

Pearls for BM Management in HER2+MBC:

A Case File Infographic

CASE 1. BASELINE BM, LOW BURDEN
(DE NOVO AT PRESENTATION)

CASE 1: K.L.

PATIENT HISTORY

- K.L. is a 49-year-old premenopausal nurse who prides herself on staying active and independent.
- Recently diagnosed with HER2+/HR- MBC, she was surprised when staging MRI revealed 2 small (6–8 mm) asymptomatic parietal lobe lesions with no edema.
- She has no prior cancer history.
- She is otherwise healthy, with normal performance status and no extracranial disease, and is eager to "hit this hard" from the start.



EXPERT RECOMMENDATIONS

- Defer local therapy, with planned MRI surveillance; initiate systemic therapy per 1L SOC (HP + taxane).
  - Consider CNS-active regimens (eg, tucatinib triplet) in trial settings, if eligible and available.
- Obtain brain MRI at baseline and every 2–3 months during follow-up; maintain a low threshold for additional imaging if symptoms develop.
- Reasonable to defer SRS unless multidisciplinary team recommendation favors early local control (eg, if the brain lesion is symptomatic or high-risk for imminent complications) or if patient preference favors SRS.

CASE 2. HIGH BURDEN/SYMPTOMATIC BM
(DE NOVO AT PRESENTATION)

CASE 2: M.R.

PATIENT HISTORY

- M.R. is a 65 year-old postmenopausal woman and a retired school principal.
- She presented for evaluation after worsening headaches, blurred vision, and balance issues.
- Imaging revealed de novo HER2+/HR+ MBC with multiple large BMs (largest 3 cm) and vasogenic edema.
- CT showed only small-volume bone metastases, no visceral involvement.
- She has not received prior systemic therapy and is concerned about losing her independence.



EXPERT RECOMMENDATIONS

- Start local therapy (eg, neurosurgical resection followed by SR, or SRS alone) for symptom relief and local control.
- Initiate systemic therapy promptly after local control (see Infographic 1 for treatment algorithm)
  - For patients with limited brain disease that can be managed locally, begin with CLEOPATRA regimen.
  - If additional BMs emerge during treatment, consider switching systemic regimens.
- Coordinate early with neuro-oncology for edema management (eg, corticosteroid taper) and supportive care.

CASE 3. ASYMPTOMATIC PROGRESSIVE BM
(PROGRESSION ON 1L)

CASE 3: J.P.

PATIENT HISTORY

- J.P. is a 46-year-old premenopausal woman and an accountant who recently returned to full-time work.
- She completed adjuvant HP + taxane 3 years ago for early-stage HER2+/HR+ breast cancer.
- She is now on HP + taxane for metastatic recurrence for 10 months.
- Her extracranial disease is stable, but surveillance MRI shows 2 new 1-cm frontal lobe lesions.
- She notes that she feels well physically and is hoping to avoid aggressive interventions unless necessary.



EXPERT RECOMMENDATIONS

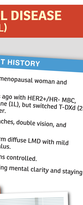
- Treat CNS progression with focal radiation (SRS) and continue current systemic therapy if extracranial disease remains controlled.
- Consider switching to a CNS-active systemic regimen (eg, tucatinib triplet or T-DXd) if further CNS progression occurs or patient meets trial eligibility.
- Monitor closely with MRI every 2–3 months; delay WBRT when possible to preserve cognitive function.

CASE 4. SYMPTOMATIC PROGRESSIVE BM
(PROGRESSION ON 1L)

CASE 4: S.D.

PATIENT HISTORY

- S.D. is a 68-year-old postmenopausal woman and grandmother of 3.
- Living with HER2+/HR- MBC on HP + taxane for 11 months, she was doing well until new right-sided weakness and headaches developed.
- MRI shows a 2.5-cm cerebellar lesion with edema plus 2 smaller supratentorial metastases.
- Her extracranial disease remains stable.
- She is worried about her mobility and being able to care for her grandchildren.



