2024 ASCO® ANNUAL MEETING

MAYO CLINIC

Outcomes of Advanced/Metastatic Breast Cancer (aMBC) Treated with Bria-IMT, an Allogeneic Whole-cell Immunotherapy

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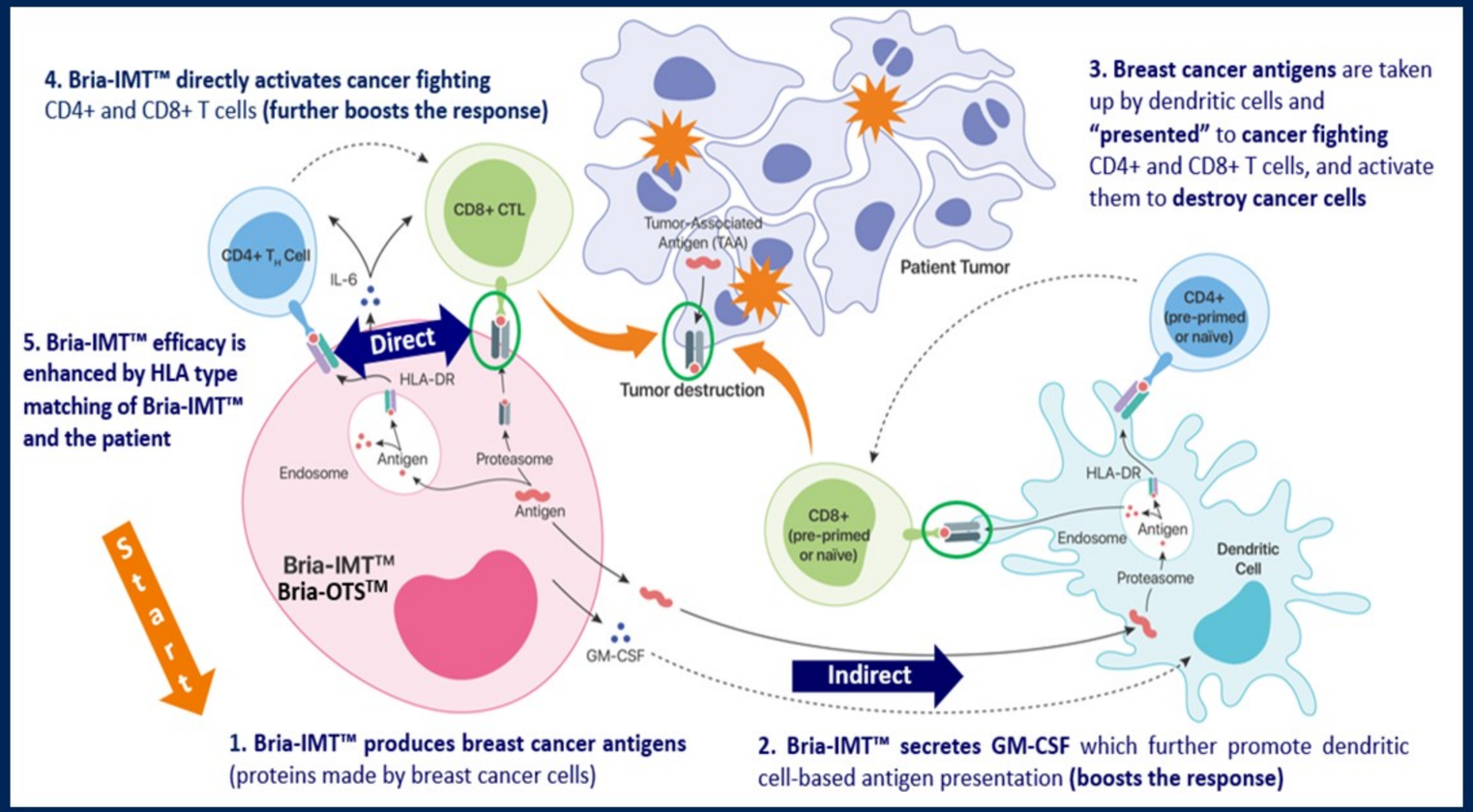
Key Takeaway

- Bria-IMT regimen is an allogenic, off-the-shelf, GM-CSF secreting, whole cell-based cancer vaccine.
- Randomized Phase I/II trial to evaluate safety and efficacy of immediate C1 vs. delayed C2 CPI with Bria-IMT regimen.
- Promising results across breast cancer subtypes were observed.
  - HR+ (ORR 10%, CBR 59%), HER2+ (ORR 50%, CBR 100%), TNBC (CBR 36%)
  - CNS responses were observed.
- Treatment is well tolerated, mainly fatigue (22%) and injection site reaction (31.5%) as the most common adverse events.
- There was no significant difference in outcomes between immediate C1 vs. delayed C2 CPI regimens.

Background: Mechanisms of Immune Activation

Bria-IMT (SV-BR-1-GM)

- Allogenic off-the-shelf whole cell-based cancer vaccine
- **Origin:** Metastatic HR-HER2+ breast cancer
- **Modification:** Secrete GM-CSF
- **Formulation:** Irradiated Shelf life > 4 years



Lacher et al. Frontier in Immunology 2018

Bria-IMT Regimen

Day -2 or -3

- Cyclophosphamide 300 mg/m^2 IV
- Retifanlimab 375 mg IV

Day 0

- 1 x 10^6 SV-BR-1-GM cells ID
- If no immediate hypersensitivity, 20 x 10^6 SV-BR-1-GM cells ID (thighs and upper back

Day 2 ± 1

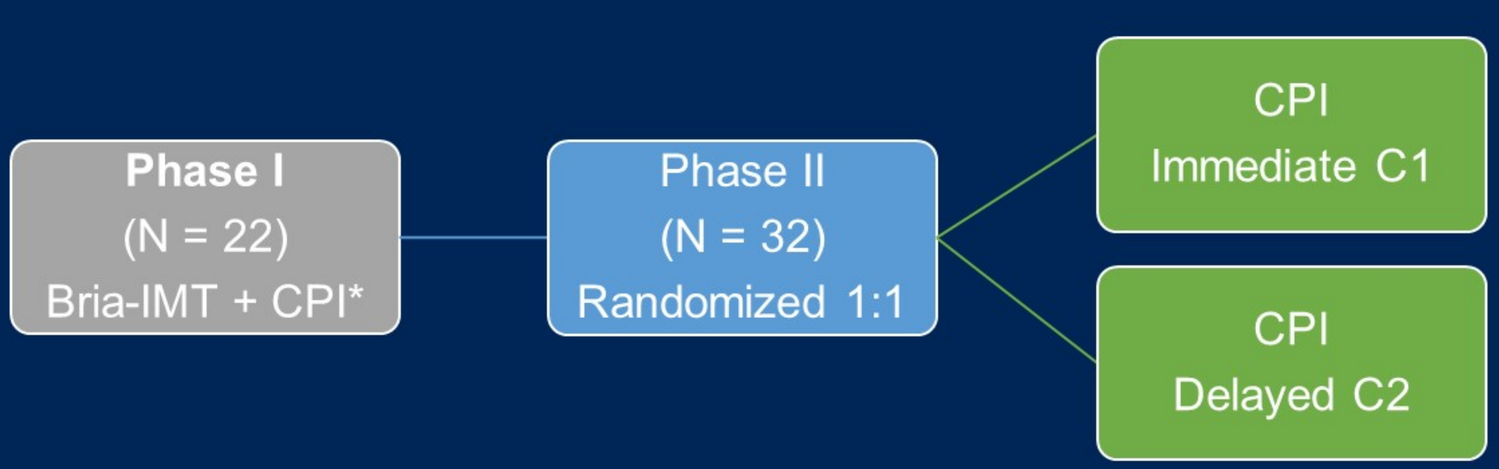
- Interferon at inoculation sites
  - IFNα-2b10,000 units ID x 4 or
  - PegIFNα-2a 0.1 mcg ID x 4

- Low dose cyclophosphamide reduces immune suppression
- Local Interferon to induce immune response
- Cycle administered every 21 days until disease progression

PRESENTED BY: Saranya Chumsri, M.D. Professor of Oncology, Mayo Clinic Breast Disease Group Research Co-Chair

Methods: Phase I/II Trial Design

- **Primary objective**
  - To determine the optimal timing of the checkpoint inhibitor (CPI) start (Immediate C1 vs. Delayed C2).
- **Secondary objectives**
  - To determine the optimal formulation of SV-BR-1-GM with or without IFNγ incubation.
  - To determine ORR, 12-week CBR, PFS, OS.



