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Expression of androgen receptor splice variant, AR-V7, in high grade serous ovarian cancer

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Background

- Androgen receptors (AR) are expressed in up to 55% of ERα-negative breast cancers overall and p to 35% of TNBC.
- Similarly expressed rates are seen in high grade serous ovarian cancer (HGSOC).
- Development of AR splice variants (AR-SV) has been shown to be a mechanism of androgen resistance in breast and prostate cancers and a poor prognostic feature
- Specifically AR-V7 splice variant is found in aggressive phenotypes of castration resistant prostate cancer marked by shorter PFS and OS

Objectives

- Determine presence of AR-V7 in HGSOC
- Evaluate any correlation with platinum sensitivity and/or treatment outcomes.

	Platinum Sensitive	Platinum Resistant
Patient n	6	6
Chemo Naïve Specimens	5	3
Platinum Treated Specimens	6	5

Methods

- Pair-matched chemo-naïve and platinum-treated HGSOC specimens were identified from our tissue repository.
- Formalin-fixed paraffin-embedded tumor (FFPE) blocks were collected and tested for expression of AR-V7.
- Gene fusion detection and variant detection were performed on mRNA isolated from a FFPE tumor sample using the Illumina NovaSeq platform (Illumina, Inc., San Diego, CA) and Agilent SureSelect Human All Exon V7 bait panel (Agilent Technologies, Santa Clara, CA).
- FFPE specimens underwent pathology review to diagnose percent tumor content and tumor size
  - Minimum of 10% of tumor content in the area for microdissection was required.

		n (%)	Sensitive	Resistant
Age (Median)	66	12 (100)	66	61.5
Range	[47, 74]		[49, 74]	[47, 71]
Grade	3		6 (100)	6 (100)
Stage				
	IIA	1 (8.3)	0 (0)	1 (16.7)
	IIIC	9 (75)	4 (66.7)	5 (83.3)
	IVA	1 (8.3)	1 (16.7)	0 (0)
	IVB	1 (8.3)	1 (16.7)	0 (0)
Outcome				
	NED	1 (8.3)	0 (0)	1 (16.7)
	Recurrence	9 (75)	4 (66.7)	5 (83.3)
	Progression	2 (16.7)	2 (33.3)	0 (0)
BMI				
	< 25	5 (42)	1 (16.7)	2 (33.3)
	≥ 25	7 (58)	5 (83.3)	4 (66.7)
BRCA 1/2				
	Mutant Type	5	5	0
	Wild Type	7	1	6

Results

- Twelve chemo-naïve specimens were collected at time of diagnosis by initial biopsy (n=8) or primary debulking surgery (n=4)
  - These were pair-matched with the patients' subsequent platinum-treated specimens from either interval debulking surgery (n=6) or biopsy of recurrence (n=6).
- At time of second pathology 50% were platinum resistant and 50% were platinum sensitive
- Only 19 of the 24 specimens submitted had sufficient RNA for testing, 8 chemo-naïve and 11 platinum-treated.
- AR-V7 variant transcript was not detected in any of the specimens submitted.

Conclusions

- AR-V7 was not expressed in any specimen before or after platinum based chemotherapy
  - This suggests AR-V7 may not be a useful prognostic marker in the management of HGSOC.
- Further investigation into gynecologic malignancies with high AR expression and treated with androgen deprivation therapy may elucidate different results.

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