

Efficacy and Safety of SV-BR-1-GM After Progression on ADC in Metastatic Breast Cancer Patients



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BACKGROUND

Antibody-drug conjugate (ADC) therapy, while effective, presents several significant therapeutic challenges for metastatic breast cancer (MBC) patients. While effective, ADCs like SG and T-DXd often lead to severe side effects, including Interstitial Lung Disease (ILD), and raise concerns of cross-resistance due to their shared cytotoxic class (topoisomerase-1 inhibitor). SV-BR-1-GM is an off-the-shelf whole cell therapeutic vaccine that expresses class I & II HLAs, secretes GM-CSF, and functions as antigen-presenting cells, with subsequent enhancements improving in-vitro characteristics¹. By expressing cancer antigens such as HER2 and PRAME, SV-BR-1-GM also serves as the reservoir of antigens to activate the patient's anti-tumor immune responses.

METHODS

This retrospective subset analysis include 23 ADC-refractory patients in the ongoing Ph2 trial (NCT03328026). The study assesses the efficacy of Bria-IMT (irradiated SV-BR-1-GM ~20x10⁶ cells, intradermally 48-72 hours after cyclophosphamide 300 mg/m², followed by low-dose interferon-alpha at the inoculation sites 2 days later), which was administered q3wks in combination with a check point inhibitor (CPI). DTH to Bria-IMT and anergy to Candin were evaluated. Bria-IMT PFS was defined as informed consent date to treatment termination. Penultimate PFS was defined as penultimate treatment start date to treatment termination.

RESULTS

Table 1: ADC-Refractory Patient Demographics

N	Age, Median (Range)	Prior Lines, Median (Range)	Prior CPI Therapy (N)	≥ 2 Prior Lines of ADC (N)
23	62, (41-83)	6, (3-13)	7	8

Conclusion: The ADC-refractory cohort was heavily pretreated

Table 2: Treatment Efficacy by MBC Subtype in ADC-refractory patients

Biomarker	HR+/HER2-	HR-/HER2low	TNBC	HER2+	ALL
N	10	4	7	2	23
Evaluable N	8	3	3	2	16
Best ORR	13% (1 / 8)	0 (0 / 3)	0 (0 / 3)	0 (0 / 2)	6% (1 / 16)
Best CBR	63% (5 / 8)	66% (2 / 3)	0 (0 / 3)	100% (2 / 2)	56% (9 / 16)

Conclusion: The ADC-refractory cohort consisted of patients with advanced metastatic breast cancer (MBC) encompassing a spectrum of molecular subtypes. Best overall objective response rate (ORR) to the treatment was 6%, with HR+/HER2- showing the highest ORR at 13%. Best clinical benefit rate (CBR) was favorable, with an overall rate of 56%. HER2+ subtype demonstrated a 100% CBR, suggesting a potential subtype-specific efficacy.

