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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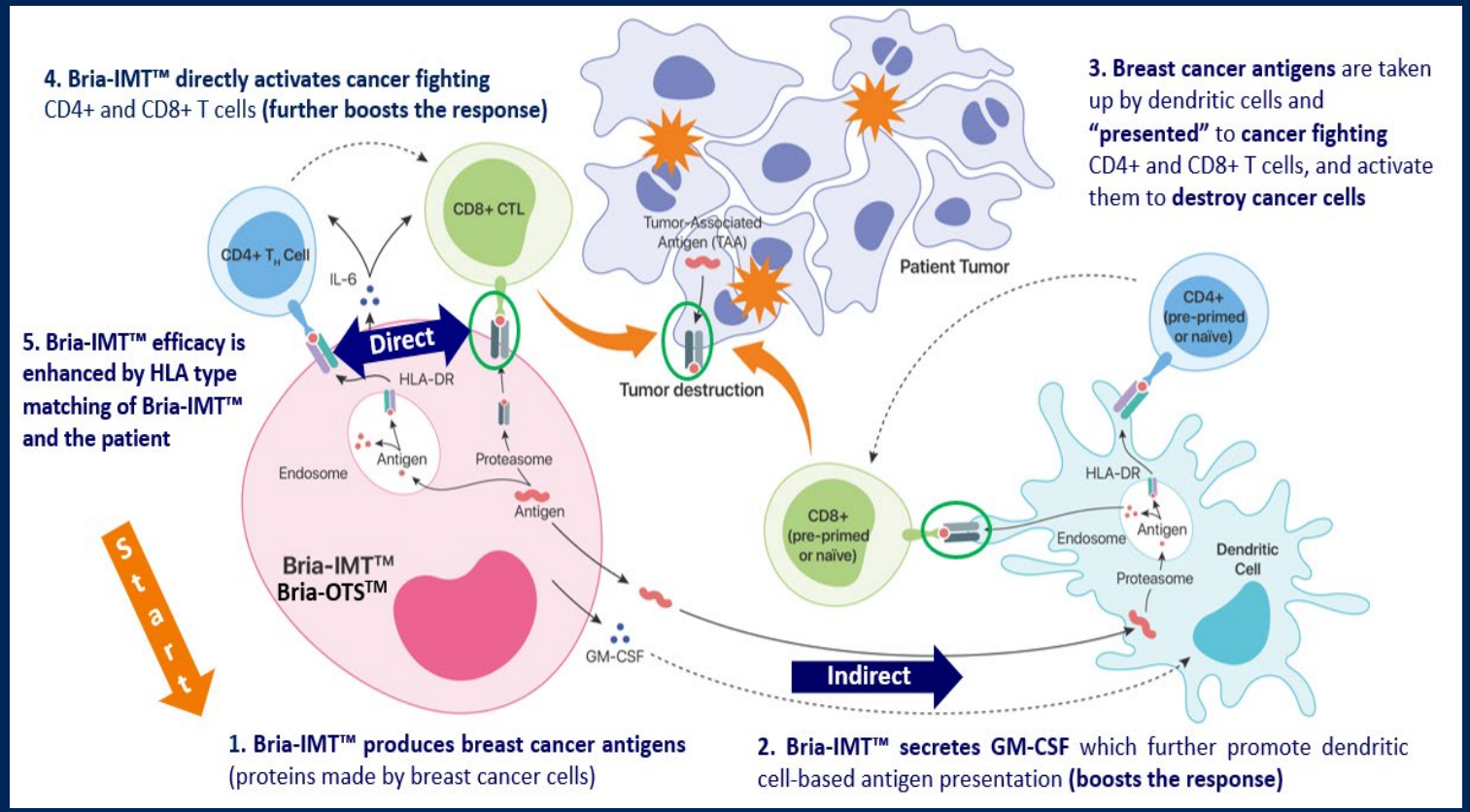
# Key Takeaway

