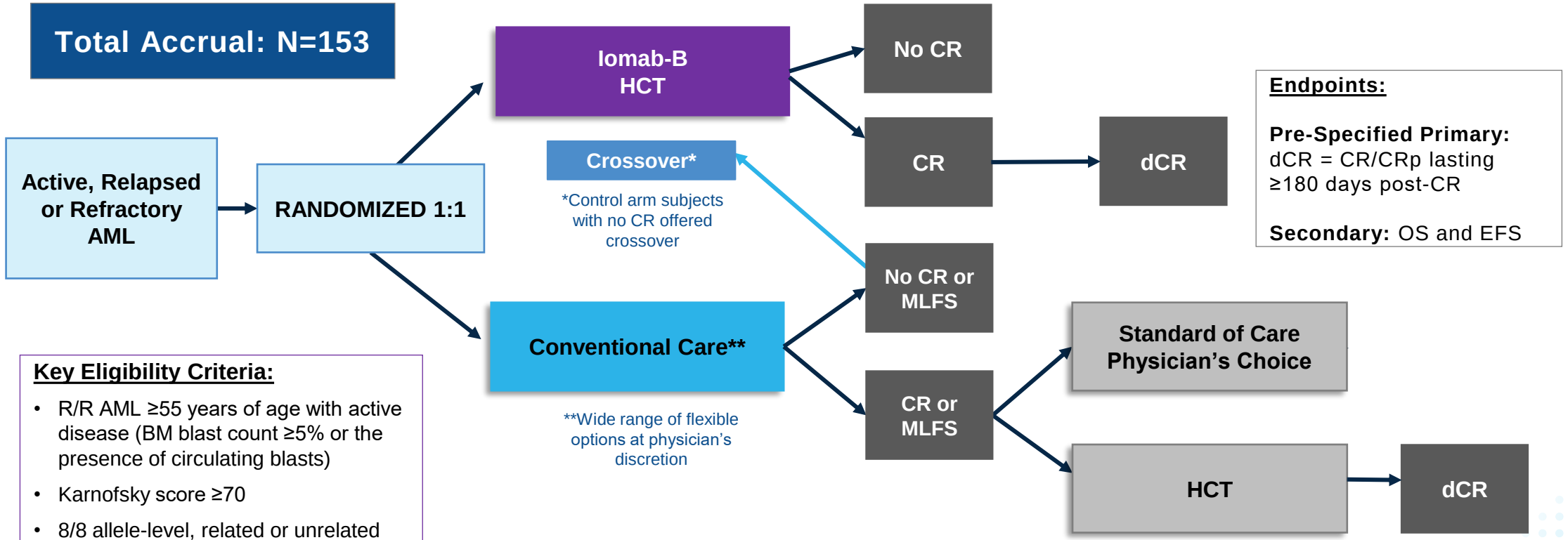
^{131}I-apamistamab-Led Allogeneic Hematopoietic Cell Transplant Significantly Improves Overall Survival in Patients with TP53 Mutated R/R AML

Hannah Choe, MD, Ben K. Tomlinson, MD, Boglarka Gyurkocza, MD, Rajneesh Nath, MD, Stuart Seropian, MD, Mark R. Litzow, MD, Camille N. Abboud, MD, Patrick J. Stiff, MD, Sunil Abhyankar, MD, James Foran, MD, Sameem Abedin, MD, George Chen, MD, Zaid Al-Kadhimi, MD, Partow Kebriaei, MD, Mitchell Sabloff, MSc, MD, FRCPC, Johnnie J. Orozco, MD, PhD, Katarzyna Joanna Jamieson, MD, Margarida Magalhaes-Silverman, MD, Koen Van Besien, MD, PhD, Michael W. Schuster, MD, Arjun D. Law, MD, Sebastian A. Mayer, MD, Hillard M. Lazarus, MD, Jennifer Spross, MA, Kate L Li, PhD, Elaina Haeuber, MS, Madhuri Vusirikala, MD, Akash Nahar, MD, MPH, Brenda M. Sandmaier, MD, John M. Pagel, MD, PhD, Sergio A. Giralt, MD, Avinash Desai, MD and Nebu Koshy, MD.