Correlative Studies
- CD8 PET imaging
- CTC and CAML
- DTH
- QoL

*Initial CPI was pembrolizumab (N = 11) but later changed to retifanlimab (N = 12); 1 subject was treated first with pembrolizumab and then retifanlimab

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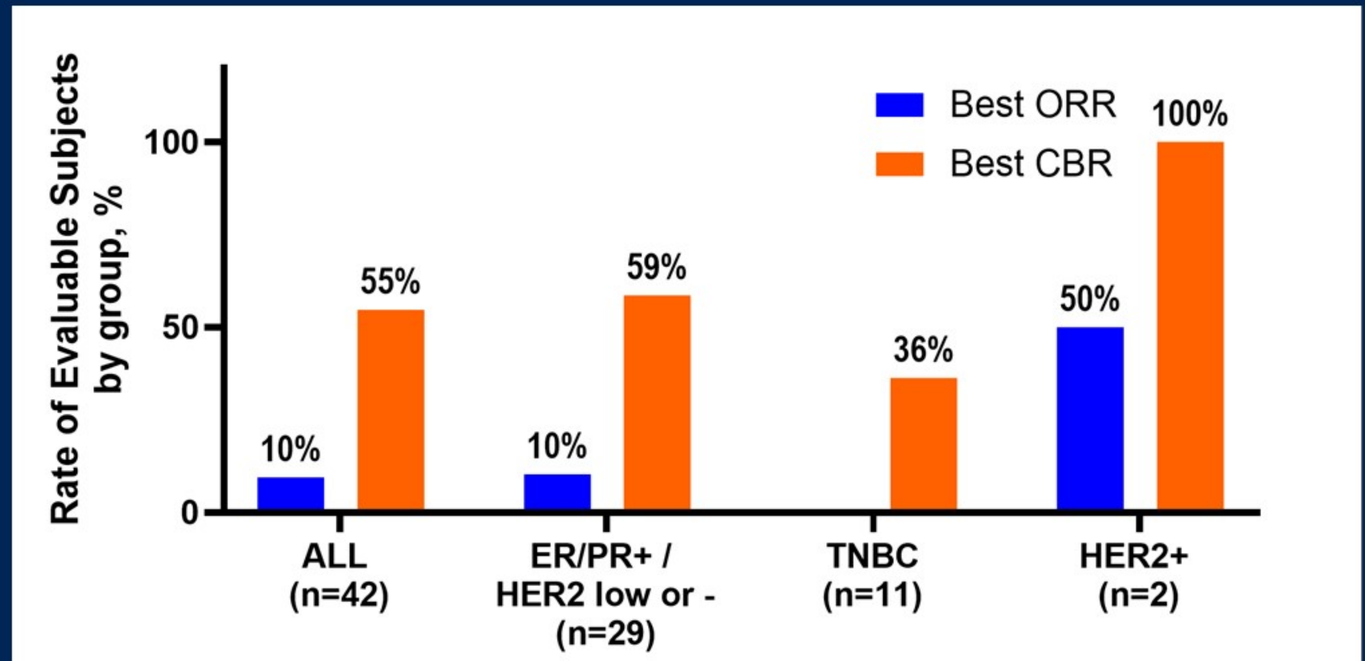
Patient Demographics (N = 54)

	N (%)
Age, Median (Range)	61 (38-81) years
BMI, Median (Range)	28.1 (18.1-42.7)
Race/Ethnicity	
• White	42 (78%)
• Black	6 (11%)
• Hispanic	10 (19%)
• Asian	3 (6%)
• Other	3 (6%)
ECOG	
• ECOG 0	29 (54%)
• ECOG 1	25 (46%)
Tumor Grade	
• Grade 1	6 (11%)
• Grade 2	15 (28%)
• Grade 3	30 (56%)
• Unknown	3 (5%)

	N (%)
Prior systemic therapy, Median (Range)	6 (2-13)
Previous therapies	
• ADC	23 (44%)
• CPI	11 (20%)
• CDK4/6 inhibitors	34 (63%)
Metastatic or Recurrent Target Lesion sites	
• Brain	4 (7%)
• Liver	25 (46%)
• Lung	10 (19%)
• Bone	12 (22%)
• Other	27 (50%)
Number of HLA Match	
• 0	12 (22%)
• 1	17 (31%)
• ≥ 2	23 (43%)
• Unknown	2 (4%)