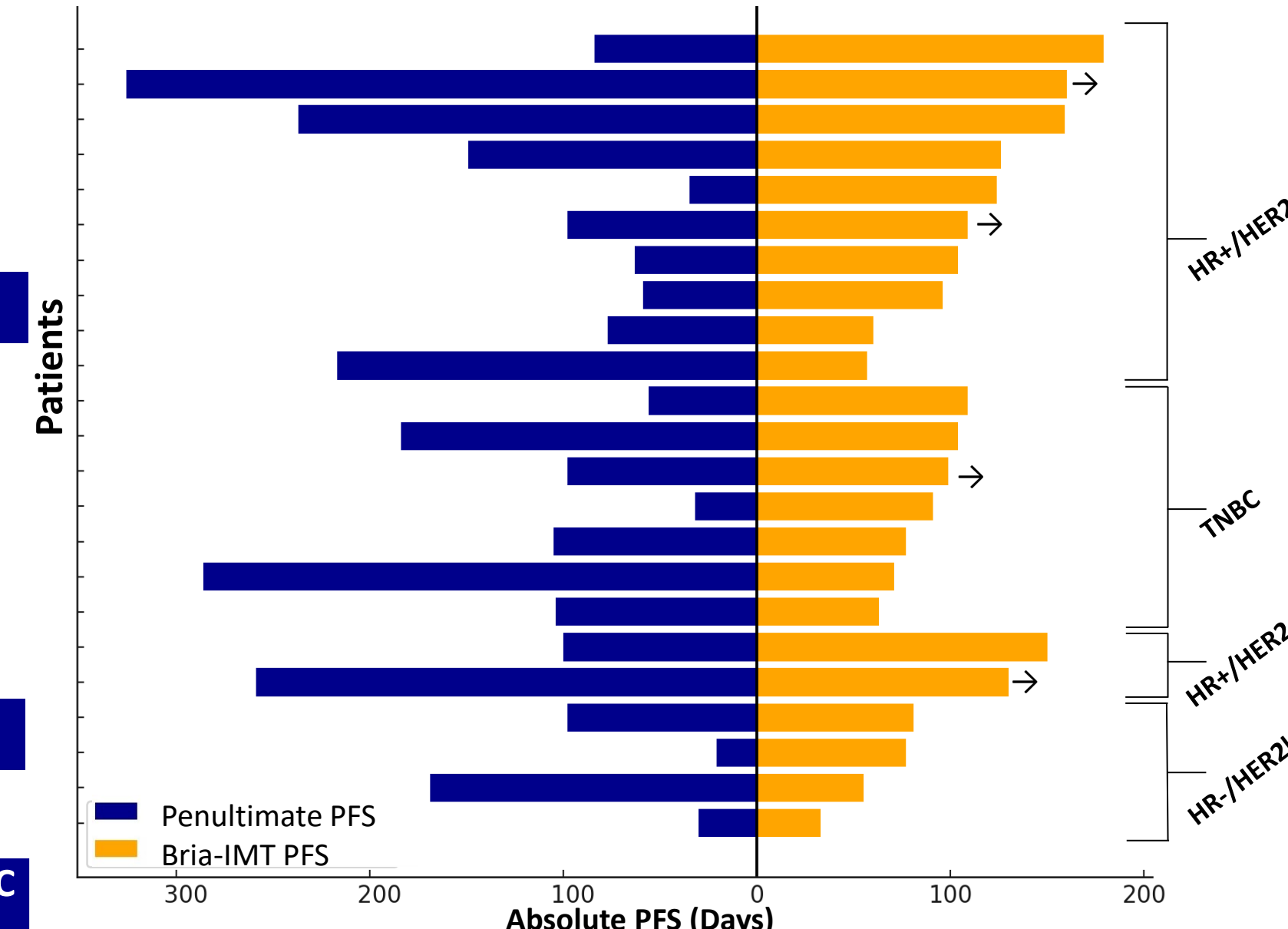
Table 3: Adverse Events in ADC-refractory patients

Toxicity-Related Treatment Discontinuations	None
Grade 3 or 4 Adverse Events (AEs) Reported	43% (10/23)
Interstitial Lung Disease (ILD) Reported	None
Adverse Events (AEs)	
Injection Site Reaction	39%
Fatigue	26%
Nausea/Vomiting	43%
Severity of Most AEs	mild to moderate
Most Clinically Significant Grade 4 AE	elevated lipase (1 case)

Conclusion: Bria-IMT was well-tolerated with no discontinuations due to toxicity, 43% experienced serious adverse events (AEs) not necessarily caused by the drug, the most commonly reported AE was injection site reaction. Notably, no instances of Interstitial Lung Disease were reported.

