

Conference Abstracts

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Beyond Binary PTEN Loss: Integrating Genomics, Long-Term Outcomes, and AI-Assisted Digital Pathology to Define Actionable PTEN Deficiency in Prostate Cancer.

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Abstract

Background

PTEN loss defines an aggressive molecular subset of prostate cancer and has gained therapeutic relevance with AKT-pathway inhibition now approved for PTEN-deficient metastatic androgen pathway modulation-naïve (APMN) prostate cancer. However, PTEN loss is not binary, and the prognostic impact of the degree of loss, spatial heterogeneity, and genomic context remain poorly described.

Methods

We are building a retrospective, multi-cohort Mayo Clinic translational study integrating PTEN-characterized prostate cancers with genomics, long-term outcomes, metastatic progression, and digital pathology. The anchor cohort is a radical prostatectomy tissue microarray of Gleason grade group 2-5 cancers with PTEN and CHD1 FISH and >15-year follow-up. Pathology accession numbers will be linked, within approved workflows, to biochemical recurrence, systemic progression, PSA and imaging trajectories (to capture PSA-

discordant radiographic progression), and sampled metastatic tissue. A second cohort with paired PTEN IHC, FISH, and sequencing will define assay concordance, and whole-slide sections will support AI-assisted quantification of percent PTEN loss and spatial heterogeneity.

Results

In the anchor cohort (409 patients with FISH; 262 in survival analysis; median follow-up 15.1 years), PTEN and CHD1 loss — assessed by FISH on Gleason pattern 4 tissue microarray cores — were present in 24.7% and 18.3% of cases, respectively. On Cox analysis, PTEN loss — but not CHD1 loss — was associated with worse biochemical recurrence, systemic progression, and prostate cancer-specific death, supporting PTEN loss as a marker of aggressive biology. Linkage to oncologic outcomes, PSA-discordant progression, assay concordance, and AI-based quantification is ongoing.

Conclusion

This study will establish an integrated clinical-pathologic-genomic framework that moves PTEN assessment beyond a binary IHC call. By linking

depth and pattern of PTEN loss to long-term outcomes, it aims to improve risk stratification, flag patients prone to PSA-discordant

progression, and refine selection for PTEN/AKT-pathway-targeted therapy.

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