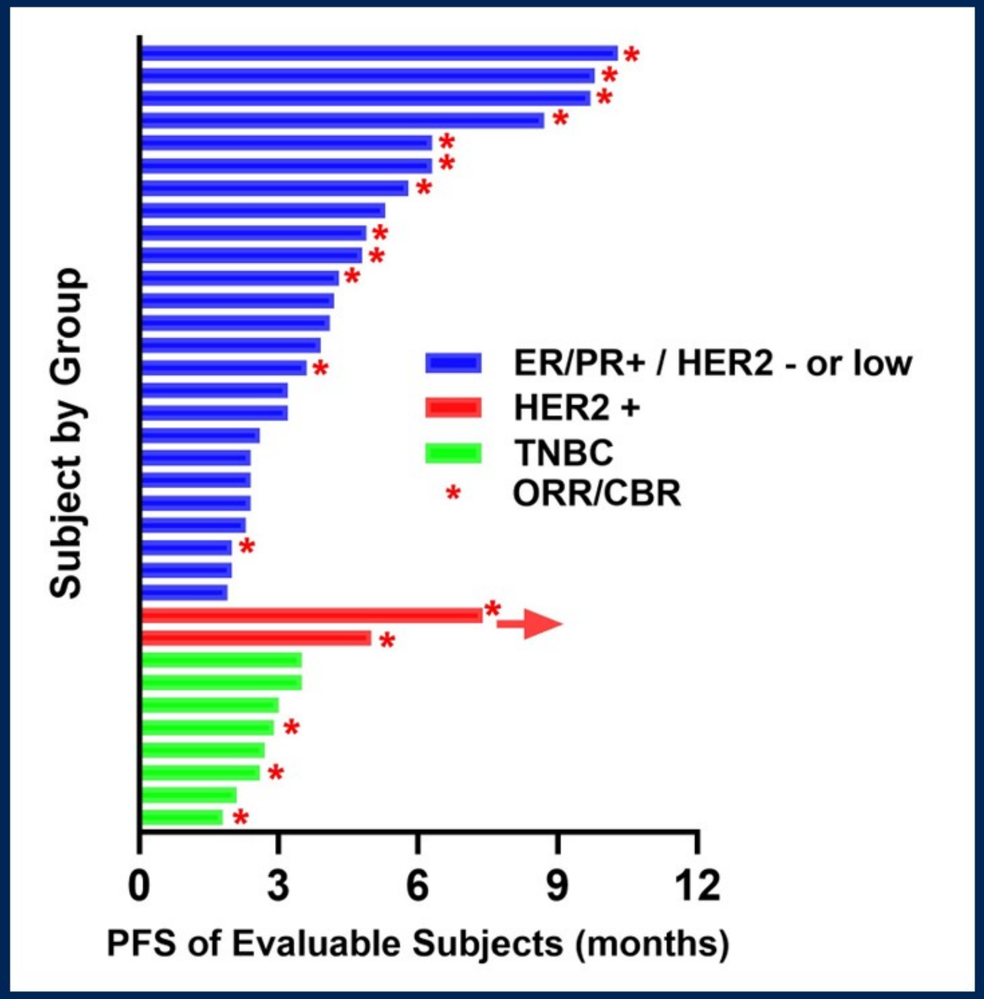
Results: ORR and CBR

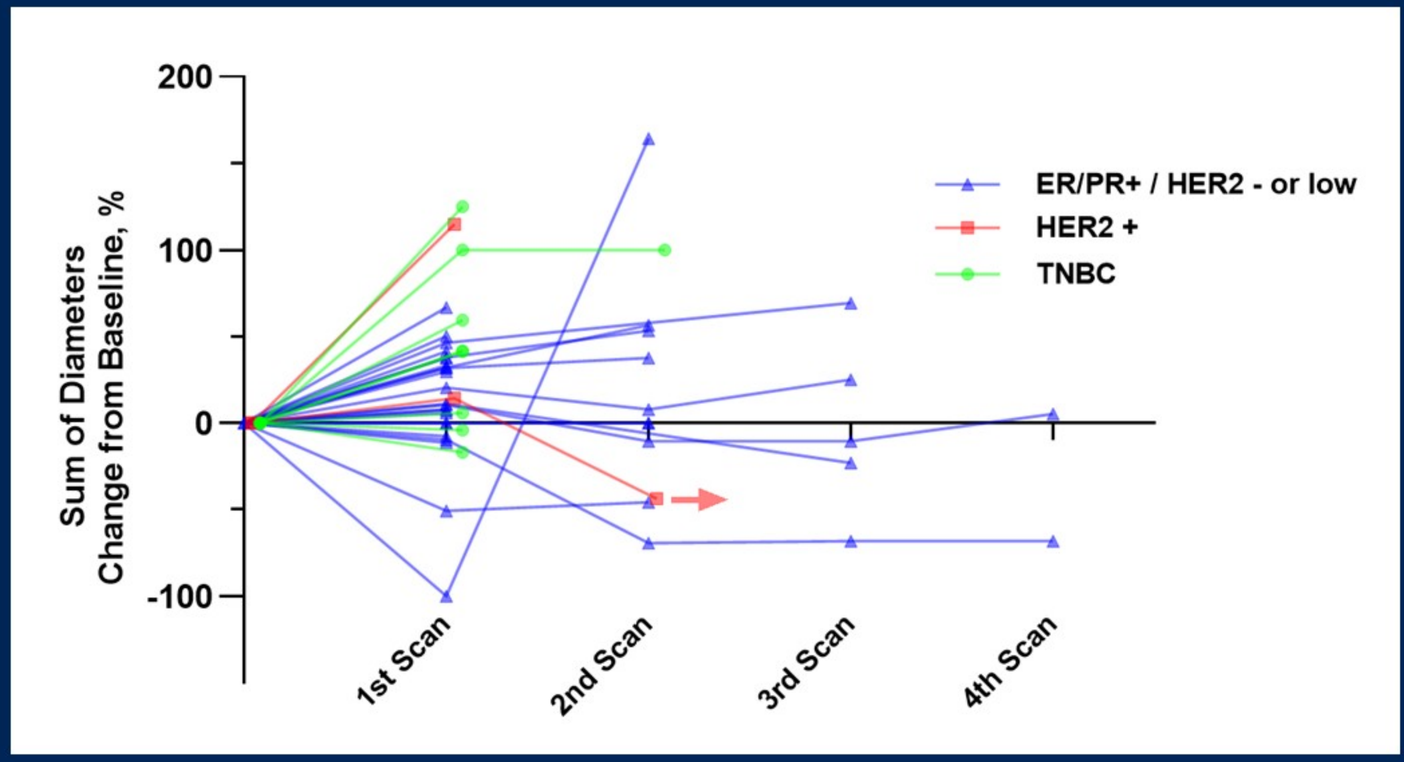
- 12-week clinical benefit seen in 55% of evaluable patients in all subtypes of breast cancer.



Duration of Response median (range) months	8.6 (5.8 - 9.8)	9.7 (5.8 - 9.8)	-	7.4+
Duration of Clinical Benefit median (range) months	5.0 (1.8 - 10.3)	3.7 (1.9 - 10.3)	2.7 (1.8 - 5.6)	6.2 (5.0 - 7.4+)

Results: PFS

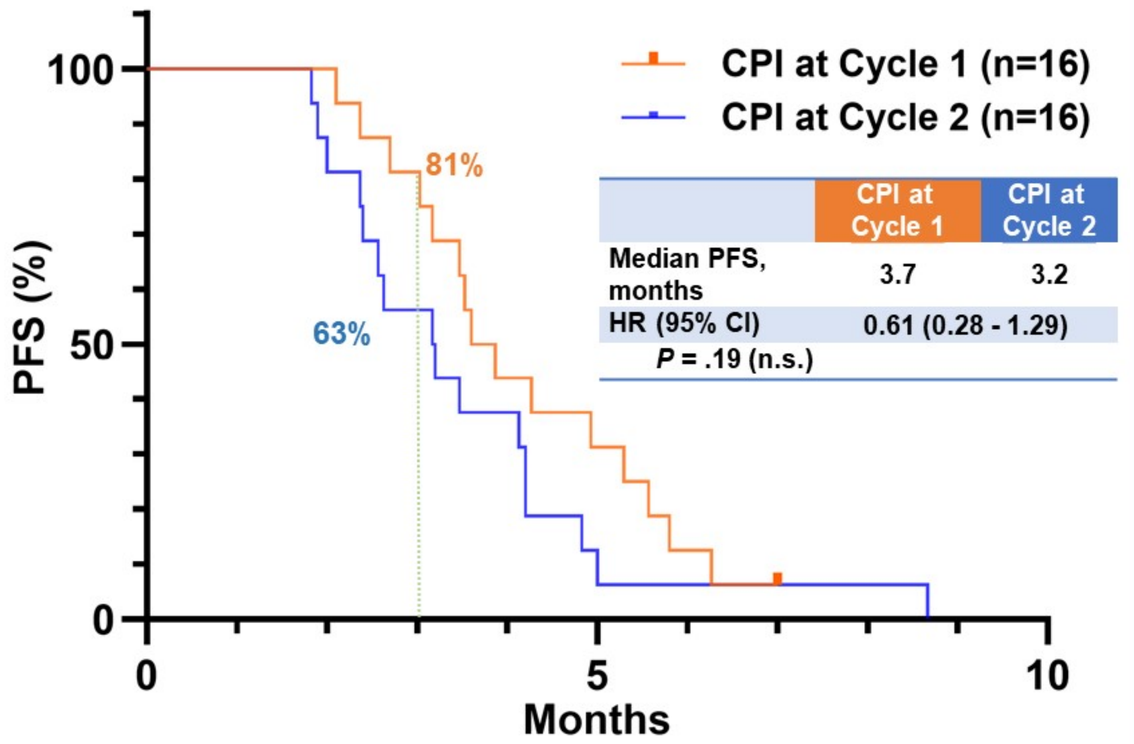




Results: Immediate C1 vs. Delayed C2

- There was no significant difference in PFS between 2 arms
  - Immediate C1: CPI starting at cycle 1, 2 days prior to SV-BR-1-GM
  - Delayed C2: CPI starting at cycle 2, 2 days after SV-BR-1-GM
- Immediate C1 implemented in Phase III trial

