2-stage design is utilized. Target accrual is 22 patients in the first stage; 13 or more patients without progressive disease within 6 months is required to proceed to second stage.

Results We report the results from the first stage. Median age was 56 years old, high grade serous and motst of the patients (90.9%) had high-grade serous carcinoma. Of the 22 patients from the first stage, 9 had progressive disease within 6 months (6-month PFS rate 66.5%, 95% CI 48.9–90.2%). The efficacy boundary to proceed to the second stage was met. No grade 4 or 5 treatment-related adverse events (TREAs) were reported, and no TRAEs leading to treatment discontinuation.

Conclusion/Implications Our findings indicate encouraging safety and activity of niraparib + bevacizumab as a maintenance therapy in platinum-sensitive ovarian cancer patients who were previously treated with a PARPi.

PR055/#936 INFLUENCE OF SPATIAL TUMOUR HETEROGENEITY ON HOMOLOGOUS RECOMBINATION DEFICIENCY SCORES FOR HIGH GRADE SEROUS OVARIAN CANCER PATIENTS

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Introduction Extensive genomic instability and heterogeneity are characteristics of high-grade serous ovarian cancer (HGSOC), with deficiency in homologous recombination (HR) repair has been reported for approximately 50% of HGSOC patients. Testing tumours for HR-deficiency (HRD) status is now a clinically applicable test, with a HR score of >42 suggestive of HRD and thus, platinum or PARP-inhibitor sensitivity in HGSOC. We aimed to determine the influence of spatial heterogeneity on HR scores in disseminated HGSOC.

Methods An algorithm detecting genomic scar HR scores was applied to genomic data from three cohorts of multi-site tumour samples – in-house Hammersmith hospital (HH) 45 patients n=5 tumours per patient; GSE38787 (n=24 patients) and GSE40546 (n=14 patients). A HR score is an unweighted sum of three independent measures of genomic instability: loss of heterozygosity (LOH), telomeric allelic imbalance (TAI), and large-scale state transition (LST). A cut-off >42 denotes HR-deficient.

Results Heterogeneity in tumour HR scores were detected in each cohort with patients presenting with either all HRD tumours, all HRP tumours or mixed HR scores, showing both HRD and HR-Proficient (HRP) tumour scores: HH (22%); GSE38787 (17%); and GSE40546 (28%). Within the HH cohort, survival analysis revealed that patients with all HRP tumours and mixed HR status had worse survival (progression-free survival p=0.0052; overall-survival p=0.00092) than patients with all HRD tumours.

Conclusion/Implications Our data demonstrating differences in HRD/HRP scores proposes that HR status may vary across disseminated HGSOC. Thus, implying that testing a single tumour biopsy may not accurately portray HGSOC tumour biology and could incorrectly guide clinical decision-making.

PR056/#32 CLINICAL CHARACTERISTICS AND ONCOLOGICAL OUTCOMES OF RECURRENT ADULT GRANULOSA CELL TUMOR OF OVARY: A RETROSPECTIVE STUDY OF SEVENTY PATIENTS

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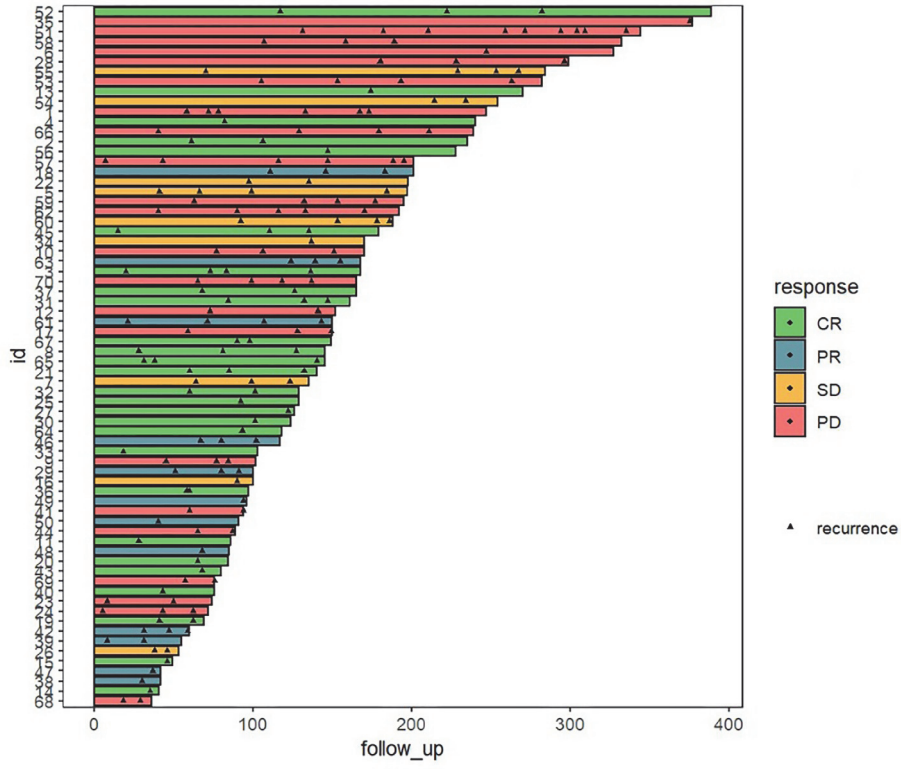
Introduction To describe the clinicopathological characteristics of recurrent adult granulosa cell tumor (AGCT) and identify the risk factors for recurrence.

