Management of HER 2 low Metastatic Breast Cancer – When to introduce Trastuzumab Deruxtecan

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

NCI Designated Cancer Center

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Disclosures:

I have no relevant financial relationships to disclose.
I3 Health and FLASCO have mitigated all relevant financial relationships.

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Case Presentation

- 37 yo premenopausal female with no significant past medical history is diagnosed (June 2017) with R IDC ER+/PR+/HER 2 2+ (FISH positive) T2N0M0 s/p NAC with FEC x 3 and TPH x 3 + Goserelin acetate (Nov 2017 – March 2018).
- Underwent bilateral mastectomies and SLNB (R) and immediate implant-based reconstruction with placement of bilateral tissue expanders.
- Final pathology showed ypT1cN0Mn/a R sided residual IDC 1.3 cm with –ve SLNB (ER+/PR+/HER 2 2+ FISH +).
- HP + AI + Goserelin acetate (May 2018-July 2018).
- April 2022: She noticed an enlarged soft tissue mass on her upper chest; biopsy proven to be ER+/PR +/HER 2 –ve MBC.
- BRCA negative.

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PATHOLOGY Sept 2017:

RIGHT BREAST AT 10 O'CLOCK:

INVASIVE DUCTAL CARCINOMA, moderately differentiated, Nottingham Grade 2,

(3+2+1=6), 1.0 cm in greatest linear microscopic dimension.

Estrogen receptor (SP1)

POSITIVE (> 50%)

Progesterone receptor (1E2)

POSITIVE (> 50%)

HER-2/neu (4B5)

HER2 amplification Positive

HER2/CEP17 ratio =4.34

Average HER2 copy number =8.08

Average CEP17 copy number =1.86

PATHOLOGY April 2018:

RIGHT BREAST MASTECTOMY (SHORT STITCH SUPERIOR, LONG LATERAL):

Residual INVASIVE DUCTAL CARCINOMA, 1.3 cm in largest dimension.

AJCC (7th Edition) Classification: ypT1c N0 (sn) Mn/a

pT1c Tumor >10 mm but ≤20 mm in greatest dimension

ER	Positive
PR	Positive
HER2	2+

HER2 FISH is positive (Ratio: 4.34)

PATHOLOGY April 2022:

SUB-CLAVIAN MASS BIOPSY:

METASTATIC CARCINOMA

E-CADHERIN	POSITIVE
ER (SP1)	POSITIVE (>50%)
PR (1E2)	NEGATIVE (<1%)
HER2 (4B5)	EQUIVOCAL (2+)

RESULT: HER2 NOT AMPLIFIED (NEGATIVE) by FISH studies

Group 5 (HER2/CEP17 ratio <2.0 and HER2 signals/cell <4.0).