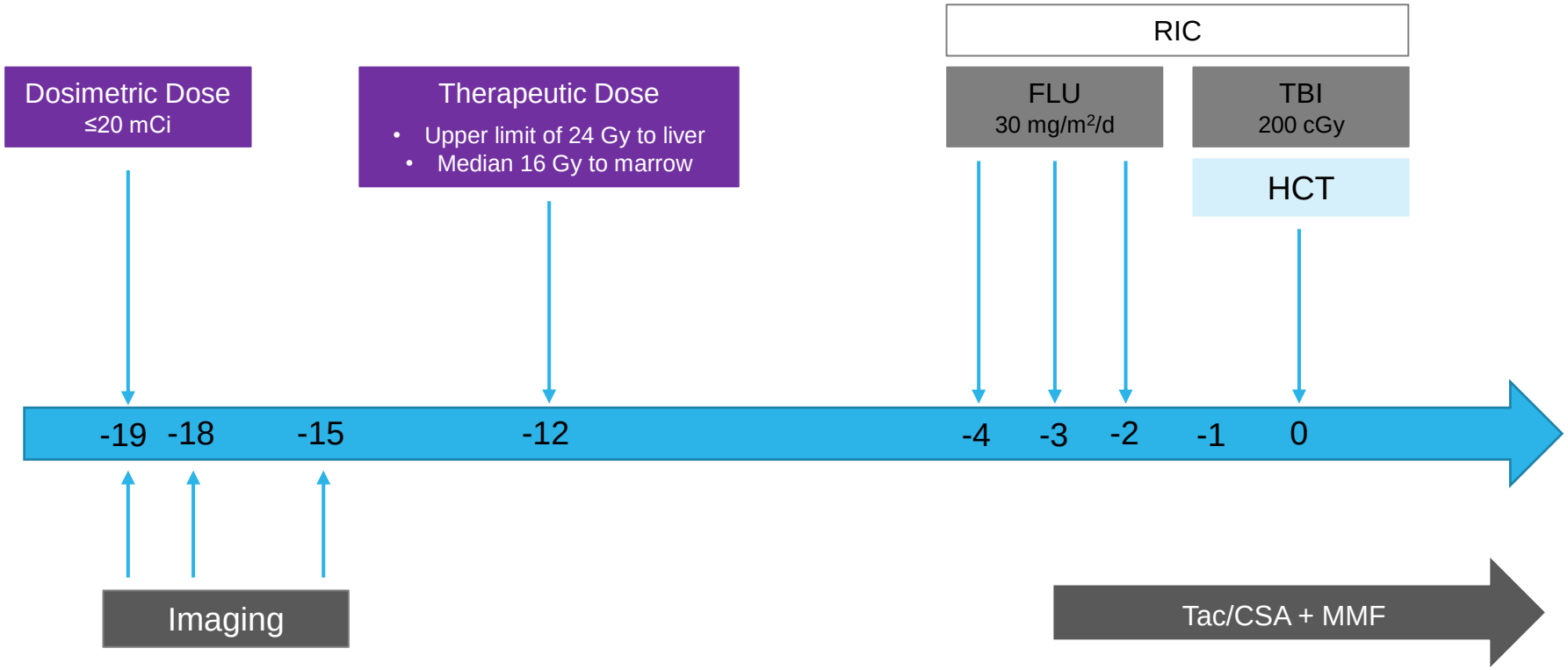
Background

- Patients with TP53 mutated R/R AML have a dismal prognosis with limited treatment options and are seldom offered alloHCT due to high post-transplant relapse rates.
- ^{131}I-apamistamab (Iomab-B) is an anti-CD45 radioimmunoconjugate designed to deliver high dose targeted radiation to hematopoietic cells, allowing for myeloablation and eradication of leukemic cells to enable alloHCT in patients with active R/R AML while limiting off-target toxicity and being mutation-agnostic
- The SIERRA trial compared Iomab-B followed by alloHCT to physician's choice of conventional care, recently reporting that the study met its primary endpoint of durable complete remission lasting at least 6 months
- We compared the outcomes and safety data in patients enrolled in the SIERRA trial with a documented TP53 mutation versus wildtype