Methods Seventy recurrent AGCT patients between 2000–2020 were retrospectively reviewed (figure 1). The primary outcomes were progression free survival after first recurrence (PFS-R), overall survival after first recurrence (OS-R) and recurrence frequency. The Kaplan-Meier (KM) analysis, Cox proportional hazard analysis, and the Prentice, Williams and Peterson counting process (PWP-CP) model were adopted.

Results The 5-year PFS-R was 29.3%, and the 5-year OS-R was 94.9%. KM analysis demonstrated that patients with distant recurrence and PFS1 ≤60 months had worse PFS-R (P<0.05), and patients with PFS-R ≤ 33 months had worse

Abstract PR056/#32 Table 1 Univariate and multivariate analysis of PFS-R and OS-R

	PFS-R				OS-R			
	Univariate		Multivariate		Univariate		Multivariate	
	P	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)
Age⩽46	0.113	1.618 (0.893, 2.931)			0.145	0.405(0.120, 1.366)		
Operation approach (TA)	0.966	0.982 (0.415, 2.322)			0.205	0.353(0.071, 1.769)		
Adjuvant chemotherapy	0.636	0.866 (0.477, 1.572)			0.787	0.846(0.252, 2.838)		
Tumor size(⩽7.1cm)	0.339	0.740 (0.399, 1.371)			0.608	0.674(0.149, 3.045)		
Recurrence site(single)	0.079	0.551 (0.284, 1.071)			0.072	0.145(0.018, 1.186)	0.056	0.116 (0.013, 1.059)
Recurrence site(local)	0.018	0.466 (0.247, 0.876)	0.027	0.488(0.259, 0.922)	0.295	0.519(0.152, 1.773)		
R0 (first recurrence surgery)	0.179	0.642 (0.336, 1.226)			0.269	0.510(0.154, 1.684)		
PFS1⩽60 months	0.017	2.007 (1.130, 3.565)	0.028	1.911(1.073, 3.402)	0.079	3.446(0.868, 13.683)	0.258	2.222 (0.557, 8.862)
PFS-R⩽33months	-	-			0.023	5.156(1.249, 21.284)	0.028	5.505 (1.199, 25.259)



Abstract PR056/#32 Figure 1

OS-R (P=0.023). PFS1≤60 months (hazard ratio, HR 1.9, 95% confidence interval, CI, 1.1–3.4, P=0.028) was an independent risk factor for PFS-R, and local lesion at recurrence (HR 0.488, 95%CI 0.3–0.9, P=0.027) was an independent protective factor for PFS-R. PFS-R ≤33 months (HR 5.5, 95% CI 1.2–25.3, P=0.028) was an independent risk factor for OS-R (table 1). The PWP-CP analysis showed laparoscopic operation could significantly increase recurrence times (P=0.002, HR=3.4), and R0 at each recurrence operation could significantly decrease recurrence frequency (P < 0.001, HR < 0.001).

Conclusion/Implications The present study is the largest report of patients with recurrent AGCT. It demonstrated that PFS1 ≤60 months and distant lesion at recurrence are independent risk factors for PFS-R, and PFS-R ≤33 months is an independent risk factor for OS-R. The PWP-CP model showed that the transabdominal approach and surgery reaching R0 could significantly decrease recurrence frequency.

PR058/#188

MICRORNA-DEPENDENT INHIBITION OF WEE1 CONTROLS CANCER STEM-LIKE CHARACTERISTICS AND MALIGNANT BEHAVIOR IN OVARIAN CANCER

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Introduction Cancer stem-like cells (CSCs) are recognized to be responsible for chemoresistance and tumor recurrence owing to their self-renewal capacity and differentiation potential. Although WEE1 is a promising target for anticancer therapies, its function in ovarian CSCs remains unknown. We present evidence that WEE1 regulates CSC properties and tumor resistance to carboplatin through a microRNA-dependent mechanism.

Methods Plasmid DNA constructs were transfected into human ovarian cancer cell lines. RNA and protein were extracted from pathologically confirmed tumor tissues. The SKOV3 spheroid tumor model were developed. Immunofluorescence analyses were performed on the xenograft tumors. miR-424 and miR-503 were detected by quantitative real-time PCR and western blot analysis. Spheroid formation assay was performed to investigate the presence and self-renewal ability of CSCs.

Results We found that WEE1 expression is upregulated in ovarian cancer spheroids because of the decreased expression of miR-424 and miR-503, which directly target WEE1. The overexpression of miR-424/503 suppressed CSC activity by inhibiting WEE1 expression, but restoring WEE1 expression reversed this effect. Furthermore, we demonstrated that NANOG modulates the miR-424/503-WEE1 axis that regulates the properties of CSCs. We also demonstrated the pharmacological restoration of the NANOG-miR-424/503-WEE1 axis and attenuation of ovarian CSC characteristics in response to atorvastatin treatment. Lastly, miR-424/503- mediated WEE1 inhibition re-sensitized chemoresistant ovarian cancer cells to carboplatin. Additionally, combined treatment with atorvastatin and carboplatin synergistically reduced tumor growth, chemoresistance, and peritoneal seeding in the intraperitoneal mouse models of ovarian cancer.

Conclusion/Implications We identified a novel NANOG-miR-424/503-WEE1 pathway for regulating ovarian CSCs, which has potential therapeutic utility in ovarian cancer treatment.