International Pathology Day 2025

The Royal College of Pathologists
Pathology: the science behind the cure

DIAGNEXIA

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ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ΑΘΗΝΩΝ ΓΕΝΝΗΜΑΤΑΣ

UNIVERSITÀ DEGLI STUDI DI TRIESTE

References

Architectural patterns and AKTs expression in HGSOC and HRD status

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Background: High-grade serous ovarian carcinoma (HGSOC) exhibits extensive morphological heterogeneity that may correlate with underlying molecular features and therapy response. The SET (Solid, pseudoEndometrioid, Transitional) architectural pattern was previously associated with homologous recombination deficiency (HRD) and better treatment response. Additionally, dysregulation of the PI3K/AKT/mTOR pathway through AKT isoform alterations represents a potential therapeutic target in HGSOC. **This study aimed to investigate the relationship between HGSOC architectural patterns, HR status, and AKT1/AKT3 expression levels**.

Methods: A retrospective analysis of 57 HGSOC cases from 2022-2025 was performed. Histological review classified tumors into SET or classic architectural patterns according to Soslow criteria. HR status was determined through BRCA1/2 testing in 46 cases using next-generation sequencing or Myriad MyChoice®CDx Plus assay. AKT1 and AKT3 expression levels were quantified by ddPCR in 33 cases. Survival analysis was conducted using Kaplan-Meier estimates and log-rank test.

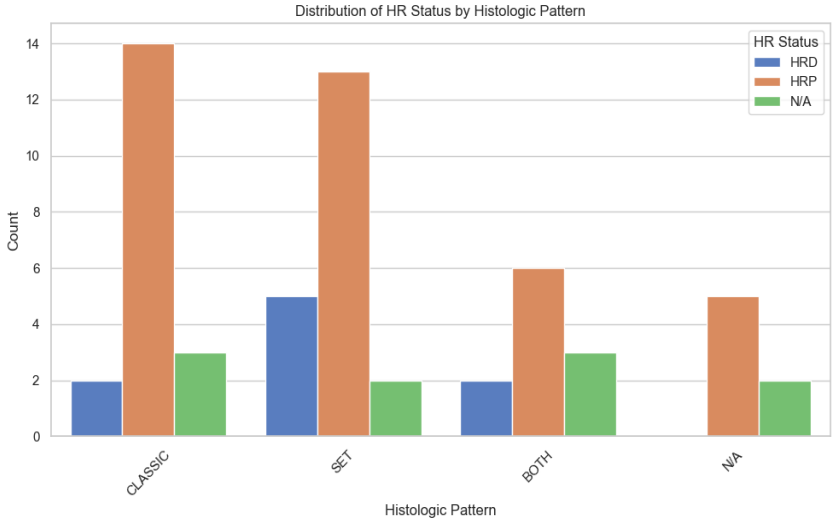

Figure 1. Descriptive statistics. Distribution of HR status by architectural pattern. Among the 38 HRP patients, 14 displayed a Classic pattern, 13 exhibited a SET pattern, 6 showed dominance of both patterns, and in 5 cases the architectural pattern could not be determined. Of the 9 HRD patients, 5 had a SET pattern, 2 a Classic pattern, and 2 had both patterns dominant (HR; Homologous Recombination, HRD; Homologous Recombination Deficiency, HRP; Homologous Recombination Proficiency, SET; Solid-pseudoEndometrioid-Transitional carcinoma cell-like, N/A; Not Available).

Results: Of 50 evaluable cases, 21 (42%) exhibited predominant SET features, 19 (38%) showed classic patterns, and 10 (20%) displayed mixed features. HRD was detected in 9/47 cases (19%). No statistically significant association was found between architectural patterns and HRD status (p = 0.6). Neither histological pattern nor HRD status significantly impacted overall survival. AKT expression analysis is ongoing in a subset of cases.

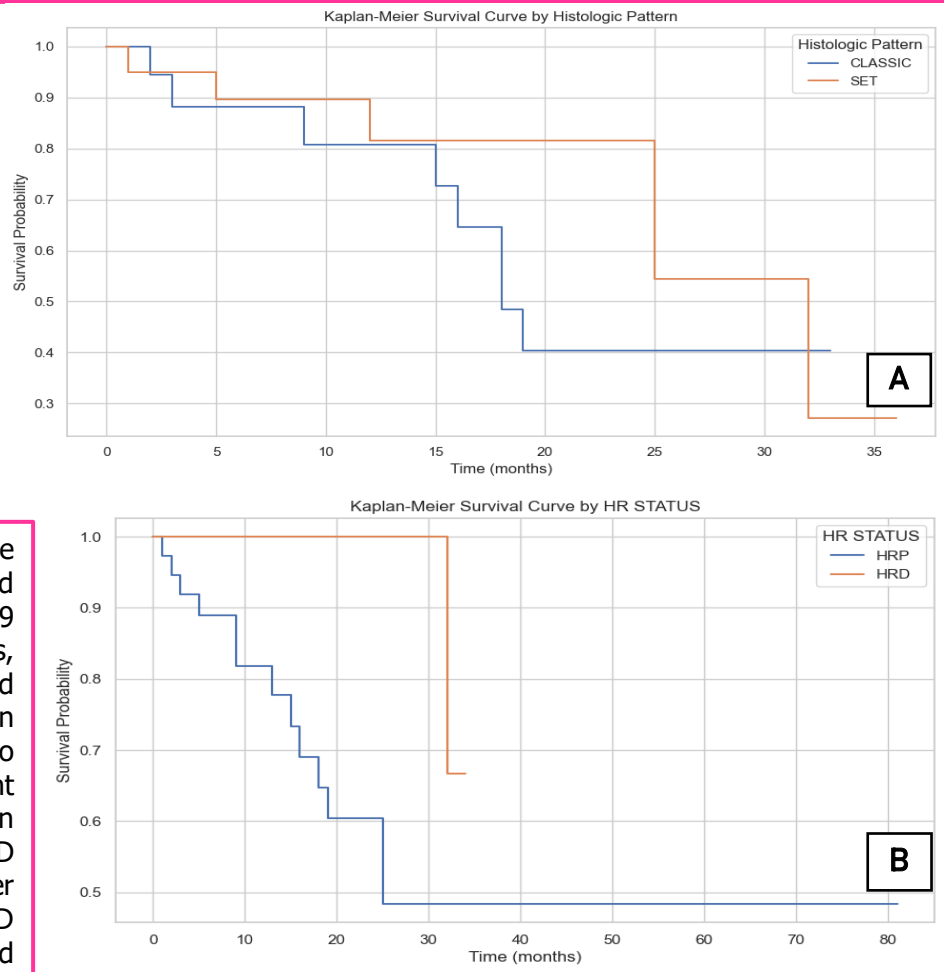

Figure 2. Kaplan–Meier curves representing the overall survival rate by histologic pattern groups (A), and HR status (B) (HR; Homologous Recombination, HRP; Homologous Recombination Proficiency, HRD; Homologous Recombination Deficiency, SET; Solid-pseudoEndometrioid-Transitional carcinoma cell-like).

Conclusions: Contrary to previous reports, our cohort did not support a significant correlation between SET morphology and HRD status in HGSOC. The lack in survival differences between pattern groups suggests that **architectural classification alone may have limited prognostic value** in this patient population, **highlighting the need for comprehensive molecular characterization**.