RESULTS

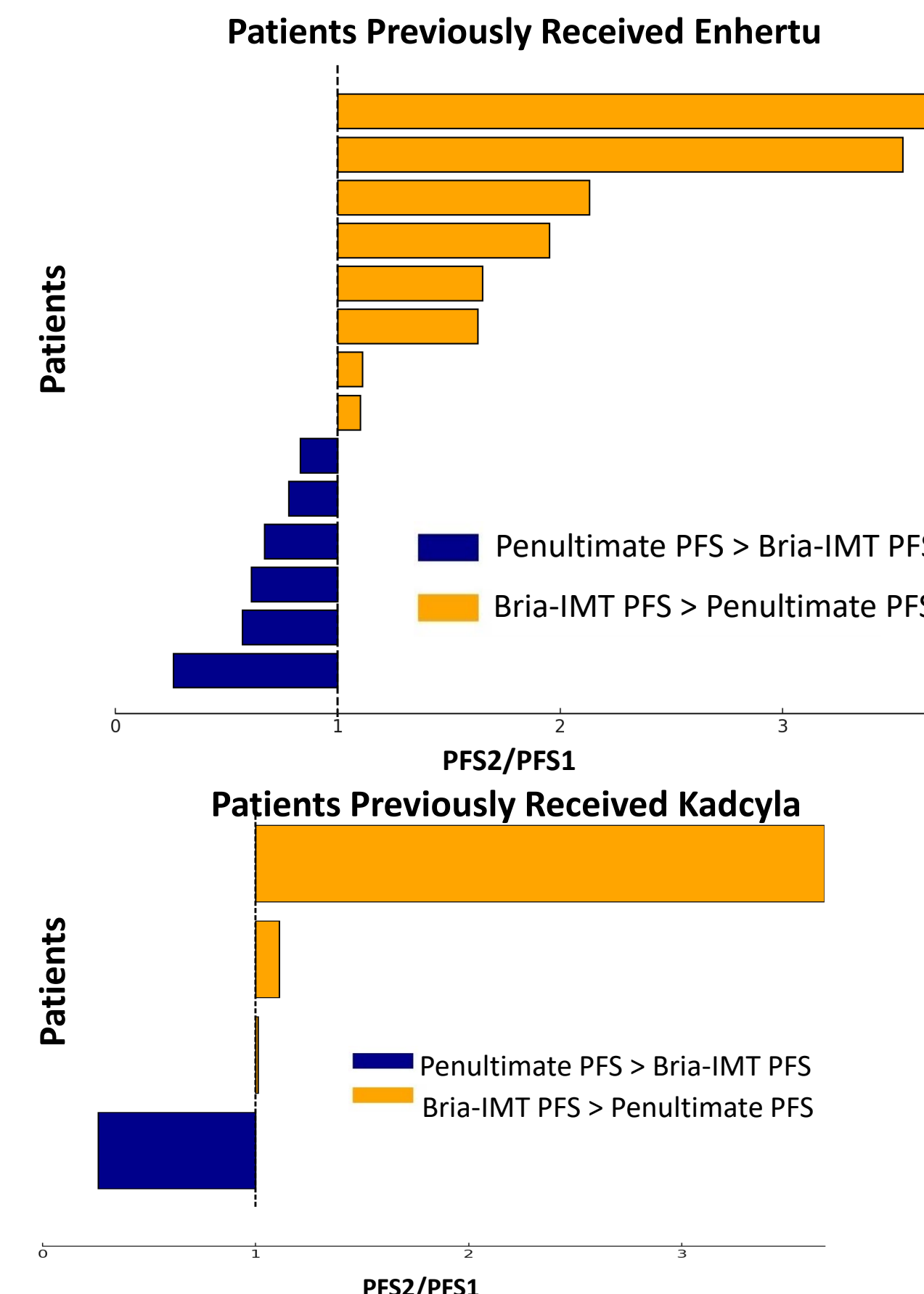
Figure 1a: Bar chart showing Bria-IMT PFS vs Penultimate Therapy PFS in ADC-refractory patients



→ indicates patient currently enrolled

Conclusion: Bria-IMTTM showed potential efficacy in reversing immune exhaustion and prolonging the duration of PFS in patients who had previously failed various ADC therapies (Trodelvy, Enhertu, Kadcyla). This suggests a potential benefit of Bria-IMTTM in patients refractory to these treatments.