- 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

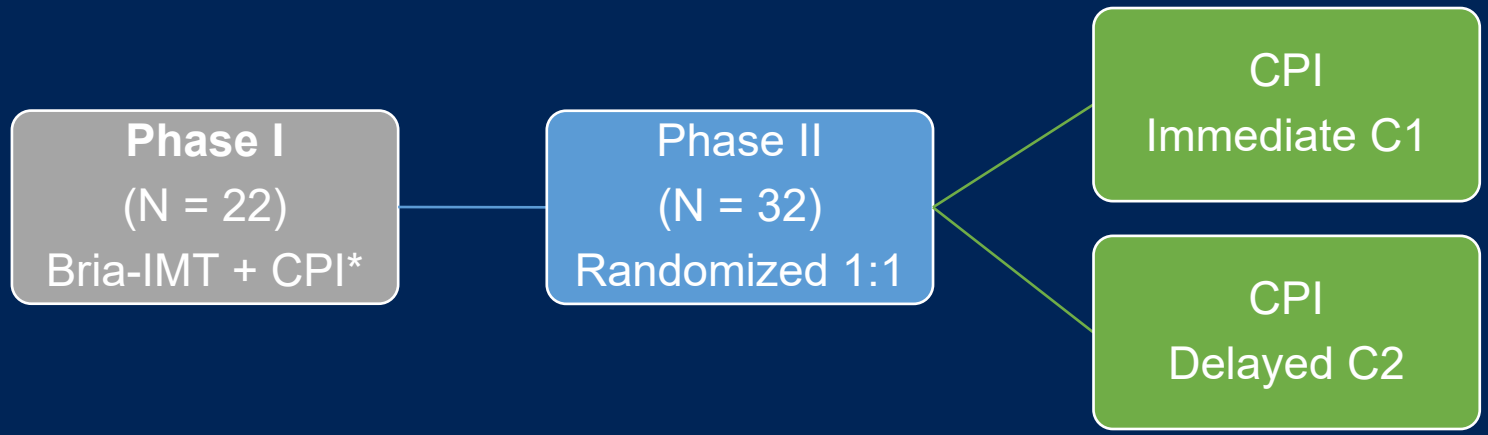
**Day 2 ± 1**

- 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

# 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

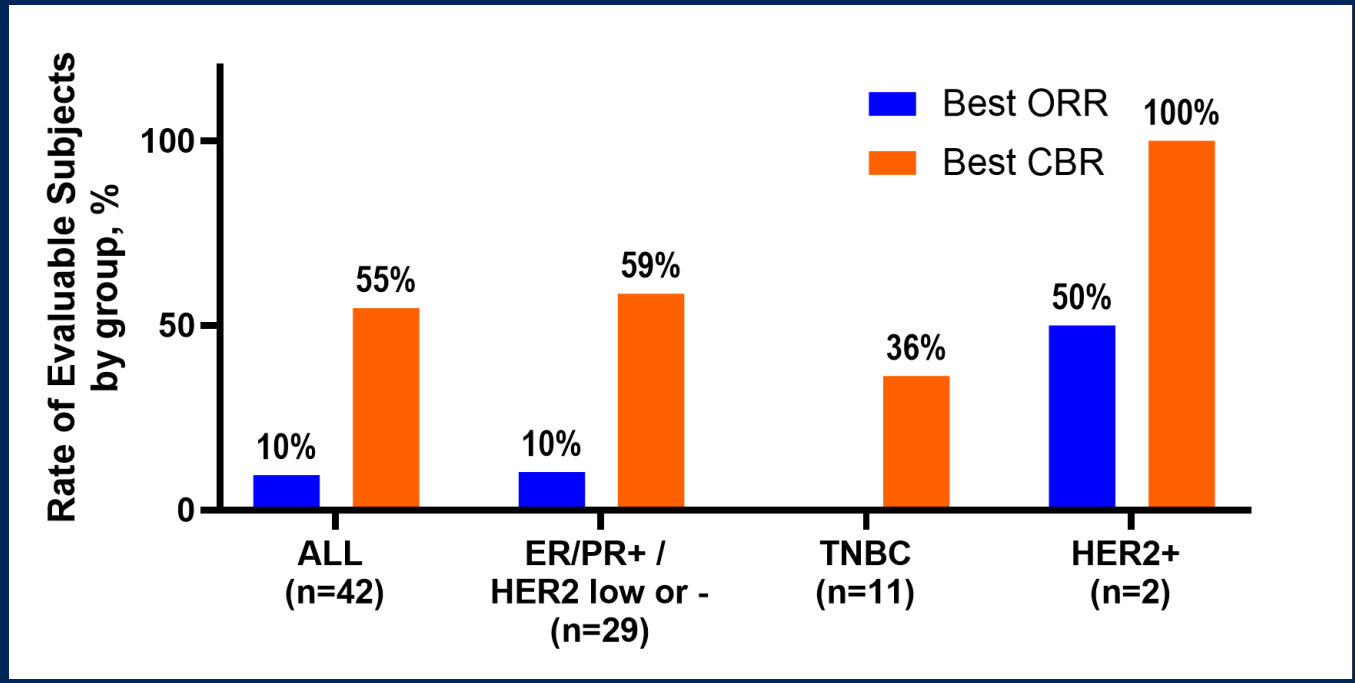
# Patient Demographics (N = 54)