Progression Free Survival in Randomized Phase II

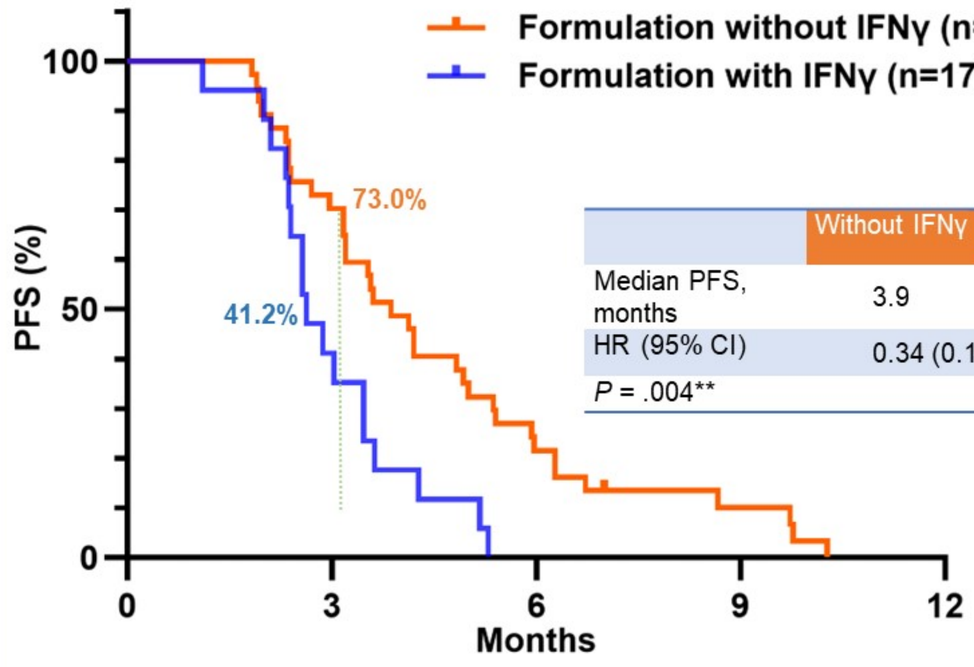


	CPI at Cycle 1	CPI at Cycle 2
Median PFS, months	3.7	3.2
HR (95% CI)	0.61 (0.28 - 1.29)	
P = .19 (n.s.)		

Results: Formulations

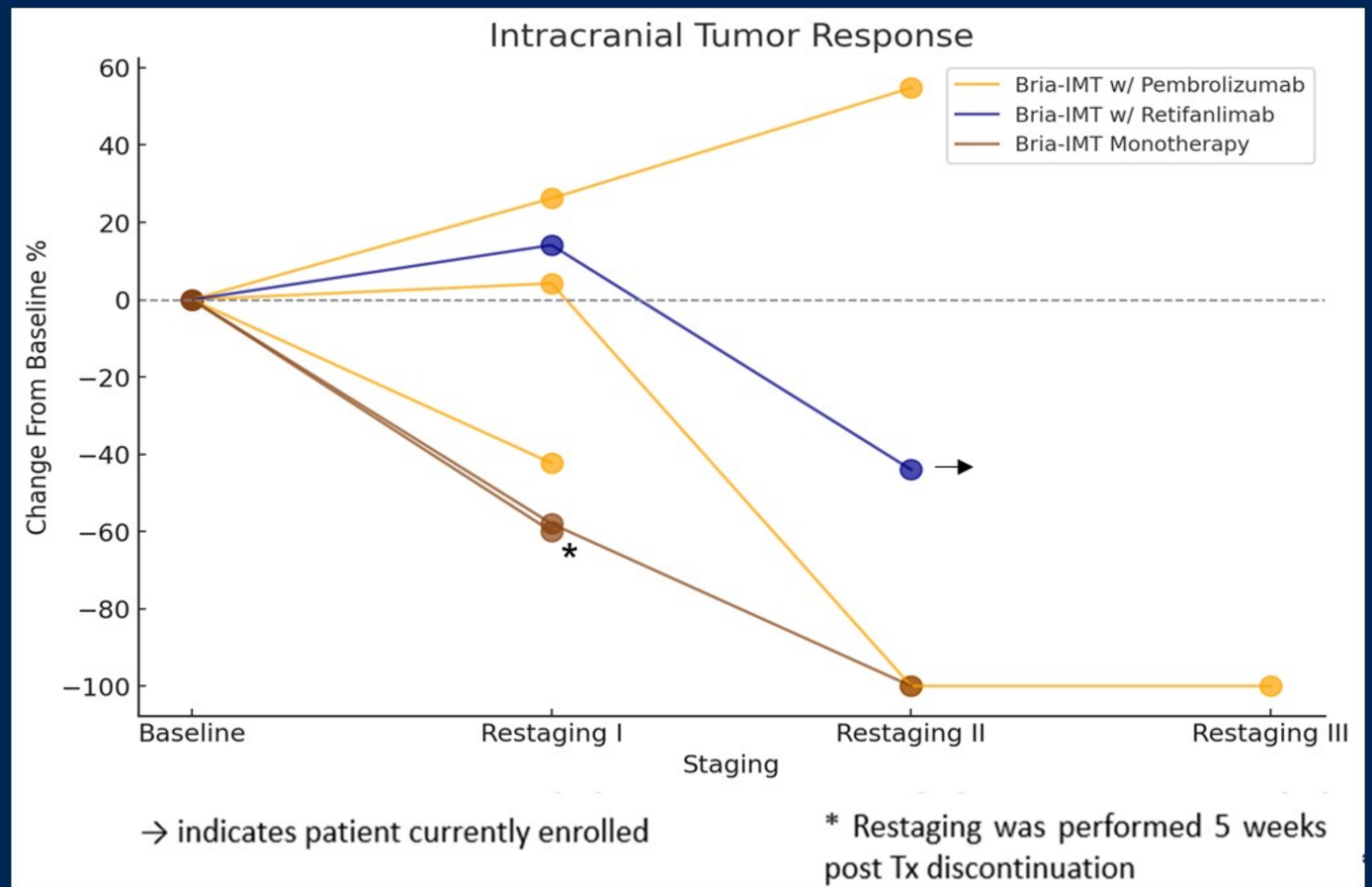
- SV-BR-1-GM has 2 formulations
  - Pulsed with IFNγ (IFNγ added in cell culture for 48 hours, then washed prior to harvesting/irradiation/cryopreservation)
  - Without IFNγ
- Patients treated with formulation without IFNγ had significantly improved PFS.
- Formulation without IFNγ will be used in the Phase III trial.