SIERRA – A Phase 3 Randomized Trial in R/R AML

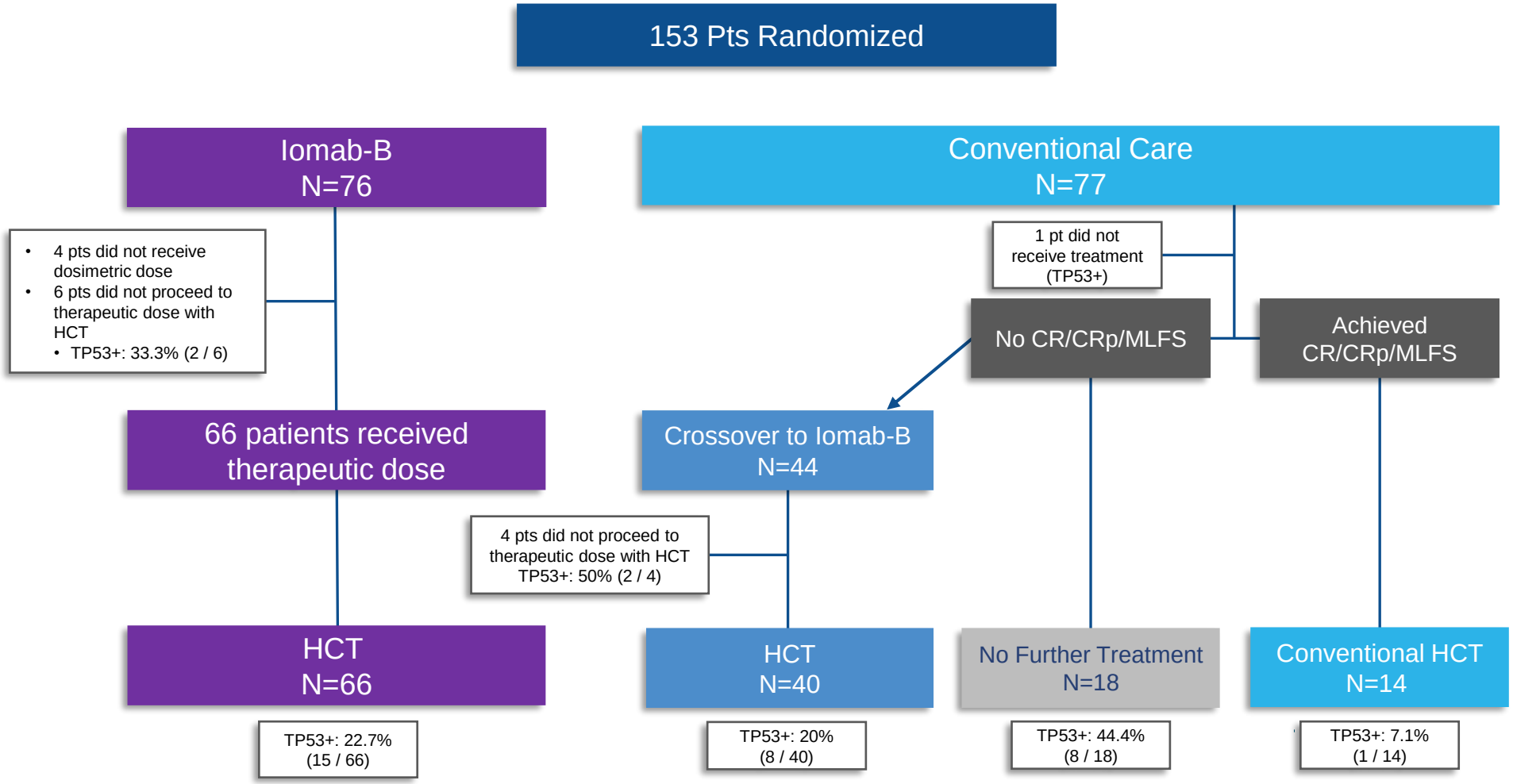


Personalized Single Dose Combined Induction/Conditioning



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

SIERRA Patient Distribution



Baseline Characteristics in Patients with TP53 Mutations (N = 37)