| | 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%) |

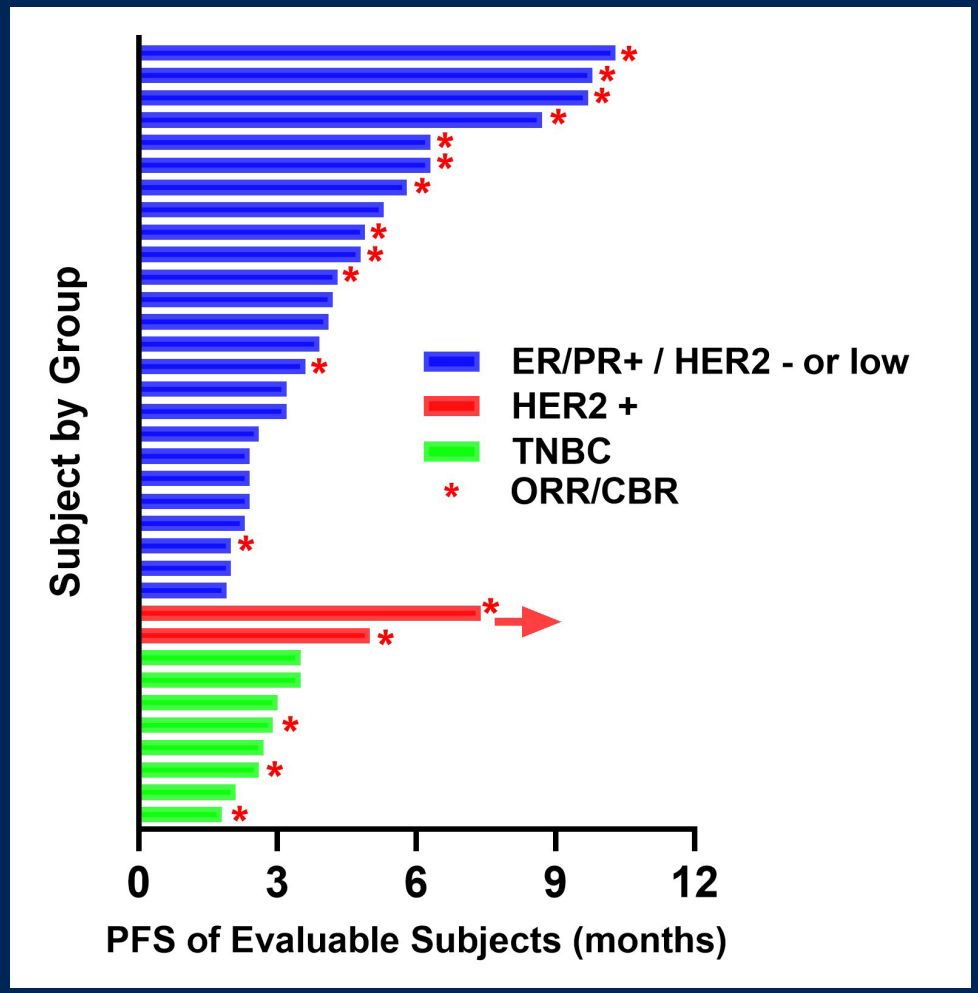
# Results: ORR and CBR

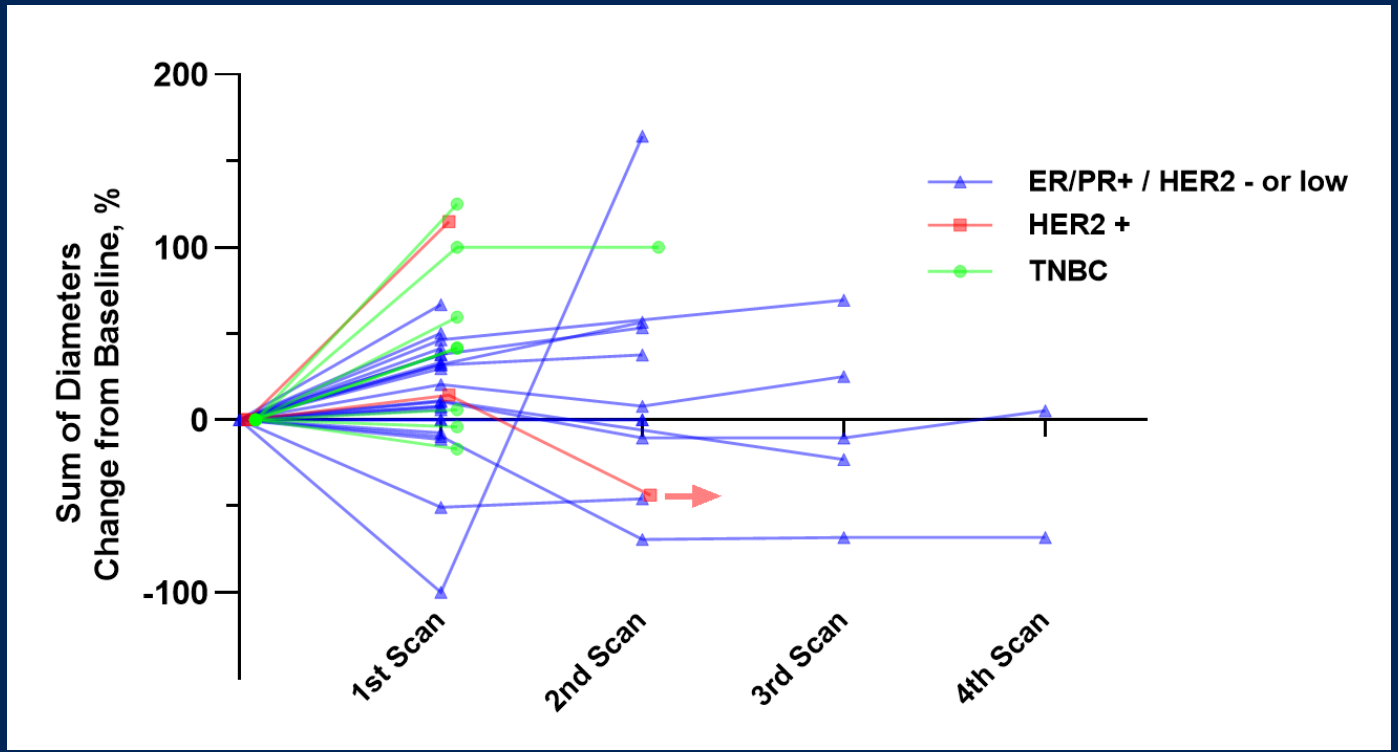
- 12-week clinical benefit seen in 55% of evaluable patients in all subtypes of breast cancer.




| | | | | |
|---|---|---|---|---|
| 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

