

# A RANDOMIZED PHASE II STUDY OF DARATUMUMAB, IXAZOMIB, AND DEXAMETHASONE (DID, ARM A) VS DARATUMUMAB, BORTEZOMIB AND DEXAMETHASONE (DVD) FOLLOWED BY DARATUMUMAB, DID (ARM B) IN NEWLY DIAGNOSED MULTIPLE MYELOMA (DERIVE) STUDY

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## Background

The safety and efficacy established by daratumumab (a CD38 monoclonal antibody)-based induction therapies for both transplant-eligible myeloma patients (based on CASSIOPEIA and GRIFFIN trials) and transplant-ineligible patients (based on MAIA trial) have gained an accelerated momentum for adoption into regular clinical practice. In this context, to find the most optimal non-IMiD based daratumumab-combination therapy as induction, we conducted a randomized phase 2 study to evaluate the safety and efficacy for in-class transition from bortezomib to ixazomib, stratified by transplant-eligibility and R-ISS

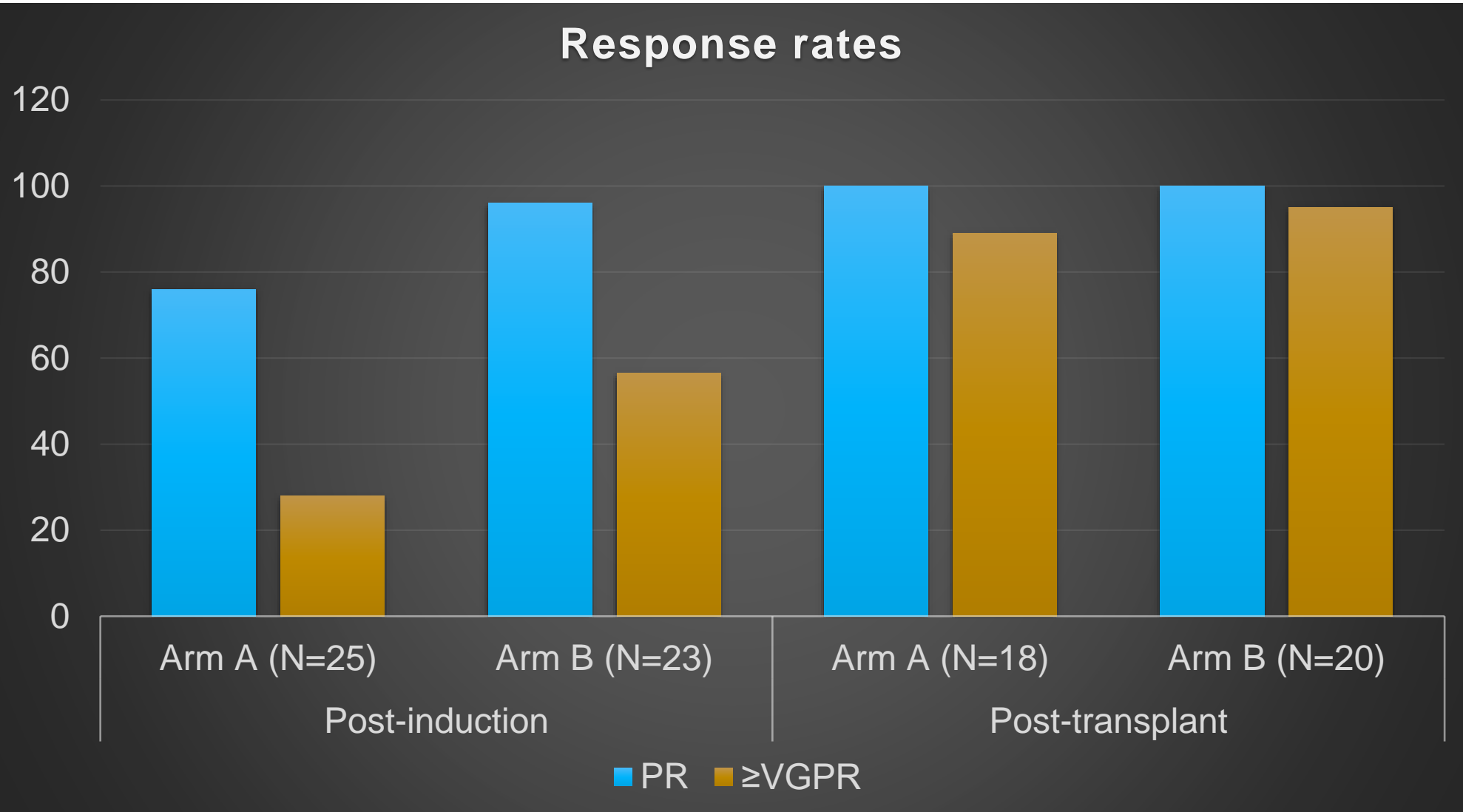
## Methods

- Randomization to Arm A [daratumumab, ixazomib and dexamethasone (DId) X 8 cycles)
  - Daratumumab IV 16 mg/kg on days 1, 8, 15, 22 every 28 days x 2 cycles; then on days 1, 15 every 28 days x 6 cycles and every 28 days during maintenance (or 1800 mg SC at the same schedule), ixazomib - 4 mg PO on Days 1, 8, and 15 every 28 days and dexamethasone - 40 mg PO on days 1, 8, 15 and 22 every 28 days