	Iomab-B (N=17)	Conventional (N=10)	Crossover (N=10)
Age, years Median (Range) N (%)	**63** (56-74) Pts >65 yrs: **6** (35.3)	**66** (61-71) Pts >65 yrs: **7** (70.0)	**64** (55-74) Pts >65 yrs: **4** (40.0)
Disease Status at Randomization N (%)	Primary Induction Failure: **12** (70.6) First Early Relapse: **4** (23.5) Relapse/Refractory: **0** (0.0) 2nd + Relapse: **1** (5.9)	Primary Induction Failure: **7** (70.0) First Early Relapse: **2** (20.0) Relapse/Refractory: **1** (10.0) 2nd + Relapse: **0** (0.0)	Primary Induction Failure: **4** (40.0) First Early Relapse: **5** (50.0) Relapse/Refractory: **0** (0.0) 2nd + Relapse: **1** (10.0)
Prior Lines of Treatment Median (Range)	**2** (1-4)	**3** (1-4)	**4** (1-6)
Prior Venetoclax Treatment N (%)	**9** (52.9.)	**6** (60.0)	**6** (60.0)
Karnofsky Performance Status N (%)	≥90: **9** (52.9) <90: **8** (47.1)	≥90: **1** (10.0) <90: **9** (90.0)	≥90: **5** (50.0) <90: **5** (50.0)
HCT Co-Morbidity Index N (%)	0-2: **9** (52.94) ≥3: **8** (47.05)	0-2: **6** (60.0) ≥3: **4** (40.0)	0-2: **6** (60.0) ≥3: **4** (40.0)