Progression Free Survival by SV-BR-1-GM Formulation



	Without IFNγ	With IFNγ
Median PFS, months	3.9	2.6
HR (95% CI)	0.34 (0.16 - 0.72)	
P = .004**		

Results: Intracranial Responses in 5/6 Evaluable Patients



→ indicates patient currently enrolled

* Restaging was performed 5 weeks post Tx discontinuation

Patient Demographics (N=7)

Patients with Intracranial Metastasis				
Median Age	Median OS (months)	Median Prior lines of therapy	Median Prior Lines of Radiation	Median Prior Surgeries
64	9	5	3	2

Median Sum of Intracranial Lesion Diameters (mm)**	
Before Bria-IMT™	After Bria-IMT™
25	8.5

**in 6 evaluable patients with measurable outcomes

Median % Change in the Sum of Intracranial Lesion Diameters (mm)**		
Bria-IMT™ w/ Pembrolizumab	Bria-IMT™ w/ Retifanlimab	Bria-IMT™ Monotherapy
-42%	-44%	-80%

**in 6 evaluable patients with measurable outcomes

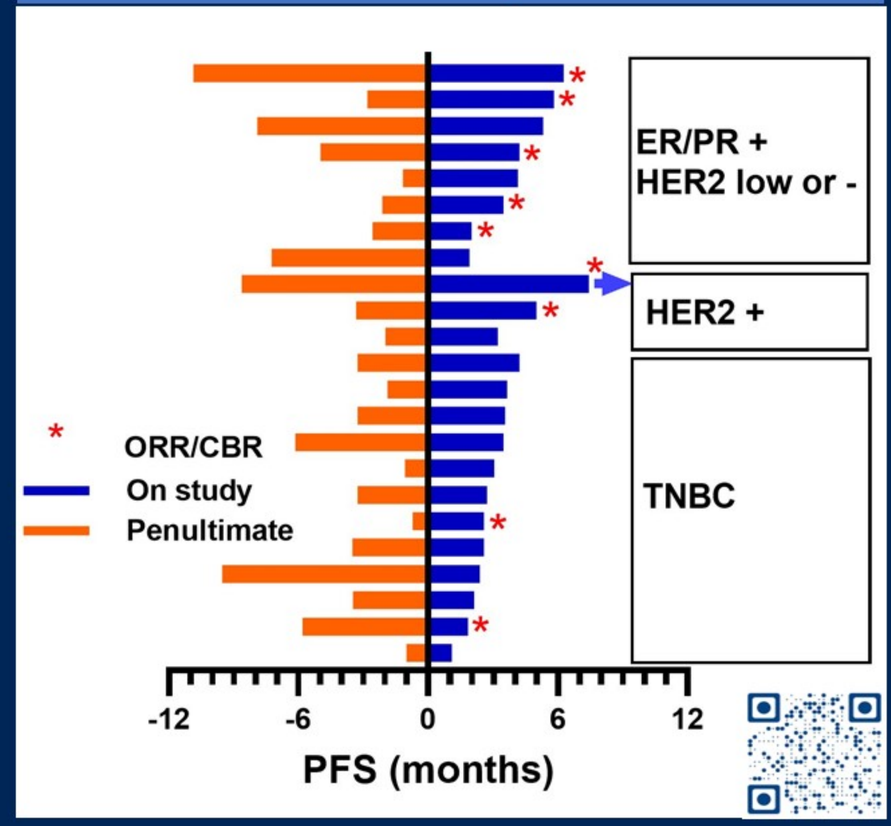
Sailaja Kamaraju, et al ; *Cancer Res* 1 April 2024; 84 (7_Supplement): CT204.

Results: CBR in ADC Resistant Patients

- Extend subsequent PFS in patients who had previously failed various ADC
  - Trastuzumab deruxtecan (T-DXd), sacituzumab govitecan, and ado-trastuzumab emtansine (T-DM 1)

Histology	All	Evaluable	Best ORR[1]	Best CBR[2]
All ADC Resistant	23	17	12% (2 / 17)	53% (9 / 17)
ER/PR + / HER2 low or -	8	8	13% (1 / 8)	63% (5 / 8)
HER2+	3	2	50% (1 / 2)	100% (2 / 2)
TNBC	12	7	0	29% (2 / 7)

Bria-IMT PFS vs Penultimate Therapy PFS in ADC-resistant patients



Chaitali Nangia, et al. ; *Cancer Res* 1 April 2024; 84 (7_Supplement): CT206.

Results: Adverse Events

- Treatment with the Bria-IMT regimen was generally well tolerated.
- No subjects came off the study due to toxicity to SV-BR-1-GM.

Most common AEs (>10% reported on Bria-IMT Regimen):

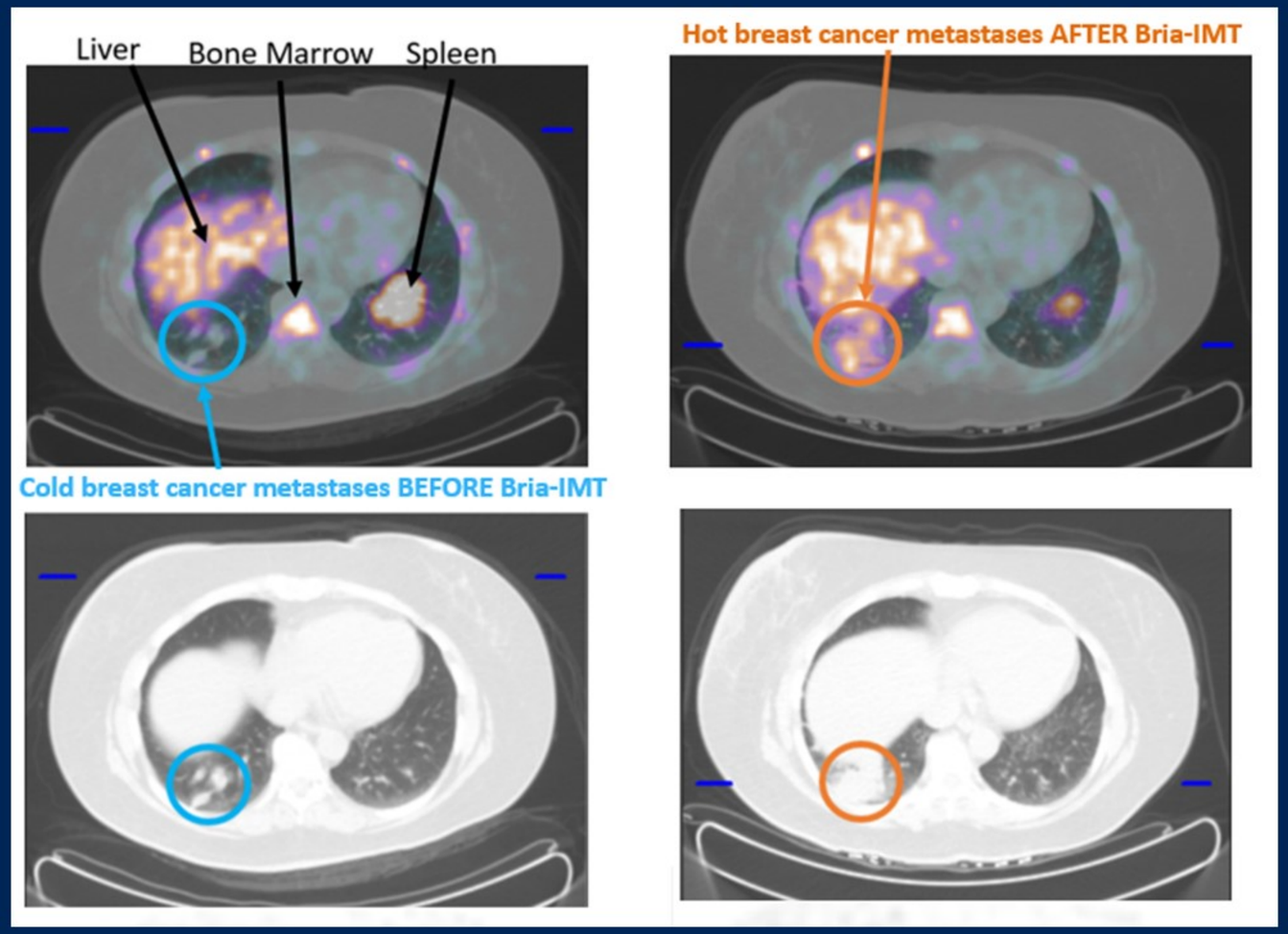
	Maximum Grade N (%)				Total Related N (%)
	Grade 1	Grade 2	Grade 3	Grade 4/5	
Fatigue	10 (18.5)	10 (18.5)	3 (5.6)	0	12 (22)
Injection Site Reaction	16 (29.6)	2 (3.7)	0	0	17 (31.5)
Nausea	11 (20)	5 (9.3)	0	0	8 (14.8)
Constipation	7 (13)	4 (7.4)	1 (1.9)	0	3 (5.6)
Diarrhea	7 (13)	3 (5.6)	0	0	1 (1.9)
Headache	8 (14.8)	2 (3.7)	0	0	2 (3.7)
Anemia	5 (9.3)	1 (1.9)	3 (5.6)	0	8 (14.8)
Rash/maculo-papular rash	6 (11.1)	1 (1.9)	1 (1.9)	0	2 (3.7)
Weakness	3 (5.6)	2 (3.7)	1 (1.9)	0	2 (3.7)