- Arm B [(daratumumab, bortezomib and dexamethsone (DVd) x 3) followed by (DId x 5 cycles)
  - Daratumumab IV 16 mg/kg on days 1, 8, 15, 22 every 28 days x 2 cycles; then on days 1, 15 every 28 days x 6 cycles and every 28 days during maintenance (or 1800 mg SC at the same schedule), bortezomib - 1.3 mg/m<sup>2</sup> SC on days 1, 4, 8 and 11 every 21 days and dexamethasone - 40 mg PO on days 1, 8, 15 and 22 every 28 days
- Primary endpoint of ≥ very good partial response rate (VGPR) rate post-induction cycle 8. Secondary endpoints: overall response rate (ORR), progression free survival (PFS) and overall survival (OS).
- Transplant eligible patients may receive transplant after cycle 8. During the maintenance phase, patients receive DId as maintenance therapy for a total of 32 cycles.

## Results

The median age was 63.5 years for the 48 evaluable subjects. 48% were black (40% vs 56.5%)

		Arm A (N=25)	Arm B (N=23)	p-value
Median Age		68.07 (48.06-86.88)	60.47 (36.8-79.73)	0.248
Sex	Male	16 (64%)	11 (48%)	0.201
	Female	9 (36%)	12 (52%)	
Race	White	15 (60%)	9 (39%)	0.245
	Black	10 (40%)	13 (56.5%)	
	American Indian		1 (4.5%)	
Risk	High risk	2 (8%)	3 (13%)	0.459
	Standard risk	23 (92%)	20 (87%)	
Transplant	Yes	18 (72%)	20 (91%)	0.1
	No	7 (28%)	2 (9%)	



