Date: 1405/08/16, 2026/11/07

Patient's Name: Z.J

Responsible Physician: Dr. Zaboli/ Dr. Omranipour

Patient Presentation:

A 39 Y/O female

Initial Diagnosis (June 2023):

Diagnosed with left breast invasive ductal carcinoma (IDC), triple-negative phenotype, Ki-67: 70%. No nodal or distant metastases were reported at initial presentation.

Neoadjuvant Treatment:

4 cycles of carboplatin + paclitaxel.

4 cycles of doxorubicin + cyclophosphamide (AC).

-Pembrolizumab: 8 cycles before surgery and 7 cycles postoperatively.

Surgery (December 2024):

Underwent left breast-conserving surgery (BCS) + axillary surgery and right LICAP flap reconstruction.

-Residual invasive tumor: 16 mm.

-ER−/PR−, HER2 2+, Ki-67: 80–85%.

-5 lymph nodes retrieved (3 sentinel nodes), all negative.

-Final stage: ypT1cN0.

Completed 28 sessions of adjuvant radiotherapy, followed by pembrolizumab and olaparib.

Molecular Testing:

-Germline BRCA1/2 testing: Negative.

-Somatic TP53 mutation: p.R175H.

-HRD-positive (reported score: 61)

-Additional findings included CDKN2A deletion, BRCA1 LOH and MYC amplification.

-MSI stable; TMB approximately 3.9 mutations/Mb.

First Loco regional Recurrence (December 2025):

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Approximately one year after surgery, multiple cutaneous nodules developed in the left breast/chest wall region.

PET/CT (January 2026): Loco regional recurrence without evidence of distant FDG-avid metastases.

Biopsy/IHC:

-ER: 0%

-PR: <1%

-HER2: Negative, HER2-ultralow expression (≤10% of tumor cells with faint membrane staining)

-Ki-67: Approximately 80%.

Systemic Treatment:

Received 3 cycles of trastuzumab deruxtecan (T-DXd; Enhertu), administered every 3 weeks. However, the number of cutaneous lesions increased during treatment.

Second Surgery (February 2026):

-Left therapeutic mastectomy with excision of involved skin and part of the underlying pectoralis muscle.

-Right prophylactic mastectomy.

-Extensive excision of recurrent cutaneous disease.

Subsequently received 4 cycles of gemcitabine + cisplatin, completed in June 2026.

Olaparib was restarted after chemotherapy (150 mg × 4 tablets daily.(

Molecular Reassessment:

Repeat NGS (CeGaT) demonstrated:

-HRD-positive (score: 88)

-TP53 p.R175H

-CDKN2A deletion and BRCA1 LOH.

-MSI stable; TMB: 5.2 mutations/Mb.

-No pathogenic BRCA1/2 or ERBB2 alterations reported.

Follow-up:

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-August 2026 PET/CT: No evidence of metabolically active disease or distant metastases.

-November 2026: Two adjacent new cutaneous/subcutaneous nodules (approximately 5.5 mm each) detected near the left mastectomy scar, inferior to the axillary scar (BI-RADS 4).

-CT chest/abdomen: Small pulmonary nodules (5–6 mm) and a sclerotic vertebral lesion, without definite evidence of distant metastatic disease.

-November 2026 biopsy: Confirmed recurrent IDC (grade 2, nuclear score 2); the second specimen was insufficient for definitive diagnosis.

Question:

What would be the optimal management strategy for this patient with rapidly recurrent locoregional TNBC despite multimodality treatment, including pembrolizumab, olaparib, T-DXd, extensive surgery, and gemcitabine/cisplatin?

Recommended Plan:

- ✓ Radiation oncology consultation is recommended to define the previous radiotherapy (RT) field.
- ✓ If the new lesions lie outside the previous RT field, re-irradiation should be considered.
- ✓ Local excision of the lesions is also recommended.
- ✓ A new systemic regimen based on sacituzumab govitecan or weekly paclitaxel is recommended.

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