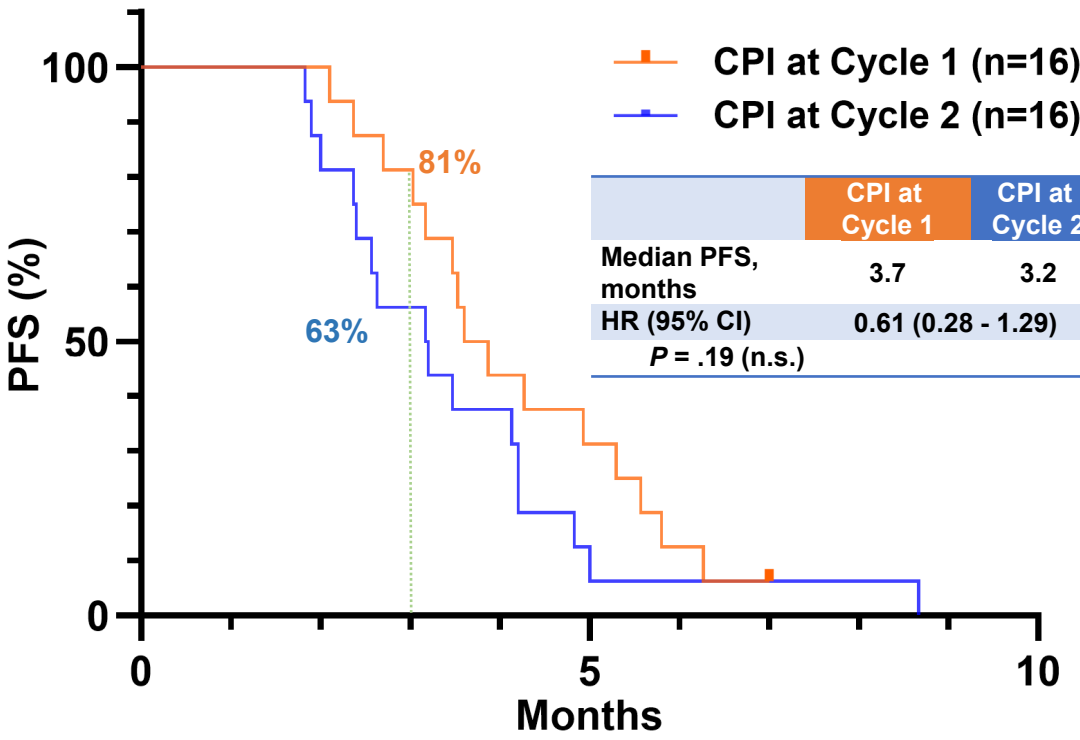


# Results: Immediate C1 vs. Delayed C2

- 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

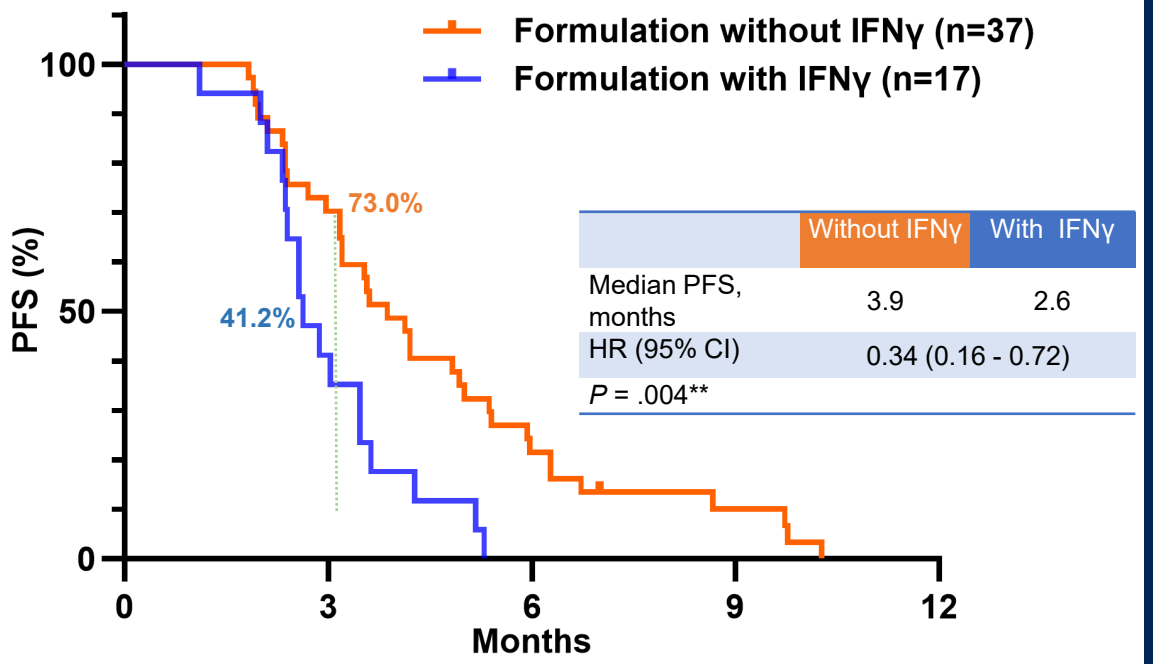



| | CPI at Cycle 1 | CPI at Cycle 2 |
|---|---|---|
| Median PFS, months | 3.7 | 3.2 |
| HR (95% CI) | 0.61 (0.28 - 1.29) | |
| *P* = .19 (n.s.) | | |

# Results: Formulations

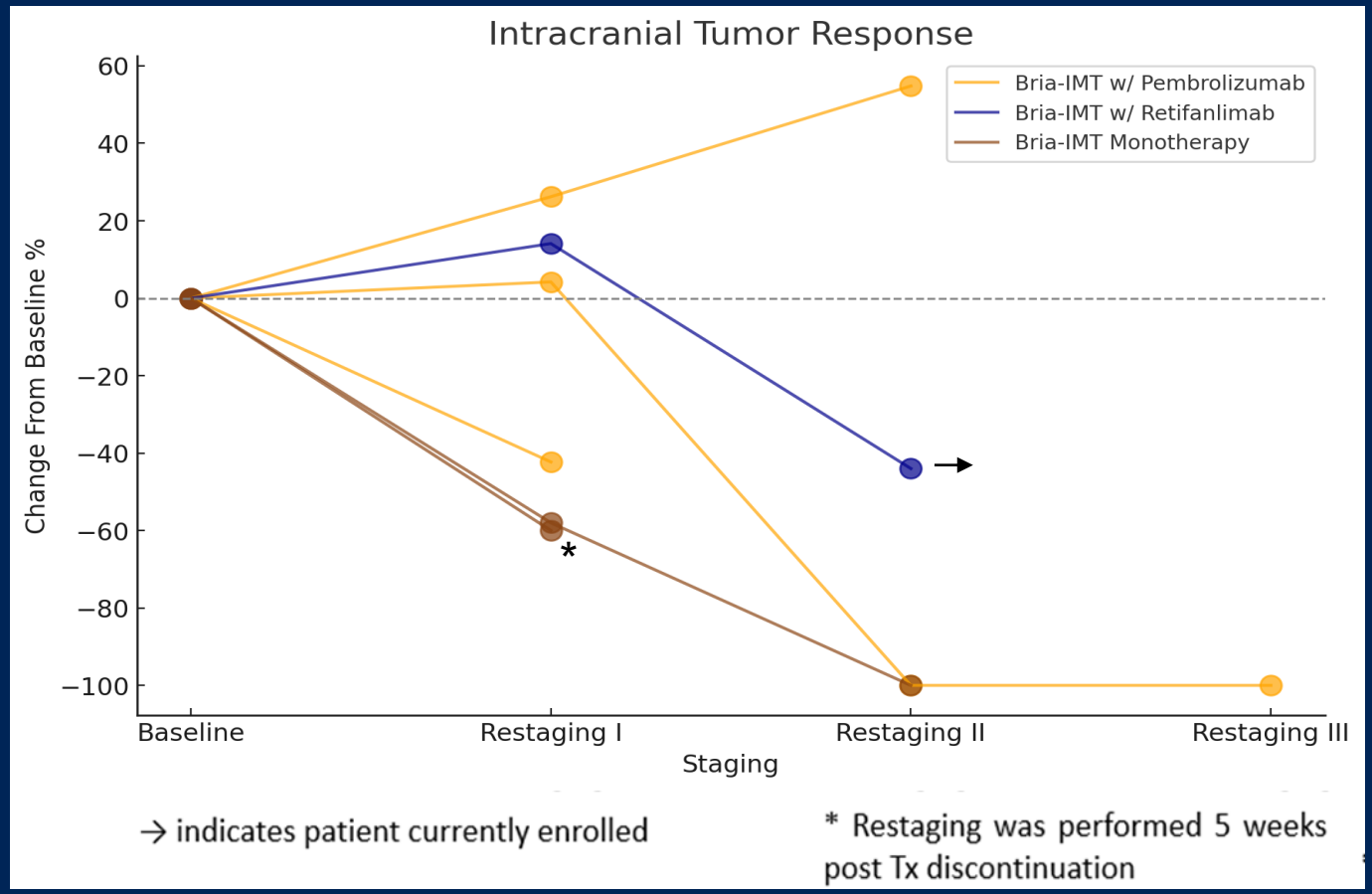
- SV-BR-1-GM has 2 formulations
  - Pulsed with IFNγ (IFNγ added in cell culture for 48 hours, then washed prior to harvesting/irradiation/cryopreservation)
  - Without IFNγ
- Patients treated with formulation without IFNγ had significantly improved PFS.
- Formulation without IFNγ will be used in the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