Figure 2: Penultimate Therapy PFS vs Bria-IMT PFS ratio by specific ADC.



Conclusion: Bria-IMTTM showed potential survival advantage over penultimate treatment, likely by reversing immune exhaustion in patients irrespective of specific prior ADC.

Figure 1b: Bar chart of PFS ratio (PFS on Bria-IMT divided by PFS penultimate therapy). In ADC-refractory patients

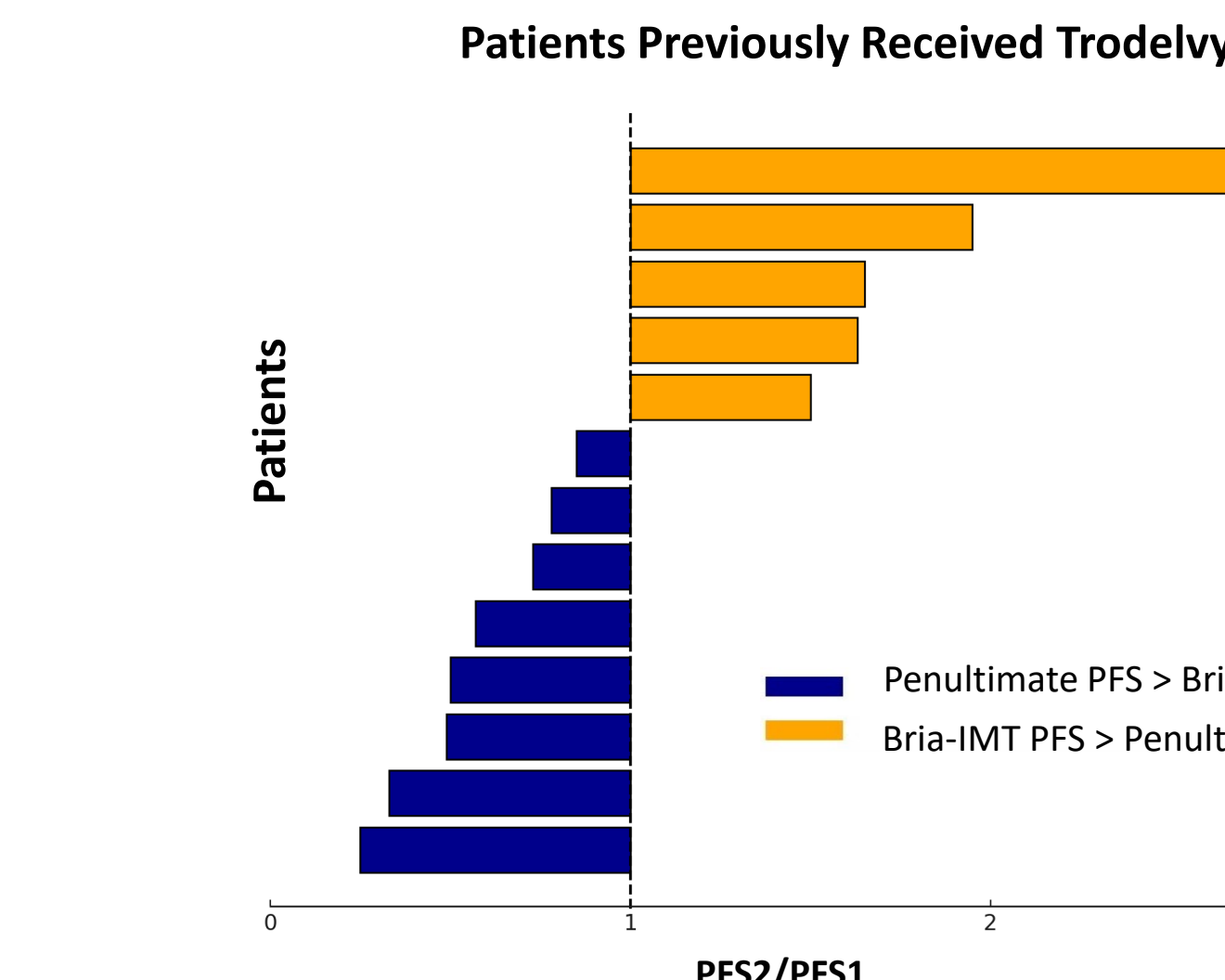
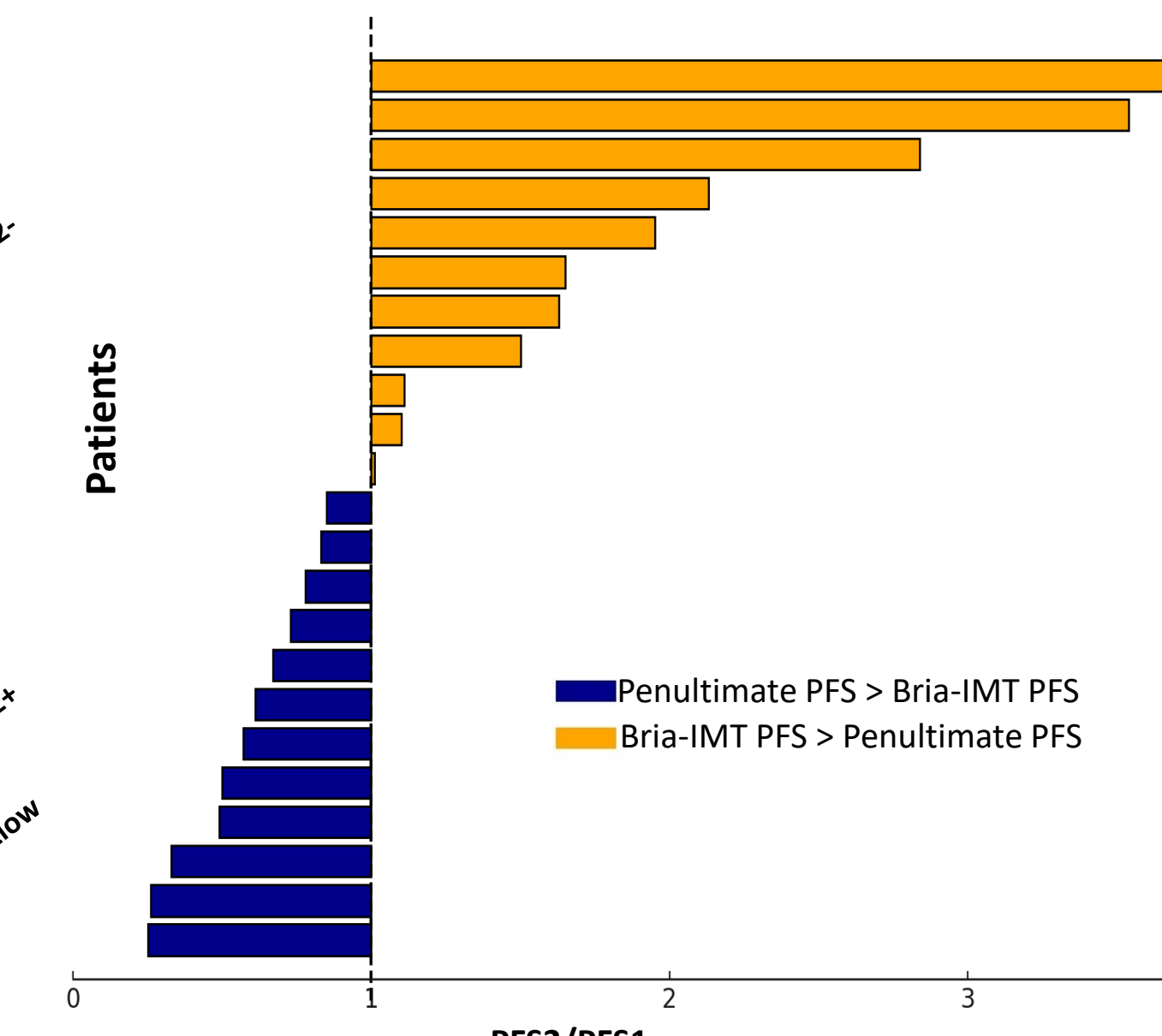
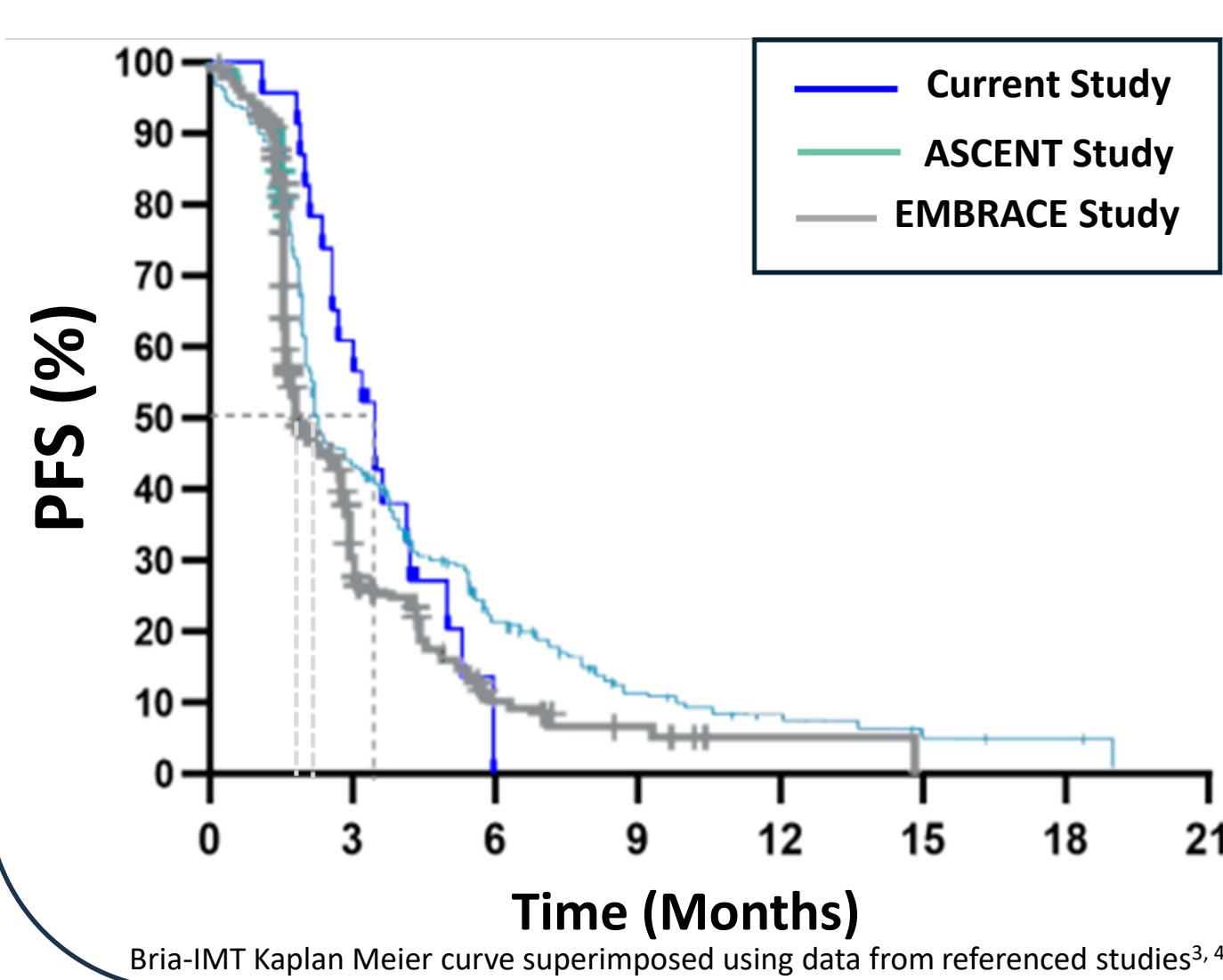