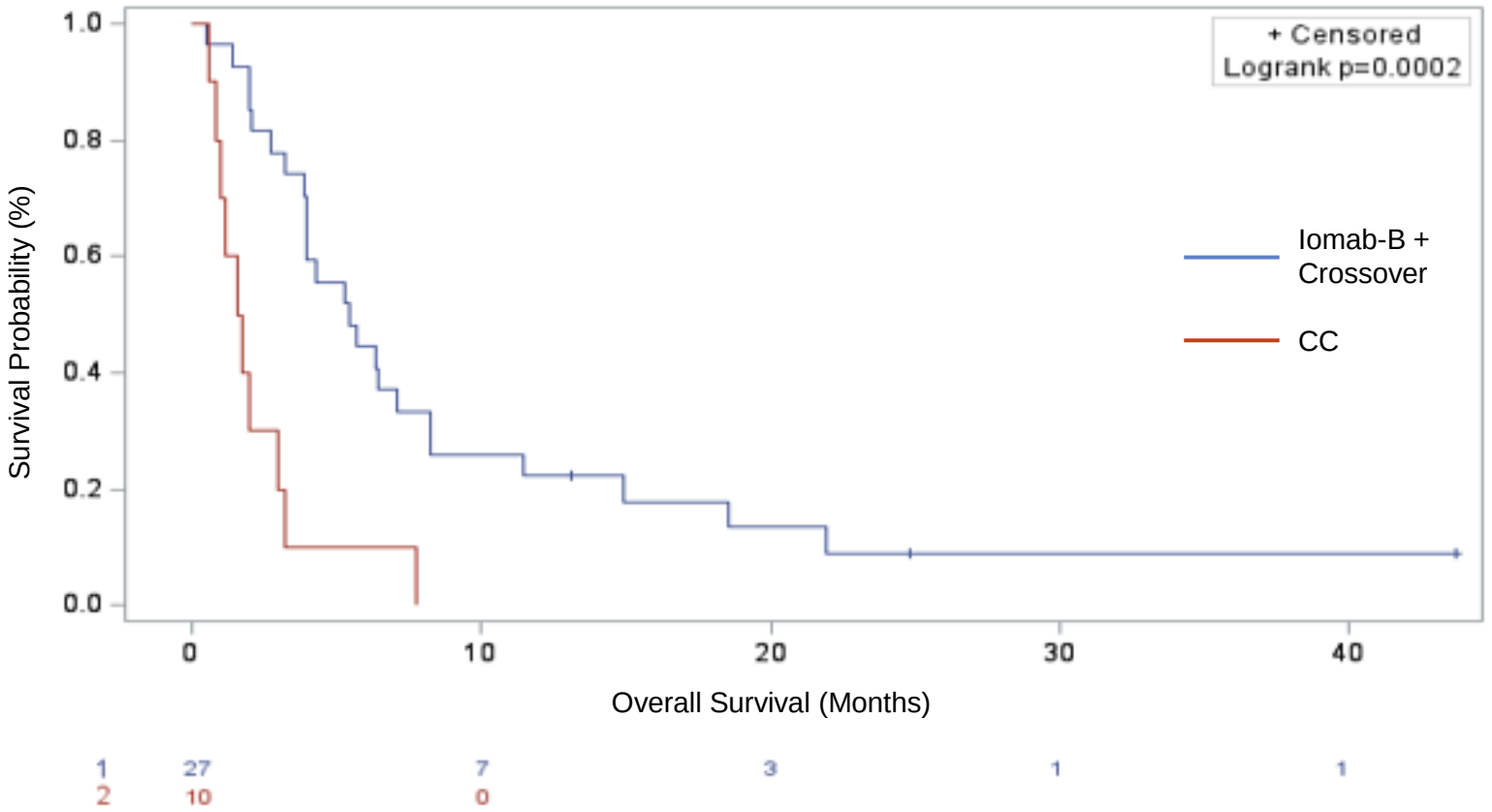
1. Per NCCN Guidelines, Version 3, 2020

CR and dCR by TP53 Mutation Status and Treatment Received

- Overall dCR Rates at 6 months were 22% in the Iomab-B group vs. 0% in the CC group (95% CI;12.29, 34.73; p<0.0001), irrespective of TP53 mutational status.
- Median OS of TP53 positive patients on CC arm was 1.66 mos versus 5.49 mos in TP53 positive patients who received Iomab-B and alloHCT

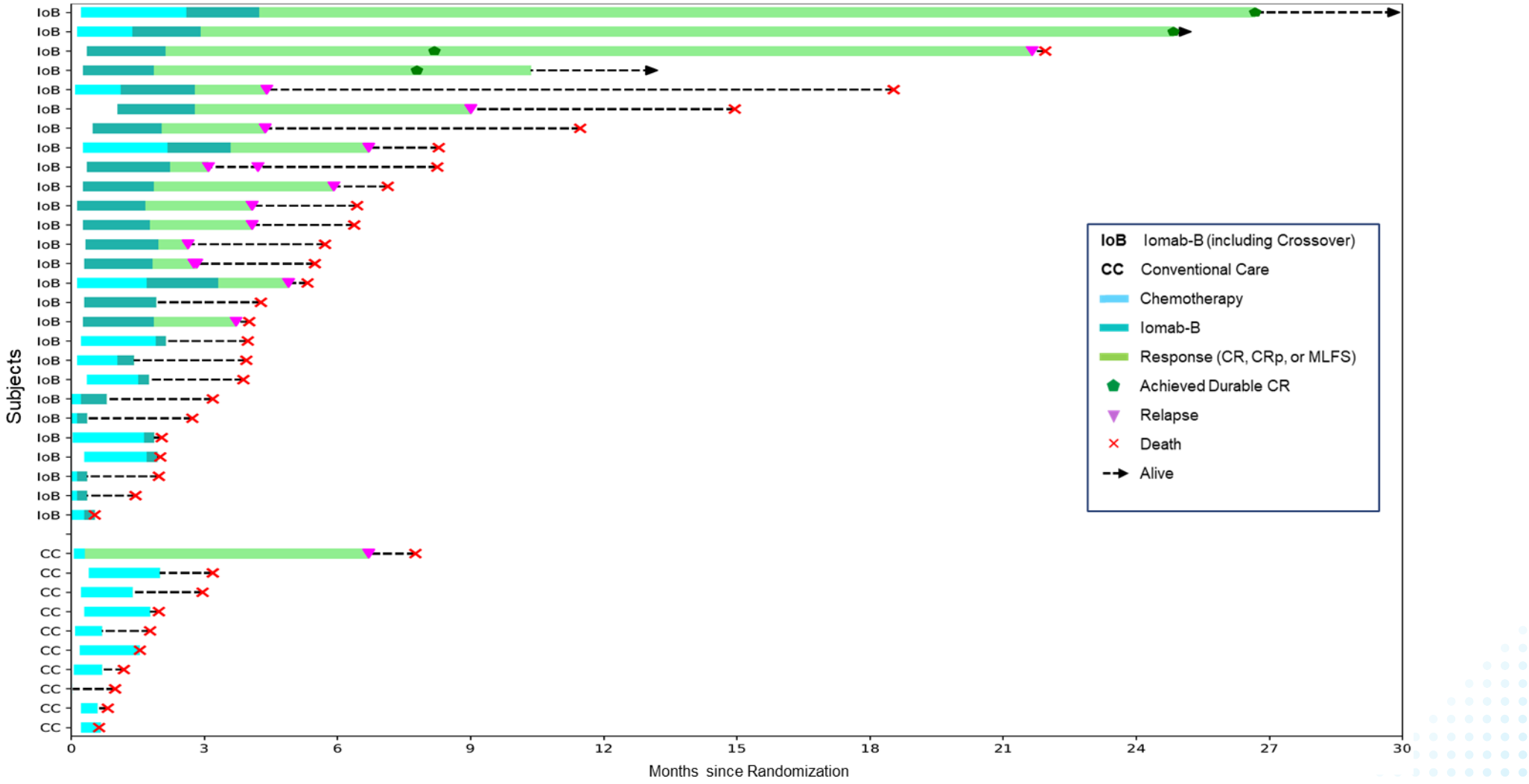
	Iomab-B + Crossover			Conventional Care		
	N	%	95% CI	N	%	95% CI
TP53 Positive	*N = 27*			*N = 10*		
CR	15	**55.56**	(35.33, 74.52)	0	**0**	-
Durable CR	4	**14.81**	(4.19, 33.73)	0	**0**	-
TP53 Wildtype	*N = 93*	**%**	95% CI	*N = 23*	**%**	95% CI
CR	54	**58.06**	(47.38, 68.22)	4	**17.39**	(4.95, 38.78)
Durable CR	15	**16.13**	(9.32, 25.20)	0	**0**	-