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

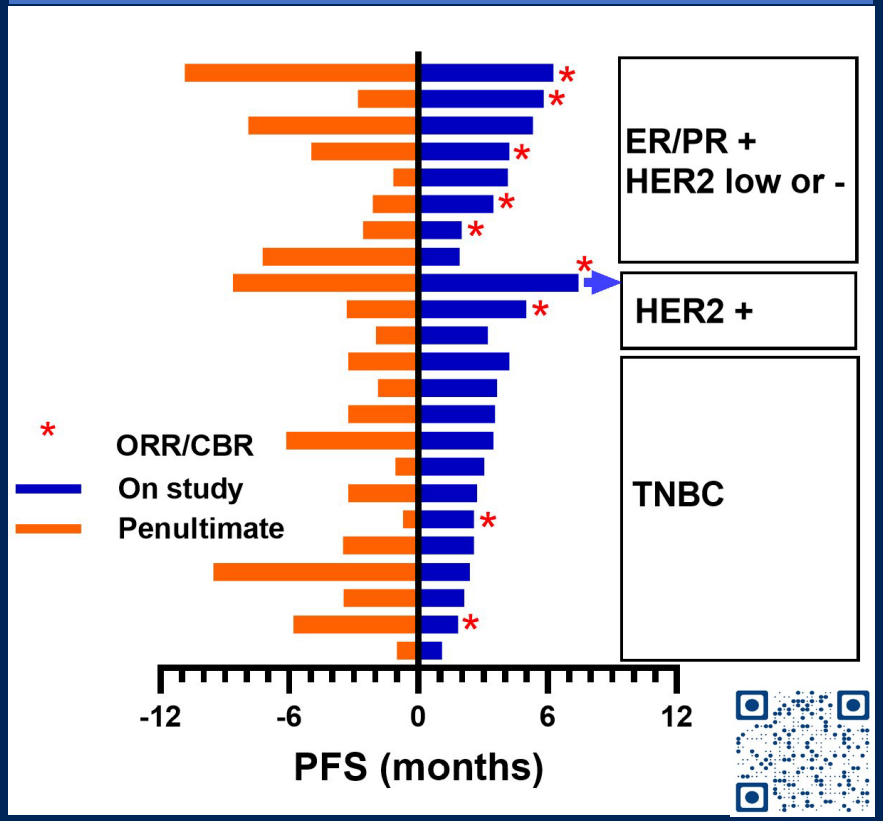
Sailaja Kamaraju, et al ; *Cancer Res* 1 April 2024; 84 (7_Supplement): CT204.

# 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.

## 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):

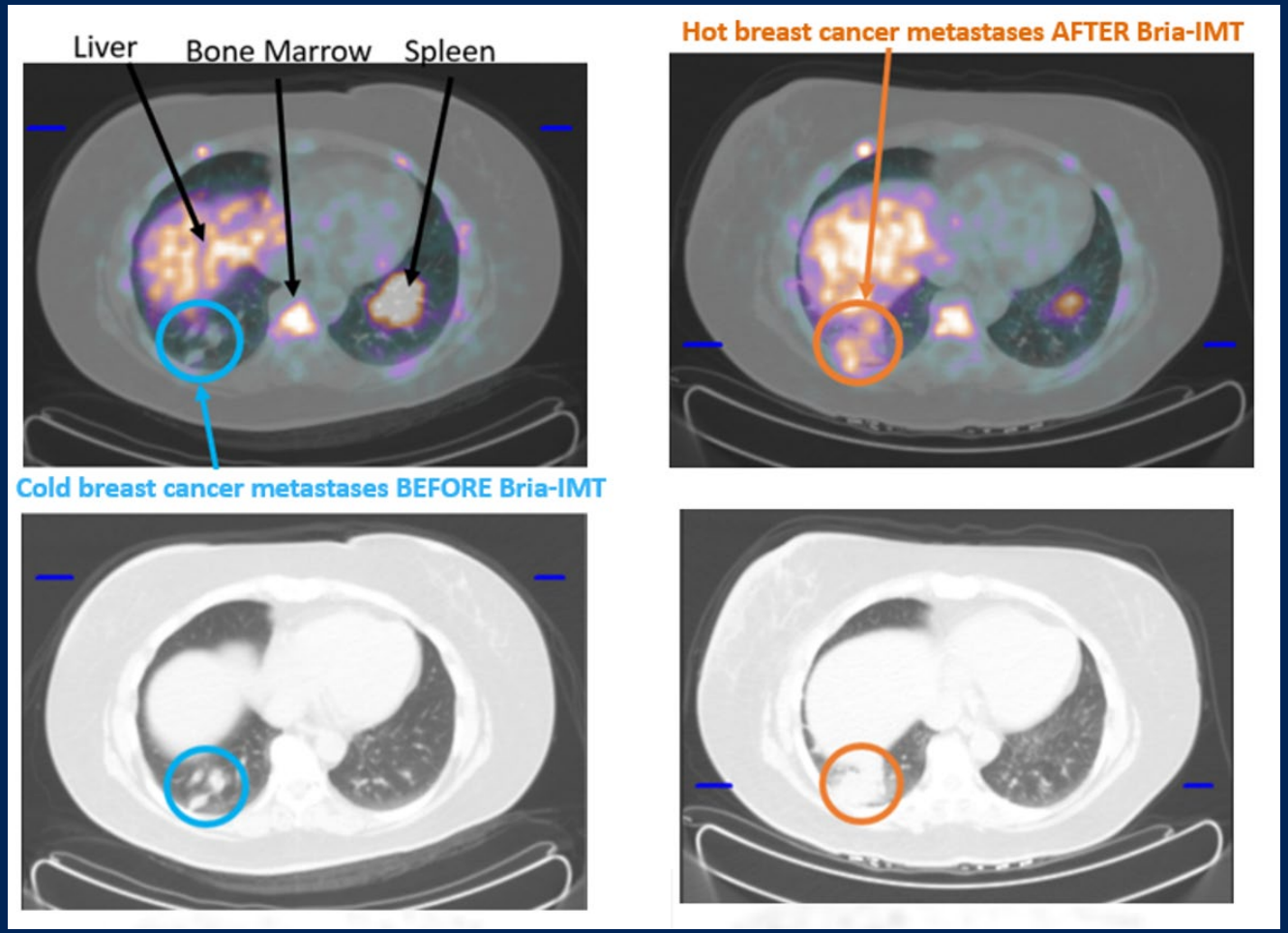
1 grade 3 intractable nausea and vomiting deemed related to study regimen (1.9%)