EXPERT RECOMMENDATIONS

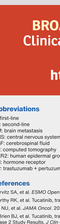
- Initiate urgent local therapy for symptomatic BMs eg, surgical resection of the large lesion followed by SRS to the cavity and all intact metastases or SRS alone if unresectable).
- Following local therapy, guidelines recommend continuing the existing systemic regimen if extracranial disease remains controlled.
- Switch to a CNS-active regimen (eg, T-DXd or tucatinib triplet) may be considered in select scenarios, such as:
  - Recurrent growth of the same BM after prior local therapy
  - Appearance of new BMs on serial imaging despite stable extracranial disease
  - Development of extracranial progression
- Coordinate multidisciplinary care early (medical oncology, neuro-oncology, radiation oncology) to individualize timing and sequencing of treatments.

CASE 5. SYMPTOMATIC PROGRESSIVE BM
(PROGRESSION ON 1L)

CASE 5: T.W.

PATIENT HISTORY

- T.W., a 44-year-old postmenopausal woman, is a graphics designer and avid traveler.
- She initially presented with de novo HER2+/HR+ MBC.
- After 14 months on T-DXd (2L), restaging shows rapid lung progression plus a single 7-mm occipital metastasis without symptoms.
- Her performance status is declining from visceral disease burden, and she's anxious about balancing aggressive treatment with quality of life.



EXPERT RECOMMENDATIONS

- Prioritize rapid systemic disease control; start a regimen with strong extracranial efficacy and, if possible, CNS activity (eg, tucatinib triplet if not previously given, or other NCCN-recommended options).
- Reasonable to defer local CNS therapy unless the brain lesion is symptomatic or high-risk for imminent complications.
- Integrate palliative and supportive care early to address quality-of-life concerns alongside aggressive treatment.

CASE 6. LEPTOMENINGEAL DISEASE
(PROGRESSION ON 2L)

CASE 6: A.H.

PATIENT HISTORY

- A.H. is a 59-year-old postmenopausal woman and business owner.
- Diagnosed de novo 3 years ago with HER2+/HR- MBC, she has received HP + taxane (1L), but switched T-DXd (2L) after progression in the liver.
- She now reports new headaches, double vision, and unsteadiness.
- MRI and CSF findings confirm diffuse LMD with mild communicating hydrocephalus.
- Her systemic disease remains controlled.
- She worries about maintaining mental clarity and staying involved in her business.

EXPERT RECOMMENDATIONS

- Start with systemic therapy that has CNS activity (eg, tucatinib triplet or T-DXd, if not previously given), choosing based on systemic disease control, toxicity profile, and patient preference.
- If ongoing systemic therapy is controlling extracranial disease and the patient is minimally symptomatic from LMD, consider intrathecal chemotherapy to allow continuation of effective systemic therapy. Avoid intrathecal therapy in highly symptomatic patients, where clinical benefit is unlikely.
- Discuss prognosis, treatment goals, and supportive care early; consider clinical trial enrollment for HER2+ LMD.

BROAD EXPERT RECOMMENDATION:
Clinical trials strongly encouraged when applicable and available.

https://www.clinicaltrials.gov

Abbreviations

1l: first-line
2L: second-line
BM: brain metastasis
CNS: central nervous system
CSF: cerebrospinal fluid
CT: computed tomography
HER2: human epidermal growth factor receptor 2
HR: hormone receptor
HP: trastuzumab + pertuzumab
LMD: leptomeningeal disease
MBC: metastatic breast cancer
MRI: magnetic resonance imaging
NCCN: National Comprehensive Cancer Network
SOC: standard of care
SRS: stereotactic
Tucatinib triplet: tucatinib, trastuzumab, and capecitabine
T-DXd: trastuzumab deruxtecan
WBRT: whole-brain radiotherapy

References

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