Figure 3: Cross-Trial Comparison: Kaplan-Meier curves presenting ADC-refractory patient data on PFS of the Bria-IMT Combination vs TPC arms from two other trials.



Bria-IMT Kaplan Meier curve superimposed using data from referenced studies^{3,4}

RESULTS

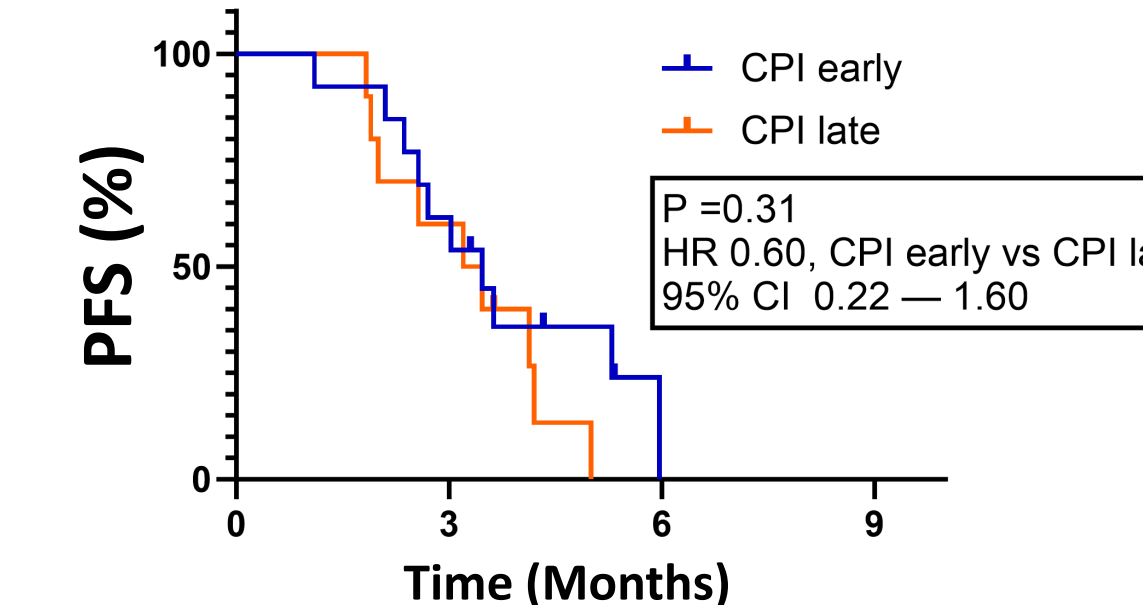
Table 5: Cross Trial Comparison of Median Progression-Free Survival (PFS) in Patients with Multiple Prior Lines of Therapy

Study	Treatment(s)	Prior Lines of Therapy, median (range)	Median PFS of TPC Arm in months	Median PFS of Experimental Arm in months
Bria-IMT (current trial, ADC-refractory subset)	Single Arm Bria-IMT regimen	6 (3-13) including ≥1 ADC	NA	3.5 (1.1 – 5.8)
EMBRACE ³	Eribulin vs TPC arm (2:1)	4 (2 – 7)	2.2 (2.0 – 2.6)	3.6 (3.3 – 3.7)
ASCENT ⁴	Sacituzumab govitecan vs TPC arm (1:1)	4 (2-14) in TNBC	1.7 (1.5 – 2.5)	4.8 (4.1 – 5.8)

