Methods Thirty-five aGCTs were subjected to massively parallel sequencing targeting 468 cancer-related genes (7 primary aGCTs that did not recur >4 years, 9 primary and matched recurrent aGCTs, 10 recurrent aGCTs). These cases and additional 12 aGCTs (n=3, primary aGCTs that did not recur; n=9, recurrent aGCTs) were subjected to Sanger sequencing analysis of the *TERT* promoter.
Results All aGCTs included harbored the *FOXL2* p.C134W hotspot mutation. A significantly higher frequency of *TERT* promoter mutations was found in recurrent (64%) than in primary aGCTs (26%; p=0.017). Moreover, aGCT recurrences harbored a higher frequency of somatic *KMT2D* and *TP53* mutations (16%, each) than primary aGCTs with subsequent recurrences (11% and 0%) and primary aGCTs without subsequent recurrences (14% and 0%). We identified a higher frequency of *CDKN2A/B* homozygous deletions in recurrent (16%) than in primary aGCTs (6%), and other gene alterations restricted to recurrent aGCTs. Pathway analysis revealed that aGCTs are underpinned by genetic alterations affecting the cell cycle pathway. Clonal decomposition of matched primary and recurrent aGCTs showed that aGCTs display multiple clones at diagnosis and relapse.
Conclusions Our findings suggest that although *FOXL2* plays a crucial role in the tumorigenesis of aGCTs, recurrences might be associated with genetic alterations affecting *TERT*, cell cycle-related genes such as *TP53* and *CDKN2A/B*, and other cancer-related genes, including *KMT2D*, *TET2* and *EPHA5*.

IGCS19-0511

13 MUCINOUS OVARIAN CARCINOMA: THERAPEUTIC OPTIONS OLD AND NEW

[1]K Gorringe*, [1]D Cheasley, [2]M Wakefield, [1]I Campbell, [3]Y Antill, [4]C Scott, [1]G GAMuT Collaborators. *[1]Peter MacCallum Cancer Centre, Research Division, Melbourne, Australia; [2]Walter and Eliza Hall Institute, Bioinformatics, Melbourne, Australia; [3]Cabrini Health, Oncology, Melbourne, Australia; [4]Walter and Eliza Hall Institute, Stem Cells and Cancer Division, Melbourne, Australia*

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Objectives Mucinous ovarian carcinoma (MOC) is a rare ovarian cancer subtype that responds poorly to conventional chemotherapy. Recurrent and advanced disease have poor survival and there are no specific guidelines for their treatment. We used a large cohort of genomic and immunohistochemical data to evaluate the likelihood of success of possible therapeutic interventions.
Methods We used DNA sequencing data (n=185) and genome-wide copy number (n=199) from primary MOC to identify key genetic events, homologous recombination deficiency scores and mismatch repair deficiency. Immunohistochemistry data was obtained for CK7, CK20, PAX8, p16, CDX2, HER2 and ER (n=162–256) and tumour infiltrating lymphocytes were counted on H&E stained slides (n=40).
Results Therapies exploiting homologous recombination deficiency are unlikely to be effective in MOC, as only 1.5% had a homologous recombination deficiency score of more than 50. Mismatch repair deficiency was very rare (<1%). Most cases had low lymphocytes counts, corresponding to a moderate mutation load. Events that suggest an existing targeted therapy include: *ERBB2* amplification(26%), *ERBB3* mutation (4%) and *BRAF* mutation(9%). Novel agents currently in clinical trials targeting genetic events such as *TP53* missense mutation(46%), *RNF43* mutation(11%), *PIK3CA* mutation(8%) and *KRAS/NRAS* mutations(66%).
Conclusions MOC is genetically diverse but with a number of potential targets. Importantly, the clinically observed lack of response to cisplatin is supported by a corresponding lack of a genomic signature, and MOC are unlikely to respond to PARP inhibitors. The role of immunotherapy is unclear. Testing novel therapeutic options in appropriate patient-derived models will be crucial and we are currently developing organoid cultures from this disease.

Plenary 3

IGCS19-0583

14 THE LONG-TERM ONCOLOGIC OUTCOMES OF MINIMALLY INVASIVE SURGERY(ROBOT-ASSISTED/ LAPAROSCOPIC) VERSUS ABDOMINAL RADICAL HYSTERECTOMY FOR EARLY-STAGE CERVICAL CANCER PATIENTS TREATED BETWEEN 2000 AND 2017 AT THE OSLO UNIVERSITY HOSPITAL

[1]MB Sert*, [1]A Dørum, [1]G Kristensen, [2]B Davidson, [3,4]A Dahl. *[1]Oslo University Hospital- The Norwegian Radium Hospital, Gynecologic Oncology, Oslo, Norway; [2]Oslo University Hospital- The Norwegian Radium Hospital, Pathology, Oslo, Norway; [3]Oslo University Hospital- The Norwegian Radium Hospital, National Resource Center for late effects after cancer treatment, Oslo, Norway; [4]Institute of Clinical Medicine, University of Oslo, Oslo, Norway*

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Objectives To compare the long-term oncologic outcomes after minimally invasive surgery (robot assisted/laparoscopic radical hysterectomy) (MIS) versus abdominal radical hysterectomy (ARH) for early-stage cervical cancer (CC).
Methods This is a large single center retrospective study. From our institution´s patient registry, we identified a total of 587 early-stage cervical cancer patients who underwent either MIS or ARH between 2000 and 2017. We excluded the following patients from the final analysis: (1) received neo-adjuvant treatment prior to surgery; (2) had histologic types other than squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma; (3) were double primary cancer cases; (4) had stages higher than stageIB1 (FIGO 2009). We included only patients who underwent radical hysterectomy for early-stage cervical cancer and radical parametriectomy for stumph cancer patients in our study population.
Results In total, 230 and 357 patients were assigned to the MIS and ARH groups, retrospectively. There were no significant differences for any demographics including age, stage, histology. Five-year recurrence free survival was 88.6% (95% CI, 83.4%- 92.3%) and 93.5% (95% CI, 90,4%- 95.7%), (p=0.04) respectively in the MIS and ARH group, and the five-year cancer specific survival was 95.4% (95% CI, 90.9%- 97.7%) and 97.4% (95% CI, 95.1%- 98.7%), (p=0.12) in the MIS and ARH group, respectively. MIS group have more peritoneal-combined relapses comparing ARH (p=0.02). The relapse rate tended to be highest for squamous cell carcinoma in MIS group (p=0.09). Disease free survival and cancer specific survival were worse in the MIS group p- value= 0.04 and 0.12 respectively.