

Ovarian carcinosarcoma shares a similar molecular profile as ovarian serous carcinoma but not endometrial carcinosarcoma

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Abstract #5560

Background: Ovarian carcinosarcomas (OCS) are rare and aggressive malignancies with limited treatment options. It is unclear if this uncommon type of cancer shares similar molecular changes as endometrial carcinosarcoma (ECS) or serous ovarian carcinoma (SOC). We compared the molecular profile of a cohort of OCS to that of SOC and ECS to explore the potential overlap in treatment paradigms.

Methods: 325 OCS, 361 ECS and 5335 SOC were evaluated using a commercial multiplatform profiling service (CARIS Life Sciences, Phoenix, AZ). Specific testing performed included a combination of gene sequencing (Sanger, NGS), protein expression (IHC) and gene amplification (CISH or FISH).

Results: TP53 was the most commonly mutated gene in all three malignancies with 76.4 % of OCS, 68.8 % of ECS and 69% of SOC. Alteration of PI3K/AKT/mTOR and MAPK pathways were noted to be similar in OCS and SOC but was less frequently altered than ECS including mutation in PIK3CA (7.6% and 2.3% vs. 22.2%, p < 0.001), FBXW7 (0% and 0.6% vs.12.1%, p < 0.001), PTEN (3.7% and 0.8% vs. 12%, p < 0.001) and KRAS (5.2% and 5.0% vs. 13.5%, p < 0.001). For homologous recombination pathway, SOC and ECS were more likely to have BRCA1 (20% and 18% vs. 9%) and BRCA 2 mutations (18% and 27% vs. 12%) than OCS. However, the differences were not statistically significant. No difference in alteration of RB, NOTCH, angiogenesis and FGFR pathways was noted among the three cohorts. Estrogen (14.6%) and 25.1% vs. 53.1%, p < 0.001) and androgen receptors (18.8% and 12.2% vs. 32.4%, p < 0.001) were expressed less frequently in OCS and ECS than SOC respectively. On the other hand, expression of progesterone receptors was more frequent in in OCS and SOC than ECS (26.5% and 30.5% vs. 20.9%, p < 0.001).

Conclusions: While ovarian carcinosarcoma and uterine carcinosarcoma are histologically similar, we reveal that OCS share molecular changes similar to that of SOC. Both OCS and SOC have significantly lower activity of PI3K/AKT/mTOR, MAPK pathways and higher progesterone receptors expression than ECS. Treatment with regimens that are active in ovarian serous could be considered when treating patients with ovarian carcinosarcoma.

or FISH).

antibodies.

• Fluorescent in-situ hybridization (FISH) was used for evaluation of the HER-2/neu [HER-2/CEP17 probe], EGFR [EGFR/CEP7 probe], and cMET [cMET/CEP7 probe] (Abbott Molecular/Vysis). HER-2/neu and cMET status were also evaluated by chromogenic in-situ hybridization (INFORM HER-2 Dual ISH DNA Probe Cocktail; commercially available cMET and chromosome 7 DIG probe; Ventana).

• Direct sequence analysis was performed on genomic DNA isolated from formalinfixed paraffin-embedded tumor samples using the Illumina MiSeq platform. Specific regions of 47 genes of the genome were amplified using the Illumina TruSeq Amplicon Cancer Hotspot panel.

Results Figure 1: Patient characteristics Average Age

Specim site

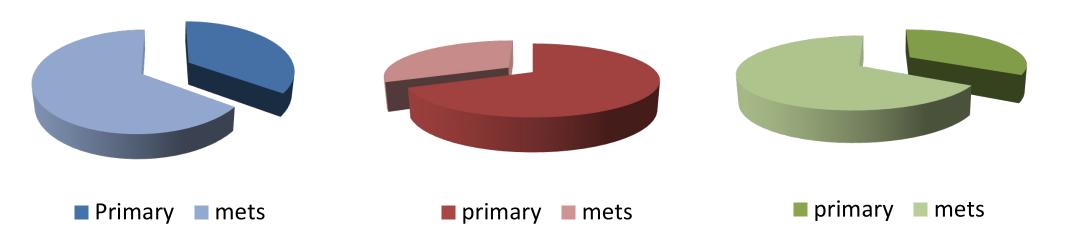
Methods

• Retrospective data analysis was done on ovarian carcinosarcoma (OCS), endometrial carcinosarcoma (ECS) and serous ovarian carcinoma (SOC) cases that were submitted to a commercial referral diagnostic laboratory (Caris Life Sciences, Phoenix, AZ) for molecular profiling aimed to provide therapeutic information based on tumor biomarkers.