Serious Adverse Events (SAEs):

1 grade 3 intractable nausea and vomiting deemed related to study regimen (1.9%)

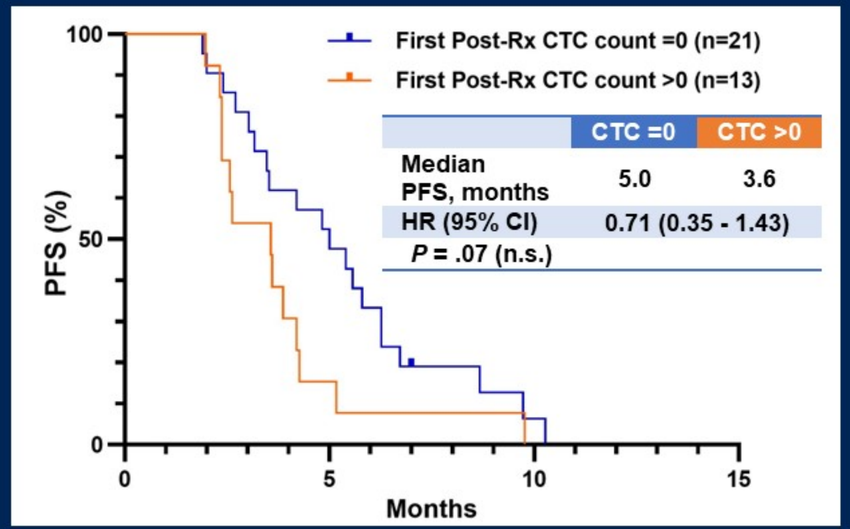
Correlative Studies: CD8 PET Imaging

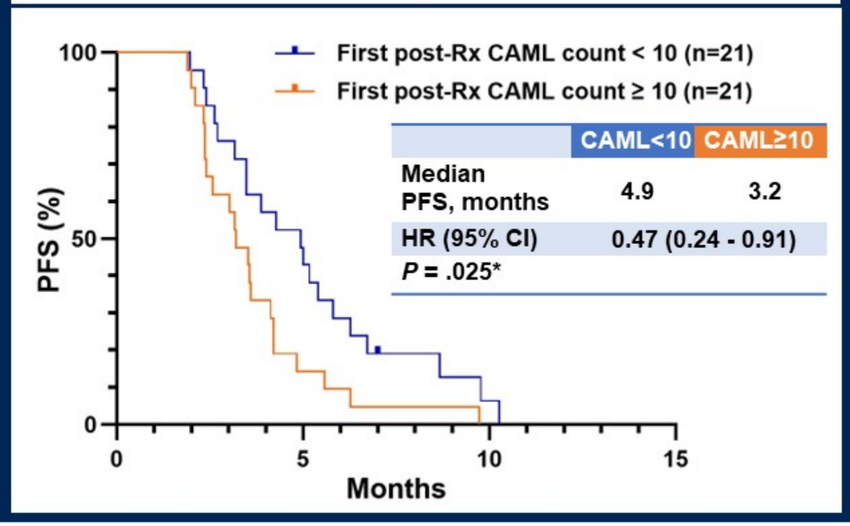
- Bria-IMT combination therapy induced CD8$^+$ T cell infiltration in metastatic breast cancer.



Correlative Studies: CTC and CAML

- Patients with lower circulating tumor cells (CTC) and cancer-associated macrophage-like cells (CAML) after the first cycle of treatment had significantly improved PFS.

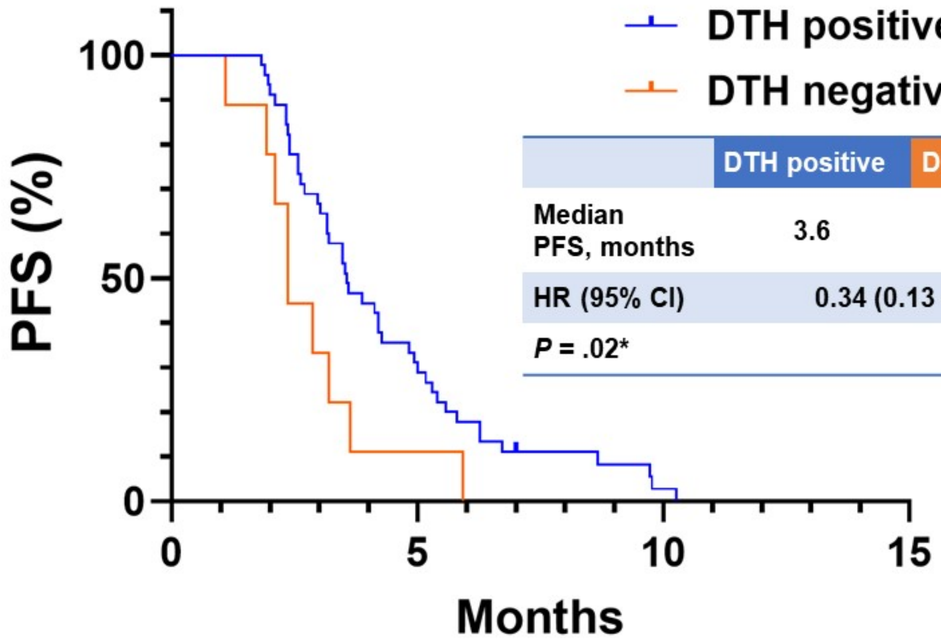




Correlative Studies: DTH Response

- Delayed type hypersensitivity (DTH)
  - A test dose of SV-BR-1-GM administer prior to full dose
  - Skin reaction (erythema/induration) measured 48 hours post-dosing
- A measure of host immune response to SV-BR-1-GM
- Statistically significant longer PFS was observed in patients with positive DTH.

