Abstract #5584: Tumor-associated immune cells and progression free survival in advanced endometrial cancer, results from the PHAEDRA Trial (ANZGOG 1601)

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Background:

- Some women with advanced endometrial carcinoma (AEC) have good response to immune checkpoint inhibitors.
- Biomarkers needed to identify those likely to respond.

Methods:

- Participants with AEC treated with durvalumab from the PHAEDRA trial[1] [n=71; 36 dMMR and 35 pMMR).
- H&E and Ventana PD-L1(SP263) immunohistochemical (IHC) stained tumor sections assessed for:
  1. **TCP:** PD-L1 staining of tumor cells
  2. **ICP:** Tumor-associated immune cells (H&E)
  3. **IC:** PD-L1 staining of immune cells

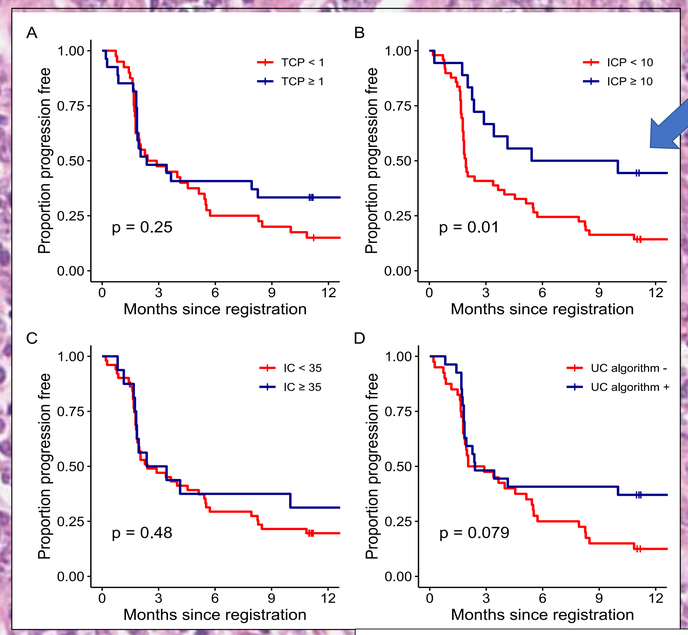
  according to Ventana interpretation guide[2].
- Area under the ROC curve, sensitivity and specificity used to determine optimal cutpoints.
- Individual optimal cutpoints compared to the Ventana PD-L1 (SP263) urothelial carcinoma (UC) algorithm and a new algorithm derived from optimal cutpoints

Results:

- **ICP≥10%**
  - **highest sensitivity (53%) and specificity (82%) of the individual cutpoints.**
  - **best predictor of tumor response and progression free survival.**
- ➢ ICP≥10% not significant after accounting for MMR status (HR 0.59, 95% CI 0.28-1.23, p=0.16).
- ➢ UC algorithm best predictor of overall survival (p=0.02) but also not significant after adjusting for MMR status (HR: 0.53, 95% CI: 0.25-1.12, p=0.10).
- ➢ Optimal cutpoint algorithm identified patients that wouldn't respond (NPV 92%).

Presence of **tumor-associated immune cells** predicts response to durvalumab better than PD-L1 status in advanced endometrial carcinoma.

	Responses below cutpoint	Responses above cutpoint	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Optimal single cutpoints:						
TCP ≥ 1%	8/40 (20%)	9/27 (33%)	33% (17%, 54%)	80% (64%, 91%)	53% (28%, 77%)	64% (49%, 77%)
ICP ≥ 10%	8/49 (16%)	9/18 (50%)	50% (26%, 74%)	84% (70%, 93%)	**53% (28%, 77%)**	**82% (69%, 91%)**
IC ≥ 35%	12/51 (24%)	5/16 (31%)	31% (11%, 59%)	76% (63%, 87%)	29% (10%, 56%)	78% (64%, 88%)
Optimal cutpoint algorithm: TCP≥1 OR ICP≥10 OR IC≥35	2/26 (8%)	15/41 (37%)	37% (22%, 53%)	**92% (75%, 99%)**	88% (64%, 99%)	48% (34%, 63%)
Urothelial carcinoma algorithm TCP>=25% OR ICP>1& IC>=25 OR ICP=1 & IC=100	6/40 (15%)	11/27 (41%)	41% (22%, 61%)	85% (70%, 94%)	65% (38%, 86%)	68% (53%, 80%)



Kaplan-Meier curve - Progression free survival for TCP (A), ICP (B), IC (C) and the urothelial algorithm.

Direction for further research:

- Validation of ICP≥10 and optimal cutpoint algorithm needed.
- Determine if MMR status and ICP≥10 are independent predictors of response.

References:
1. Antill et al. Clinical Activity of Durvalumab for Patients with Advanced Mismatch Repair-Deficient and -Proficient Endometrial Cancer A Nonrandomized Phase 2 Clinical Trial. Journal for ImmunoTherapy of Cancer – In press.
2. https://diagnostics.roche.com/content/dam/diagnostics/us/en/products/v/ventana-pd-l1-sp263-assay/PD-L1-SP263-Bladder-Cancer-Sell-Sheet.pdf

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