• Specific testing was performed per physician request and included a combination of sequencing (Sanger, NGS), protein expression (IHC) and gene amplification (CISH

• IHC analysis was performed on formalin-fixed paraffin-embedded tumor samples using commercially available detection kits, automated staining techniques (Benchmark XT, Ventana, and AutostainerLink 48, Dako), and commercially available

	Ovarian carcinosarcomas (OCS)		Endometrial carcinosarcoma (ECS)		Serous ovarian carcinoma (SOC)	
je						
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	Ovary and				Ovary and Fallopian	
men e	Fallopian tube	35.1%	Uterus	68.4%	tube	33.2%
	Pelvis, NOS	18.5%	Peritoneal tissue	6.9%	Peritoneal tissue	33.4%
	Peritoneal tissue	16.9%	Vagina & vulva	3.9%	GI tract	8.4%
	GI tract	7.4%	Lymph nodes	3.6%	Pelvis	5.2%
	Abdomen	6.8%	Pelvis	3.6%	Connective tissue	4.7%
	connective tissue	4.9%	lung	3.0%	Lymph nodes	4.4%
	Liver	3.1%	GI tract	2.8%	Abdomen	4.1%
	Other	7.4%	Other	7.8%	Other	6.7%



Results

Figure 2: Biomarker frequency distribution, corresponding cancer pathways and associated therapies in OCS, ECS and SOC Associated

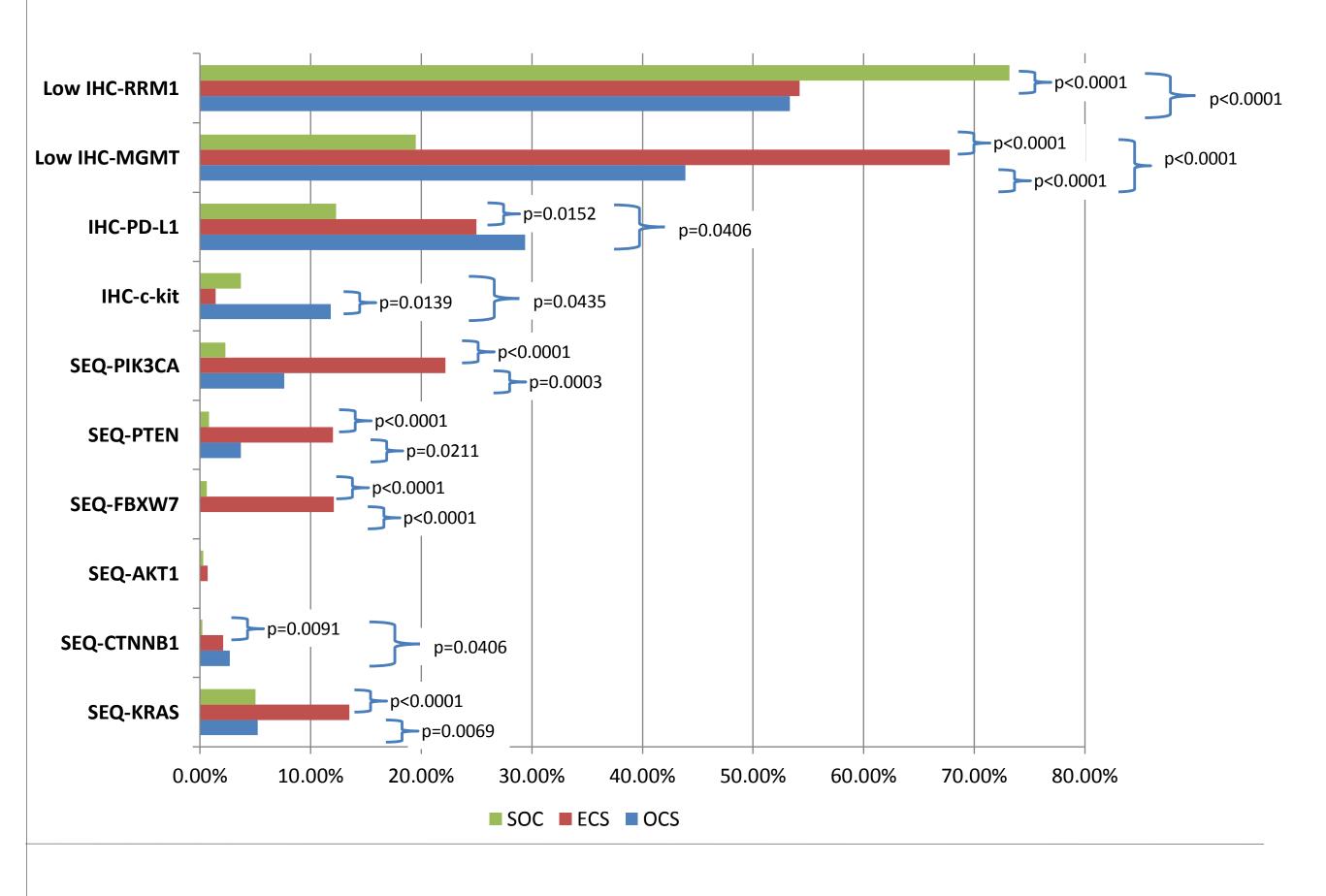
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Agents that are not routinely considered



Results

Figure 3: Biomarkers that are significantly different among OCS, ECS and SOC



Conclusions

- TP53 carries the highest mutation rate in ECS, OCS and SOC.
- Carcinosarcomas of the ovary and endometrium show higher PD-L1 expression, higher RRM1 expression and lower MGMT expression than serous ovarian cancer, suggesting immune-checkpoint inhibitors and temozolomide as promising agents that warrant further investigation in ECS and OCS, while gemcitabine may be more effective in SOC.
- EOC and OCS show molecular similarities when compared to ECS, as shown by low activation of PI3K/Akt/mTOR pathway and KRAS mutation, suggesting PI3K/Akt/mTOR inhibitors and MEK inhibitors as promising therapies to be investigated in ECS.
- Based on similarities in tumor profiles detected by multiple testing technologies, treatment with regimens that are active in ovarian serous cancer could be considered when treating patients with ovarian carcinosarcoma.