HER2/chromosome enumeration probe 17 (CEP17) ratio = 1.2

Average number of HER2 signals per cell = 2.2

Number of scored nuclei = 50

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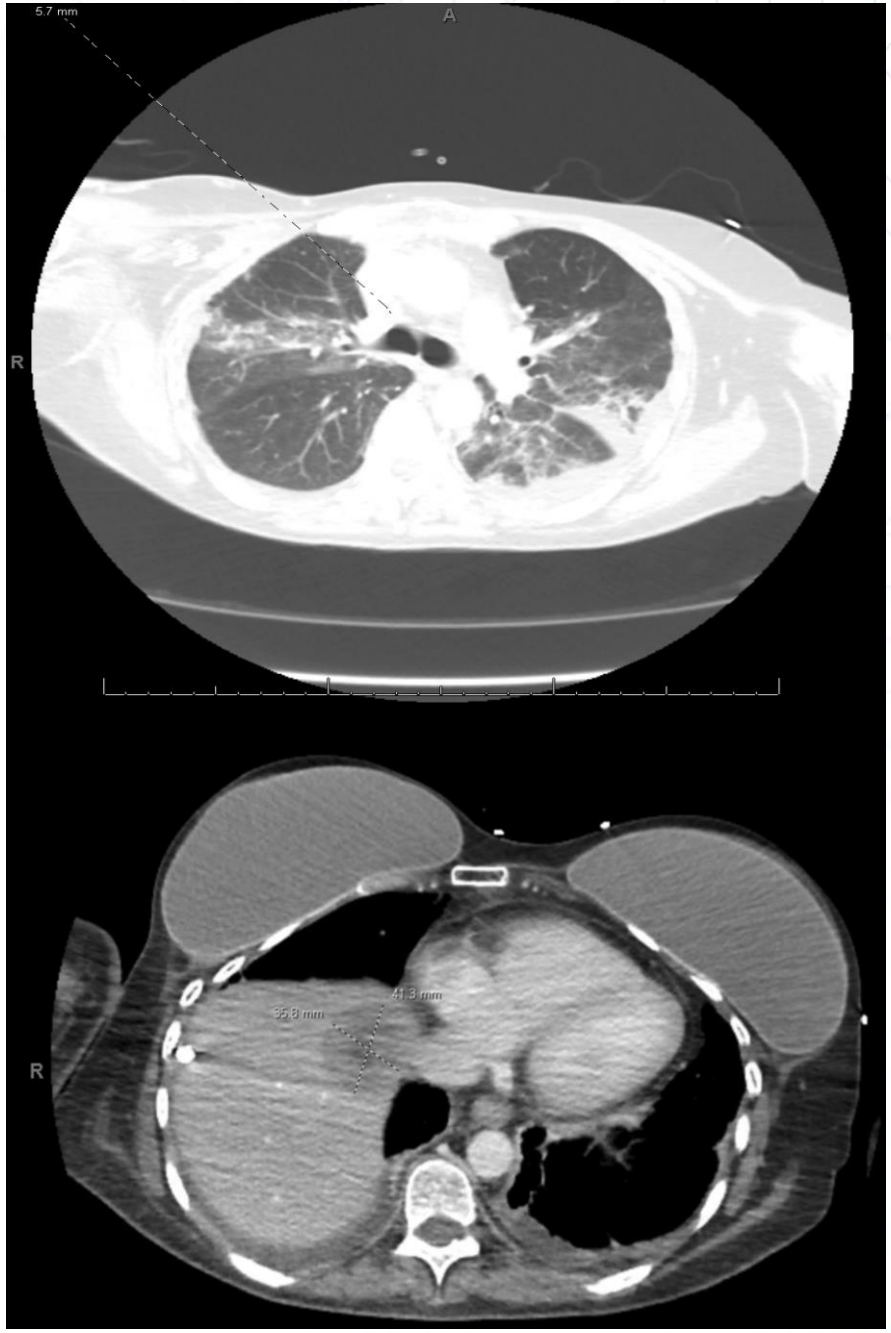
Case Presentation

- Started on Palbociclib + AI June 2022. XRT June 2022 – Aug 2022
- October 2023: Progression on CT chest, ESR1 mutation on Guardant360. Switched to Elacestrant 345 mg daily
- February 2024: Worsening metastases to BL lungs, liver, bones. MRI brain with supra and infratentorial CNS mets.
- Started on Gemcitabine/Paclitaxel q3 weeks (received 2 cycles only due to recurrent hospitalizations for CAP/pneumonitis).
- CT C/A/P April 2024 with worsening progression →**Trastuzumab Deruxtecan started**



Case Presentation

- Mixed response on surveillance imaging in July 2024. MRIs obtained in Oct 2024 to further characterize bone lesions showed clear progression (9 cycles later).

Q → Would you have started HER 2 targeted therapy earlier?

- She developed binocular diplopia, R full facial paralysis, partial CN III palsy (L eye), CN VI palsy on the R eye, R CN VII palsy (Nov 2024).

- MRI brain:

1.Interval progression of metastatic disease with increased size and number of previously seen enhancing metastatic supratentorial and posterior fossa lesions. No evidence of significant vasogenic edema or mass effect.

2.New lesions in the right dorsal pons causing partial effacement of the fourth ventricle.

3.Extensive new intra-axial and leptomeningeal deposits in the bilateral cerebellum.

Case Presentation

- She completed C4/4 HD MTX and proceeded afterwards with proton craniospinal irradiation.
- Repeat MRI brain after HD MTX showed an increase in the volume of the numerous supra and infratentorial metastases.
- She also has a new PIK3A mutation on new liquid Guardant 360 testing making her a candidate for Alpelisib after completion of RT.

Q → Thoughts on next step in management plan?

Thank you

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