No subjects came off the study due to toxicity to SV-BR-1-GM


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

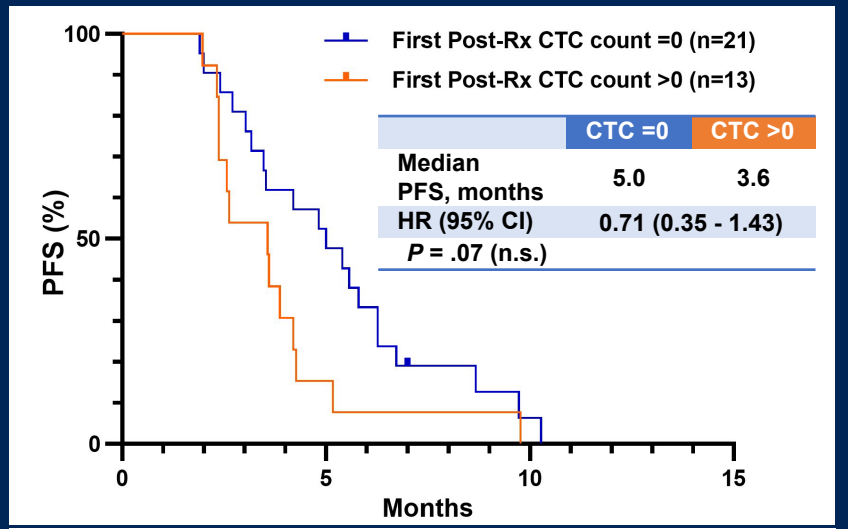
# Correlative Studies: CD8 PET Imaging

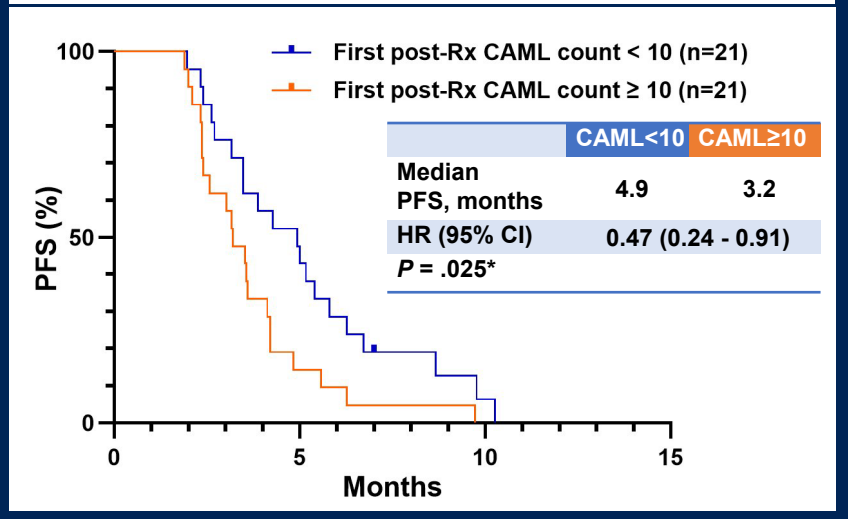
- Bria-IMT combination therapy induced CD8$^+$ T cell infiltration in metastatic breast cancer.



# 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.

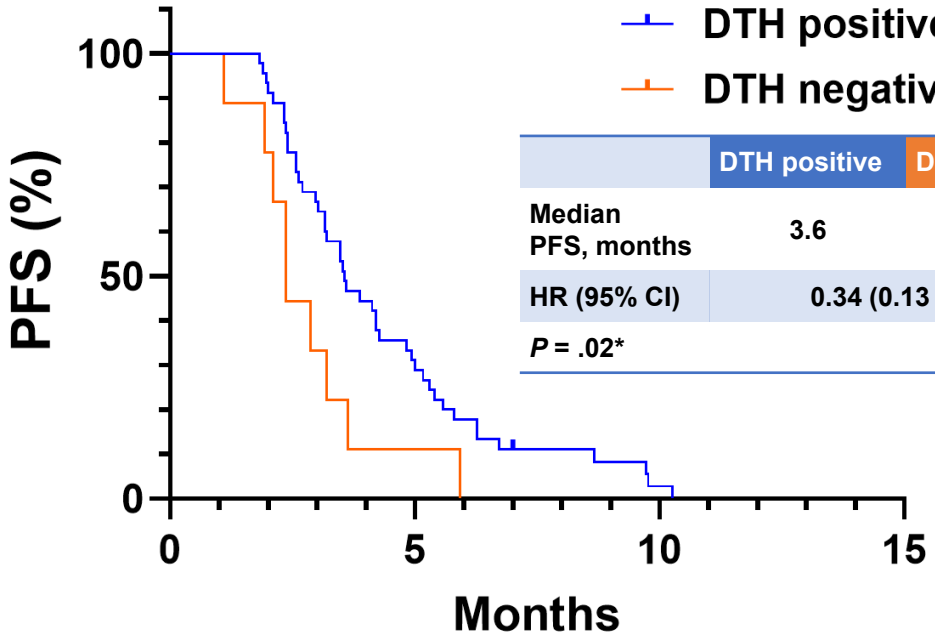


# Correlative Studies: DTH Response

- 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.

