Transformation of ER/PR Positive Invasive Ductal Carcinoma to Triple-Negative Metastatic Breast Cancer Following Adjuvant Abemaciclib: A Case Report

Allison Poles, MD (RUSH), Shalini Atluri, BS (RUSH), Ruta Rao, MD (RUSH)

Introduction

- Abemaciclib is an oral CDK 4/6 inhibitor approved by the FDA October 2021 for adjuvant treatment of HR-pos, HER-2 neg early breast cancer in combination with endocrine therapy
- Few reports have shared the transformation of HR-positive disease to triple-negative while on a CDK4/6i

Initial Presentation

45F with bilateral locally advanced invasive ductal carcinoma (IDC): Stage IIIB (cT2, cN3c(f), cM0)

- Biopsies: R breast ER 70%, PR 90%, HER2 0, Ki-67 90% (hot spots). L breast ER > 90%, PR 5-10%, HER2 0, Ki-67 > 20%
- Histology: Nottingham grade 3 (3+3+2=8) in both tumors
- Lymph nodes: Bilateral axillary nodes positive for macromestatic carcinoma
- Staging at diagnosis: CT CAP and bone scan negative for distant metastases
- Germline testing: Negative (including TP53)

Initial Treatment:

- Neoadjuvant dose-dense ddAC-T [doxorubicin (60mg/m2) and cyclophosphamide (600mg/m2) x 6 cycles followed by paclitaxel (175mg/m2) x 2 cycles]
- Bilateral mastectomies with radiation to entire chest wall
  - Pathologic Response: R breast tissue with rare tumor cells in lymphovascular spaces, no tumor cells in L breast tissue
  - 1 of 5 sentinel lymph nodes on both R and L with isolated cytokeratin positive tumor cells measuring less than 2mm in a background of therapy-associated changes
- Oophorectomy and adjuvant letrozole for ovarian suppression
- Abemaciclib started 6 months post-mastectomy

Subsequent Clinical Course

- 8 months after starting abemaciclib, new osseous metastases (C2/C3, T11, L4, left acetabulum) were incidentally found during a hospitalization (Fig 1)
- L acetabular lesion biopsy: ER 5%, PR %, HER2 1+
- FES PET confirmed ER loss (Fig 2)
- Germline testing: three new TP53 mutations, along with pathogenic ARID1A, ELOC, HNF1A, LRP1B, RAD1
  - TP35 Splice region variant – LOF (pathogenic)
  - TP53 p.R267P – c.800G>C Missense variant – LOF (pathogenic)
  - TP53 p.N268d – c.802A>G Missense variant (VUS)
- Disease progression reflected phenotypic conversion to ER-negative disease under therapeutic pressure. Transitioned off endocrine/CDK4/6 therapy.
- Clinical update: the patient has progressed on multiple adjuvant regimens, including capecitabine, trastuzumab deruxtecan and sacituzumab. She has significant osseous metastases and innumerable liver metastases. She is now starting eribulin

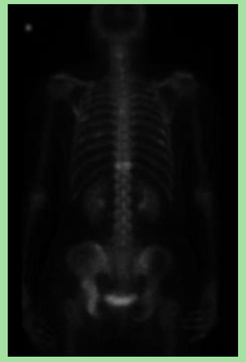


Figure 1: Bone scan with new osseous metastases (C2/C3, T11, L4, left acetabulum)

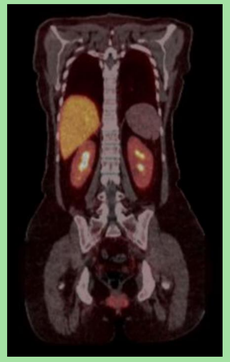


Figure 2: FES PET/CT showing absence of ER uptake at recurrence

Conclusion

- ER loss and TP53 mutation can occur early after adjuvant abemaciclib in patients with ER+ breast cancer
- Corti et al. (2025): showed ~9% recurrence in high-risk, HR–pos, HER2-neg early breast cancer treated with adjuvant abemaciclib plus endocrine therapy. 50% of those patients had HR loss and some had p53 alterations (of the 10 who underwent genomic sequencing 90% had p53 alterations)
- Re-biopsy and molecular profiling are essential to guide therapy at recurrence

- *Future Directions*: Further studies should evaluate the frequency of new p53 mutations in patients treated with abemaciclib and its role in the transition of HR status

References

- Rastogi P, O'Shaughnessy J, Martin M, et al. Adjuvant Abemaciclib Plus Endocrine Therapy for Hormone Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative, High-Risk Early Breast Cancer: Results From a Preplanned monarchE Overall Survival Interim Analysis, Including 5-Year Efficacy Outcomes. J Clin Oncol 2024; 42:987-993
- Corti C, Martin AR, Kurnia PT, et al. Clinicopathological features and genomics of ER-positive/HER2-negative breast cancer relapsing on adjuvant abemaciclib. ESMO Open. 2025 Jun 3;10(6):105126. doi: 10.1016/j.esmoop.2025.105126

Acknowledgements

We would like to thank our patient and the Rush University Medical Center care team.

Contact Allison_Poles@rush.edu for further questions.