AE profile was similar across both cohorts

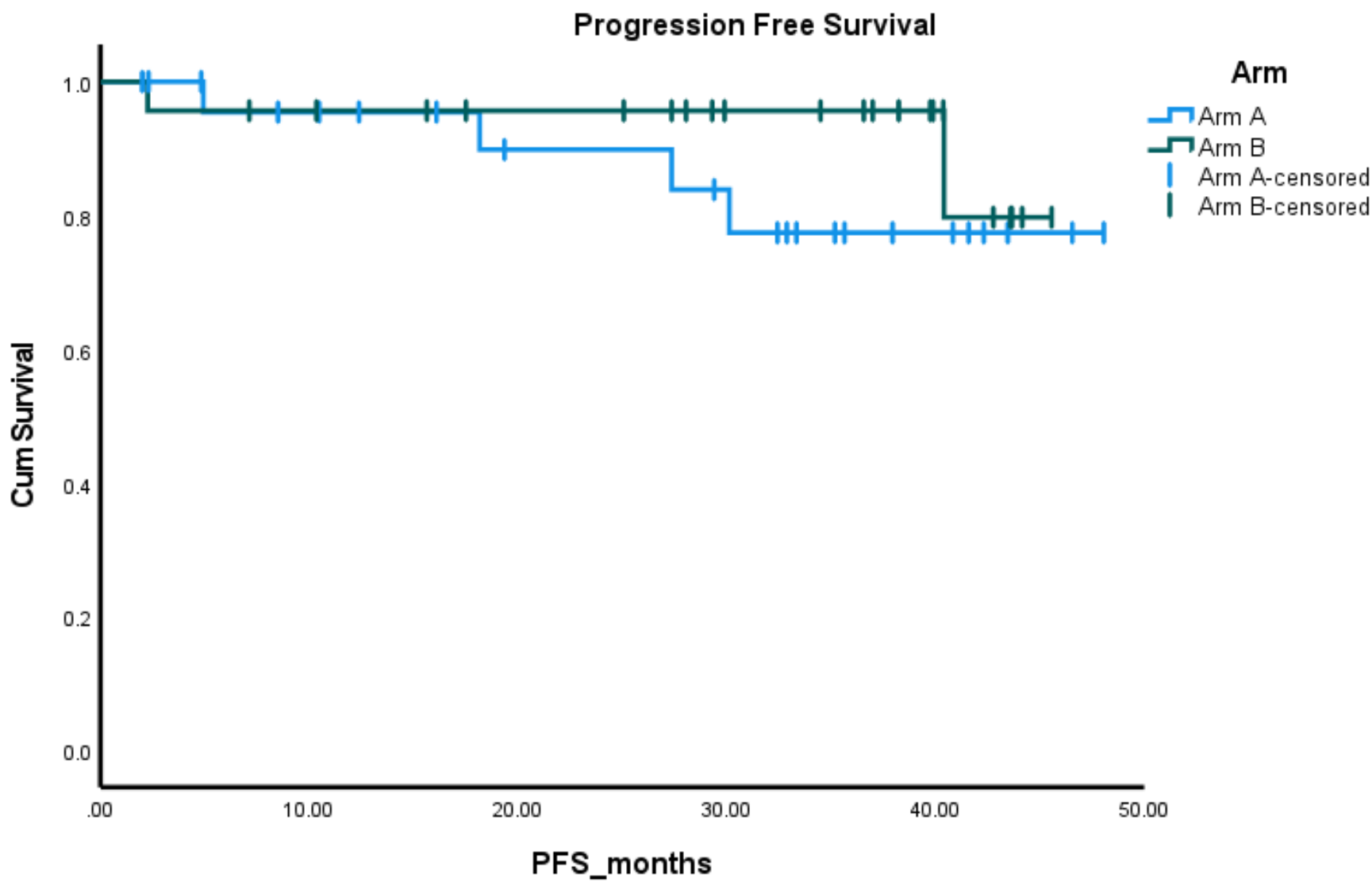
- grade 3/4 events occurred in 6 (24%) vs 7 (30%) for Arm A and B, respectively, p=0.27).

There was no grade 3/4 peripheral neuropathy (PN)

- grade 1/2 PNs were higher in Arm B.

There were two secondary primary malignancies reported in Arm B (prostate, esophageal adenocarcinoma)

## Results Continued



## Conclusion

- This is one of the first studies showing the safety and efficacy of non-IMiD based dara-combination induction therapies with in-class transition of bortezomib to ixazomib yielding higher response rates post-induction and post-transplant without compromising safety.
- 3-year PFS rate of close to 80% across both arms for daratumumab and proteasome inhibitor combination therapy are highly encouraging.

## Data Application to Patient Care

- The study results suggest in class transition of DVd→DId may be an alternative regimen for patients that may not tolerate IMiDs or that have a contraindication to receive IMiDs

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