Improved Survival with ^{131}I-apamistamab in Patients with TP53 Mutation



	Iomab-B + Crossover	Conventional Care
	N = 27	N = 10
Median OS (mos) (95% CI)	**5.49** (3.94, 8.25)	**1.66** (0.99, 2.96)
Hazard Ratio (95% CI)	**0.23** (0.10, 0.52)	
p value (log-rank)	**0.0002**	

SIERRA Trial Patients with TP53 Mutation



Treatment-Emergent Adverse Events (Grade ≥3)

	TP53 Positive Patients Receiving Iomab-B + HCT[1] N = 23	TP53 Negative Patients Receiving Iomab-B + HCT[1] N = 83	Standard HCT N = 14
Febrile Neutropenia N (%)	**11** (47.8)	**35** (42.2)	**7** (50.0)
Mucositis[2] N (%)	**4** (17.4)	**13** (15.7)	**3** (21.4)
Sepsis N (%)	**4** (17.4)	**8** (9.6)	**4** (28.6)
Cumulative Incidence aGVHD (Gr III-IV) % (95% CI)	**8.7** (1.4, 24.7)	**8.6** (3.8, 16.1)	**14.3** (2.1 , 37.6)

- TP53 mutations are not associated with increased transplant-related toxicity
- Safety data in TP53 positive patients transplanted with Iomab-B aligns that of the entire Iomab-B-treated population

1. Includes patients randomized to Iomab-B arm and CC patients who crossed over to Iomab-B
2. 'Mucositis' includes the Preferred Terms 'Stomatitis' and 'Mucosal Inflammation'

Conclusions

- Patients with TP53-mutated relapsed or refractory AML have a dismal prognosis and are generally unable to access potentially curative alloHCT due to resistant disease.
- ^{131}I-apamistamab led alloHCT significantly improves survival outcomes in this very high-risk patient population with TP53 mutations, with response rates and overall survival commensurate with those observed in patients without this mutation.
- The safety profile in this population was similar to the overall SIERRA trial, and Iomab-B was well-tolerated with a low rate of serious adverse events.
- These data support the use of ^{131}I-apamistamab led induction/conditioning and alloHCT in R/R AML, especially in patients with difficult-to-treat, TP53-mutated disease.