Progression Free Survival by DTH Response



	DTH positive	DTH negative
Median PFS, months	3.6	2.4
HR (95% CI)	0.34 (0.13 - 0.90)	
P = .02*		

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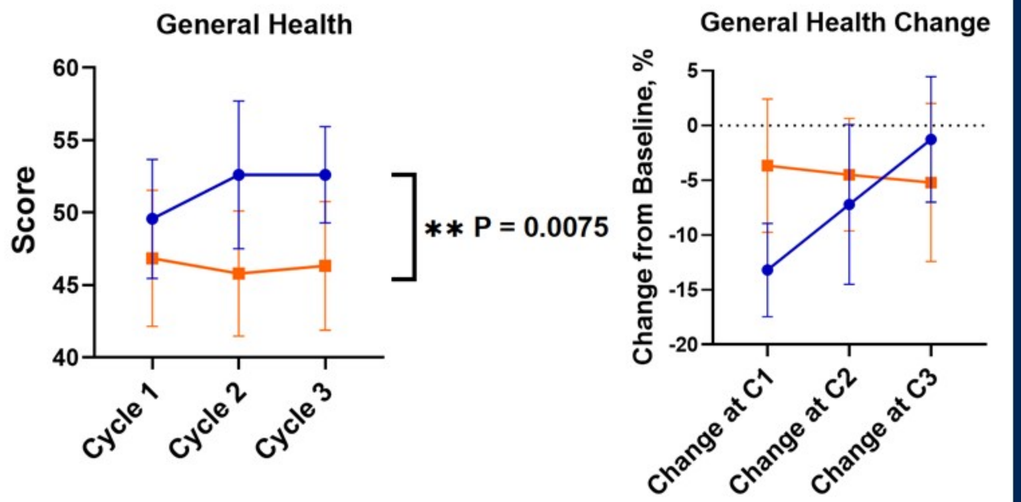
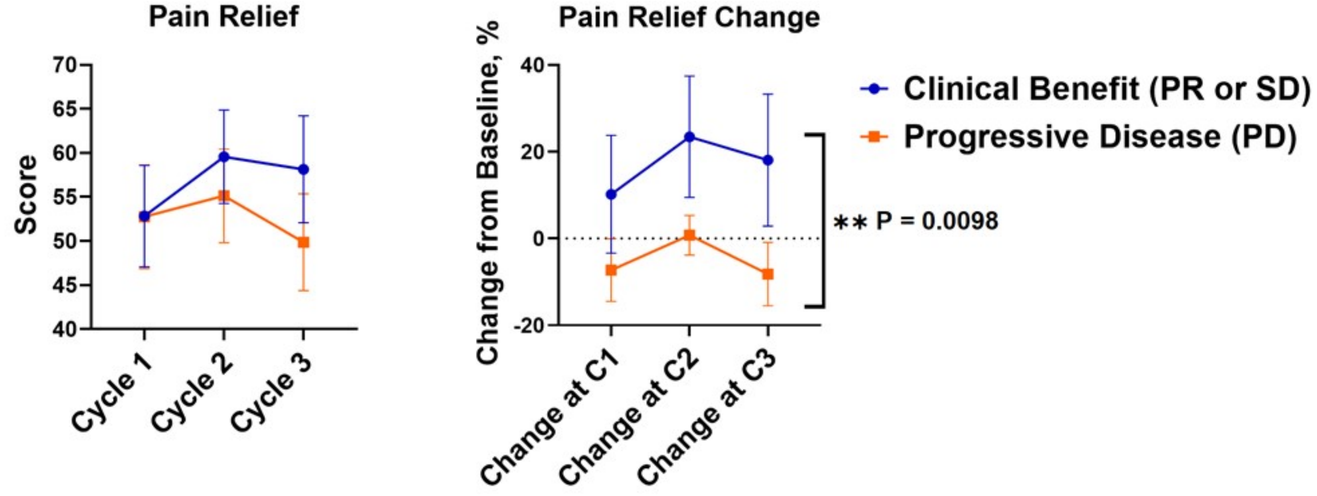
Correlative Studies: Quality of Life (SF-36)

General Health



General health scores significantly correlate with disease control.

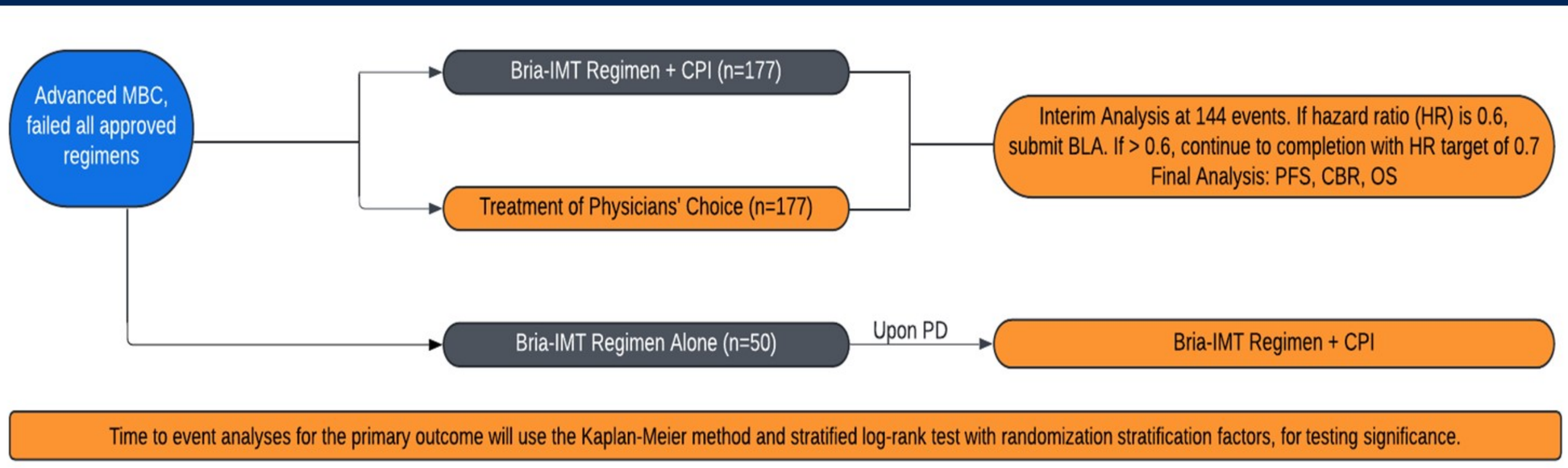
Pain Relief



Pain relief score changes from baseline significantly correlate with disease control.

Limitation and Future Direction

- Small sample size. A randomized phase III trial is ongoing.



Hurvitz *et al.* Poster Session TPS1137 – Breast Cancer – Metastatic 6/2/2024 9:00 am-12:00 PM

Conclusions

- In heavily pretreated breast cancer patients, the BRIA-IMT regimen showed promising results across breast cancer subtypes.
  - HR+ (ORR 10%, CBR 59%), HER2+ (ORR 50%, CBR 100%), TNBC (CBR 36%)
  - CNS responses were observed.
- Treatment is well tolerated, mainly fatigue (22%) and injection site reaction (31.5%) as the most common adverse events.
- There was no significant difference in outcomes between immediate C1 vs. delayed C2 CPI regimens.
- The Phase III trial comparing the BRIA-IMT regimen to the physician's choice standard of care therapy is ongoing.

Lay Term Summary

- Bria-IMT regimen is an off-the-shelf, whole cell-based breast cancer vaccine.
- Randomized Phase I/II trial to evaluate the safety and efficacy of the Bria-IMT regimen.
- Promising results across breast cancer subtypes were observed.
  - Hormone receptor-positive (response rate 10%, clinical benefit rate 59%), HER2-positive (response rate 50%, clinical benefit rate 100%), triple-negative breast cancer (clinical benefit rate 36%)
  - Brain metastasis responses were observed.
- Treatment is well tolerated. The most common side effects are mainly fatigue (22%) and injection site reaction (31.5%).
- The Phase III trial comparing the BRIA-IMT regimen to the physician's choice standard of care therapy is ongoing.

