Oral Abstract 8: Antibody drug conjugate target expression profiling in tubo-ovarian high grade serous carcinoma (HGSC)

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Topic
Ovarian

Objectives
Antibody-drug conjugates (ADCs) are promising therapeutics for HGSC. Two ADCs have current U.S. Food and Drug Administration approval for use in HGSC, targeting folate receptor alpha (FOLR1) and HER2, with additional targets under investigation. Our objective was to evaluate patterns of target antigen expression in HGSC samples.

Methods
214 unique 1mm-core regions of adnexal and omental HGSC samples representing 23 patients were profiled for expression of 4 antigens (FOLR1, B7-H3, TROP2 and CLDN6). Histochemical (H) scores were calculated for TROP2, B7-H3 and CLDN6 expression and PS2 scoring was implemented for FOLR1, with H score positivity defined as ≥100 and PS2 ≥75. The intraclass correlation coefficient (ICC), a ratio representing the between patient variance to total variance, was calculated using a linear mixed effects model.

Results
The mean H score across 214 cores was 140.9 for TROP2, 64.0 for CLDN6 and 32.8 for B7-H3, and the mean PS2 score for FOLR1 was 51.9. Positivity rates were 19/23 (83%) for TROP2, 2/23 (9%) for FOLR1, 5/23 (22%) for CLDN6, and 3/23 (13%) for B7-H3. Core positivity rates were 169/214 (79%) for TROP2, 66/214 (31%) for FOLR1, 59/214 (28%) for CLDN6 and 31/214 (15%) for B7-H3. 22/23 (96%) patients had at least one core sample that was positive for at least one target. The ICC for TROP2 was 0.733 (95% CI 0.347, 0.676), 0.541 (95% CI 0.347, 0.676) for CLDN6, 0.660 (95% CI 0.461, 0.772) for B7-H3, and 0.527 (95% CI 0.302, 0.680) for FOLR1.

Conclusions
There was substantial patient-level heterogeneity in the expression of most ADC targets. The majority of HGSCs were positive for TROP2, with consistent expression amongst cores. Most antigens were expressed with slightly more variance between patients than among individual core samples. Nearly all patients had at least one core that was positive for an ADC target. Variability of antigen expression in individual patients may reduce the reliability of limited tissue testing in making determinations of tumor antigen expression, a challenge in the recurrent setting where tumor samples may be limited.

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