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TARGETED MOLECULAR TESTING IN ENDOMETRIAL CARCINOMA: VALIDATION OF A RESTRICTED TESTING PROTOCOL

E-Poster Viewing
ORAL FEATURED POSTERS

Lecture Title:

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Objectives: The World Health Organization (WHO) endorsed molecular classification of endometrial carcinoma (EC) to be incorporated in routine diagnostic workup, by evaluating p53 and mismatch repair (MMR) protein immunohistochemistry (IHC), as well as pathogenic mutations in the gene encoding DNA polymerase epsilon (POLE). The latter is currently the least affordable or accessible step. We investigated whether POLE testing can be omitted in patients who based on stage, grade and lymphovascular space invasion (LVI) criteria would not usually be directed to adjuvant therapy.

Methods: Using data from a single cancer centre (n=460) in Vancouver, and a population-based cohort in Tubingen (n=452), we compared the WHO recommended molecular testing of the entire cohort (n=912) with a restricted protocol: p53 and MMR IHC on all cases, but POLE sequencing not done on “very low-risk” ECs, defined as Stage 1A, G1/G2, no LVI, MMR proficient and without p53 abnormalities.

Results: 30% of full cohort and 38% of population-based patients were classified as “very low-risk”, and did not undergo POLE testing. “Very low-risk” ECs with unknown POLE status showed excellent clinical outcomes in both univariable and multivariable survival models. Amongst G1/G2 EEC, 14/566 (2.5%) were p53abn, and G1/G2 EEC constituted 14/166 (8.4%) of all p53abn ECs.

Conclusions: Molecular classification of EC can be safely and more pragmatically incorporated into routine clinical practice using universal MMR and p53 IHC, and foregoing POLE testing in “very low-risk” ECs where this has no therapeutic impact. Restricting molecular testing to high-grade/high-risk EC would miss some p53abn patients.