References

Lacher MD, and Bauer G, et al. SV-BR-1-GM, a Clinically Effective GM-CSF-Secreting Breast Cancer Cell Line, Expresses an Immune Signature and Directly Activates CD4 + T Lymphocytes. Frontiers in Immunology, 2018, Volume 9, Article 776

Sailaja Kamaraju; Blaise Bayer; Mingjin Chang; William Williams; Charles Wiseman; Giuseppe Del Priore. Cancer Res (2024) 84 (7_Supplement): CT204. https://doi.org/10.1158/1538-7445.AM2024-CT204

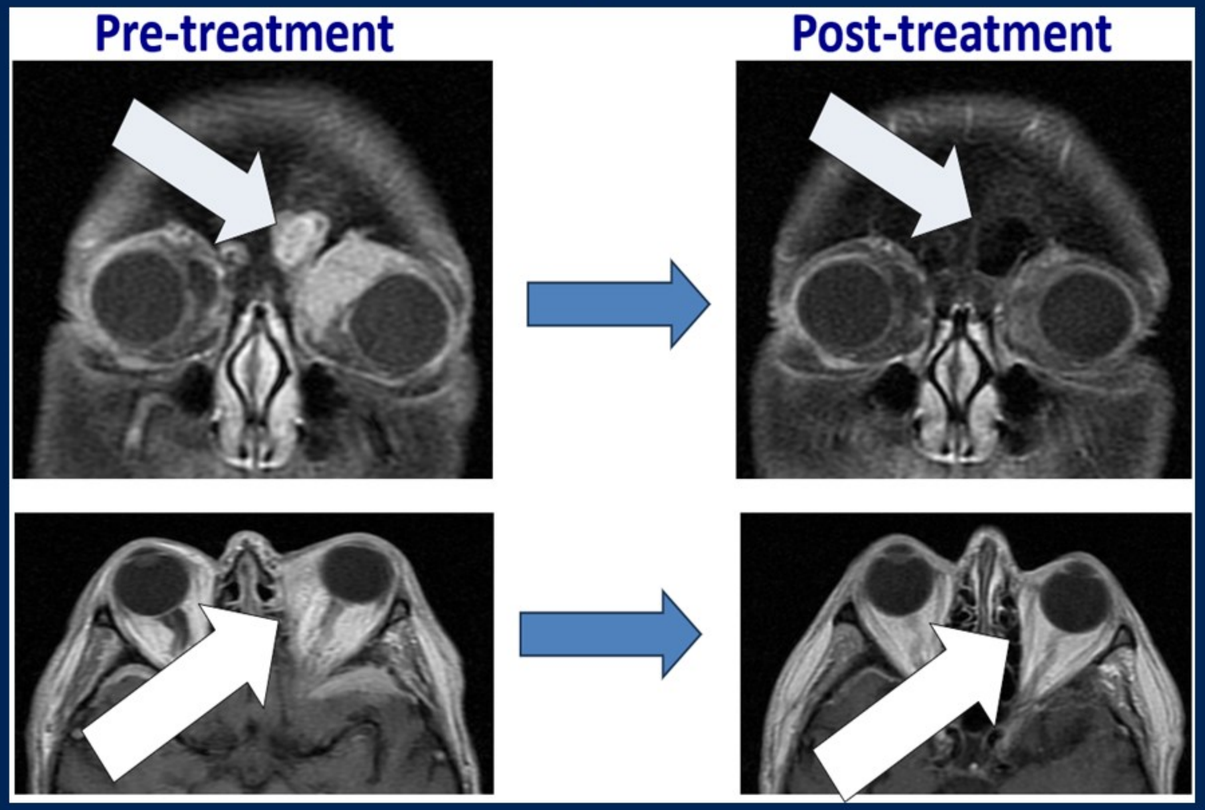
Chaitali Nangia; Carmen Calfa; Blaise Bayer; Mingjin Chang; William Williams; Giuseppe Del Priore; Charles Wiseman; Saranya Chumsri. Cancer Res (2024) 84 (7_Supplement): CT206. https://doi.org/10.1158/1538-7445.AM2024-CT206

Calfa C, Nangia C et al. Randomized Phase 2 of Bria-MT, an Allogenic Human Cell Line with Antigen Presenting Activity in Heavily Pretreated Metastatic Breast Cancer. Cancer Res. December 2023, Presentation ID P03-05-12

Results: Intracranial Responses

MRI showing *complete response* of orbital lesion

Subject 1



MRI showing *ongoing regression* of orbital lesion

Subject 2

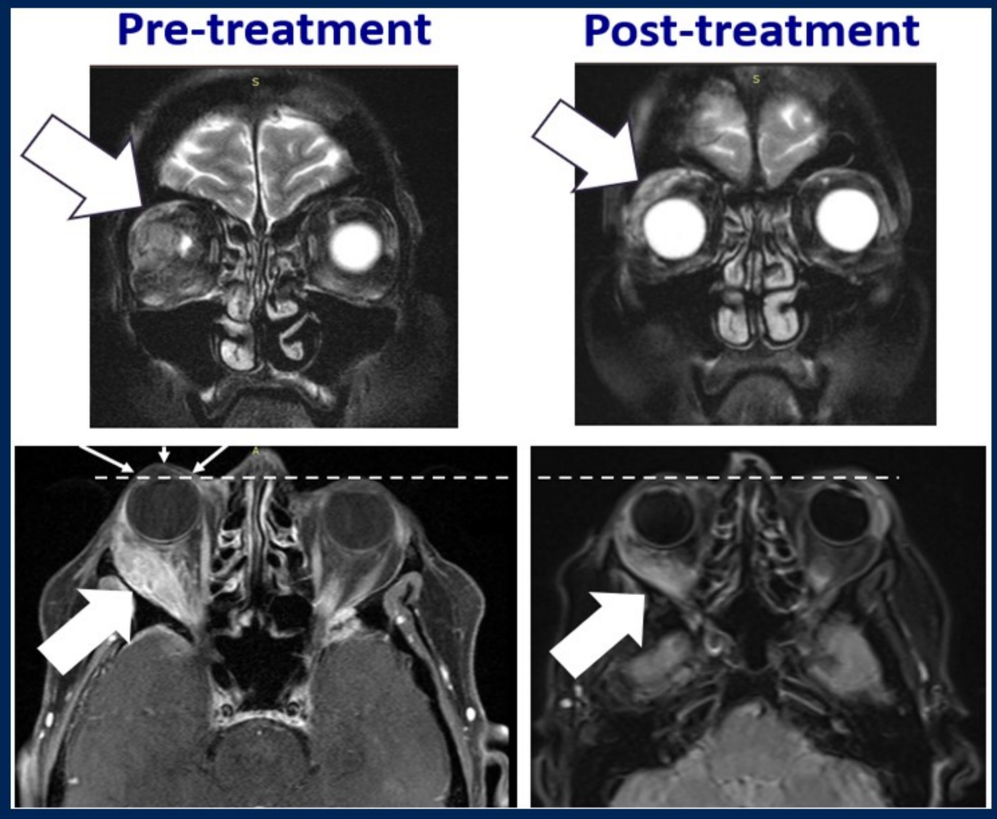


Figure courtesy of Russ Kuker MD, U Miami