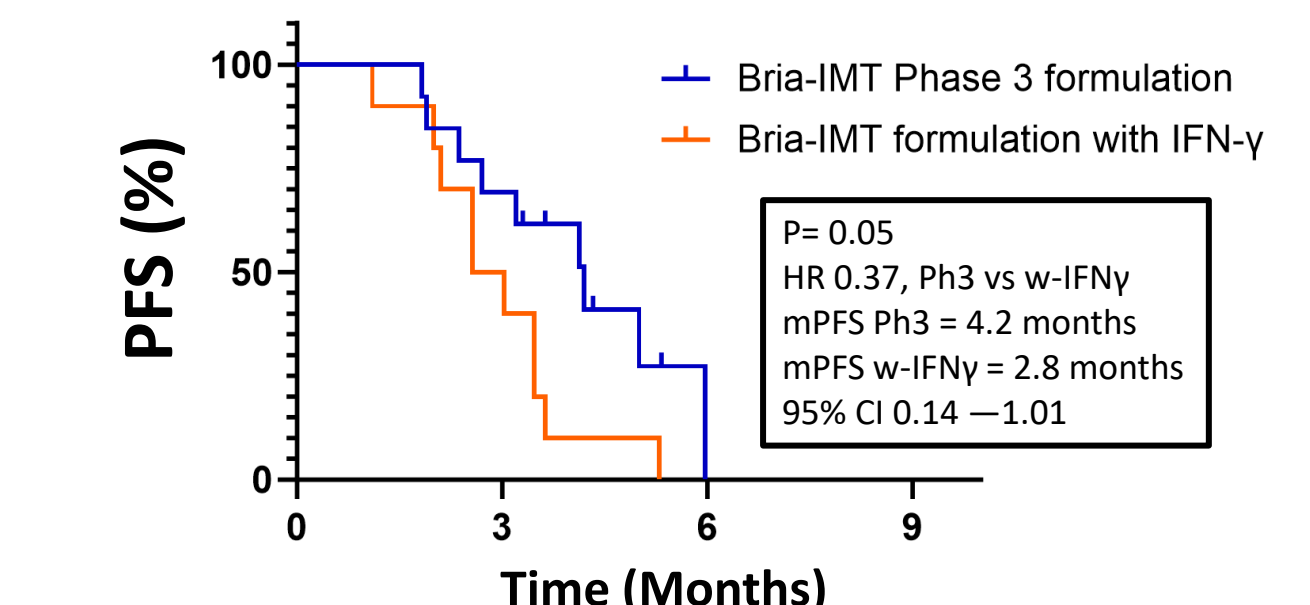
Conclusion: Compared to the Treatment of Physician's Choice (TPC) arms from two other Ph3 trials, Bria-IMT's ADC-refractory cohort had higher median PFS despite more prior lines of therapy, suggesting potential superior efficacy by overcoming immune exhaustion in heavily pretreated populations.

Figure 4: Kaplan-Meier curves presenting Treatment sequence and IP formulation and their effects on PFS in ADC-refractory cohort

Treatment Sequence: In the Bria-IMT regimen, CPI was administered either 1-2 days prior to the SV-BR-1-GM (CPI early) or skipped in cycle 1 and administered starting in Cycle 2 at 2-3 days after SV-BR-1-GM (CPI late)



IP formulation: During manufacturing, interferon-γ (IFN-γ) was either added or omitted to stimulate cells, before harvesting and formulation. The formulation omitting IFN-γ was chosen for the ongoing Bria-IMT phase 3 study (NCT06072612).



Conclusion: Sequencing of CPI and SV-BR-1-GM does not have an effect on PFS, while different IP formulations show near-significant effect on PFS in the ADC-refractory cohort. The IP formulation omitting IFN-γ is chosen for the ongoing Phase 3 trial comparing the Bria-IMT regimen + CPI vs Treatment of Physician's Choice.

CONCLUSION

This subset analysis of the Bria-IMTTM regimen in ADC refractory MBC patients suggests clinical benefit and a potential treatment option for this patient population. The absence of serious AEs, notably interstitial lung disease (ILD), and no toxicity-related treatment discontinuations, underscores the regimen's favorable safety profile. Future studies are warranted to confirm these results and explore the potential of Bria-IMTTM in broad clinical settings of heavily pretreated contemporary MBC patients.

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