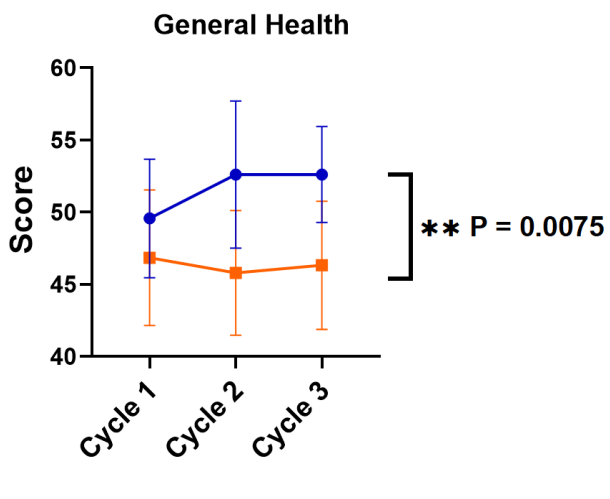
## Progression Free Survival by DTH Response

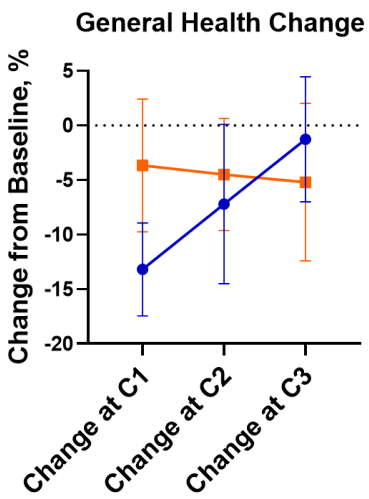



| | DTH positive | DTH negative |
|---|---|---|
| Median PFS, months | 3.6 | 2.4 |
| HR (95% CI) | 0.34 (0.13 - 0.90) | |
| *P* = .02* | | |

# Correlative Studies: Quality of Life (SF-36)

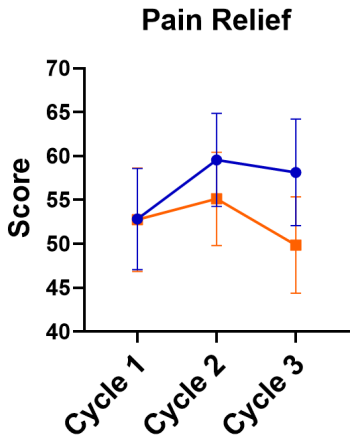
## General Health

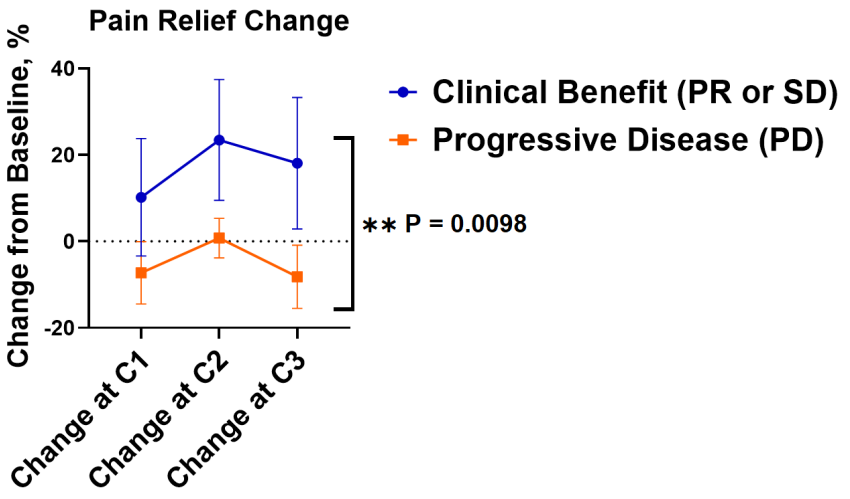



General health scores significantly correlate with disease control.

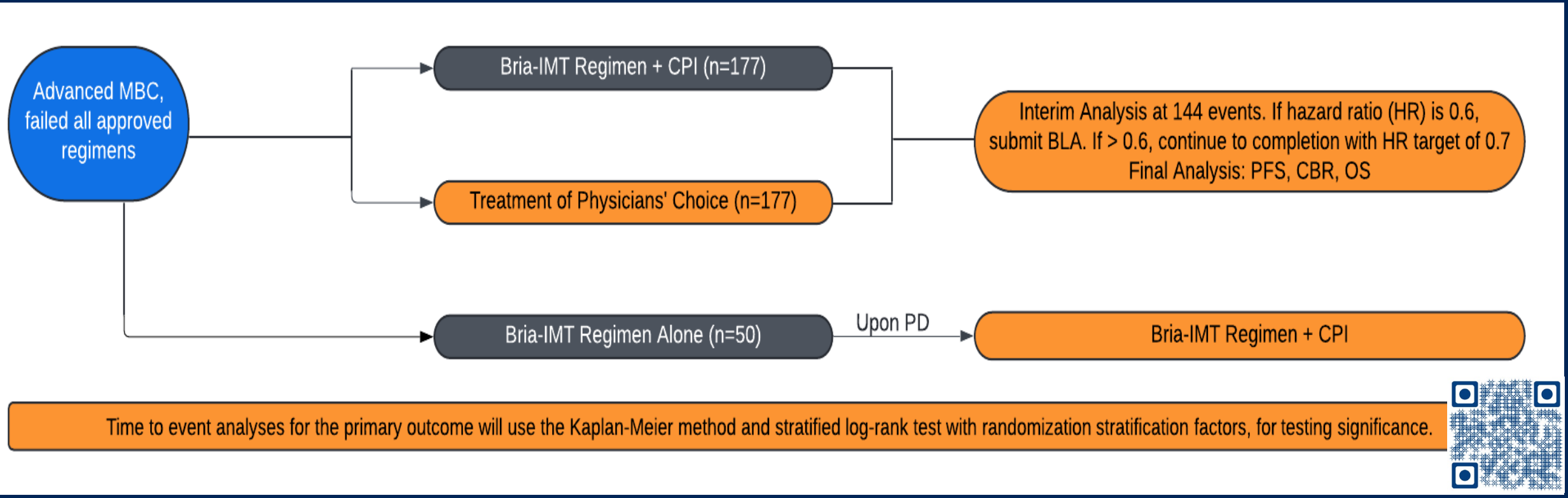
## Pain Relief




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

# Phase III Study Design




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.

# 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

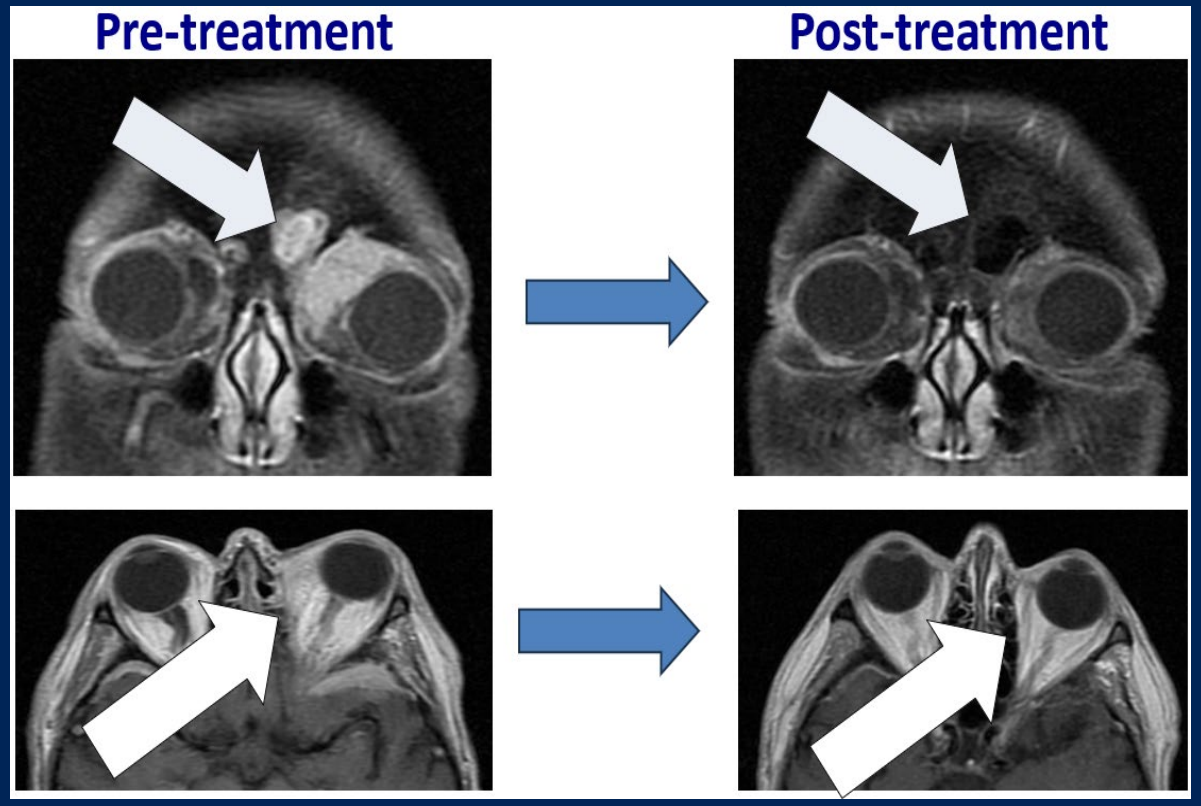
Chaitali Nangia; Carmen Calfa; Blaise Bayer; Mingjin Chang; William Williams; Giuseppe Del Priore; Charles Wiseman; Saranya Chumsri. Cancer Res (2024) 84 (7_Supplement): CT206. https://doi.org/10.1158/1538-7445.AM2024-CT206

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

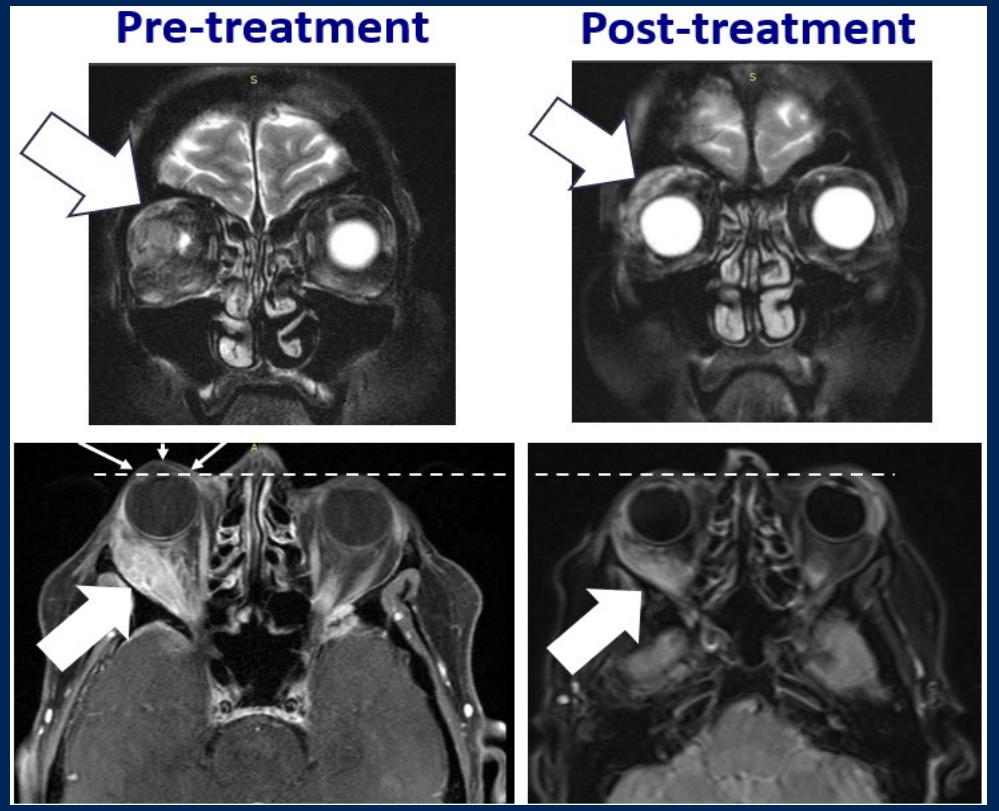



Figure courtesy of Russ Kuker MD, U Miami