GCT-30 Surgical management of ovarian germ cell tumours

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Background: Surgical resection of advanced epithelial ovarian cancer aims for macroscopic nil residual disease (NR) which improves survival. However, in patients with advanced ovarian germ cell tumours, the extent of surgery is debated. The role of peritoneal and nodal staging is unclear.
Methods: Aim to determine optimal surgical management of ovarian germ cell tumours. Multicentre cohort study in four large UK cancer centres over 12 years.
Results: 138 patients, median follow-up 56.6 months. Overall survival: 93%, event-ree survival (EFS): 72%. Histological subtype powerfully predicted EFS (log-rank $p = 4.9 \times 10^{-7}$). Only 17/137(12%) surgical patients had peritoneal biopsies; 5/17(29%) upstaged. Only 23/137 (17%) had para-aortic/pelvic lymphadenectomy, 6/23(26%) upstaged. 37 dysgerminoma: mostly fertility-preserving operations including 2 patients >1 cm residual disease salvaged with BEP chemotherapy. By contrast, 2(stage 2 and 3c) had non-fertility-preserving surgery leaving NR had BEP. All 42 immature teratoma (IT) had surgery; 3/42 (7%) received neoadjuvant BEP; 6/42 (14%) received adjuvant BEP. None responded to chemotherapy. 3 IT patients relapsed – successfully treated with surgery only (including excision of brain metastases). The only survivor 1/4 PNET (at 2201 days) had radical surgery (resection left hemi-thorax/lung) with NR at time of relapse. 8/53 deaths in yolk sac tumours – no difference by surgery. In summary, peritoneal biopsies and para-aortic/pelvic lymphadenectomy should be considered if results could change management. Fertility-preserving surgery, even in advanced dysgerminoma, is reasonable. Surgical management alone for IT should be considered, in keeping with paediatric practice, even at relapse. Radical surgery should be considered in PNET. Yolk-sac tumour has a poor prognosis.

Debate

GCT-31 Debate: This house believes that there is no place for chemotherapy in the management of immature teratoma: Proposing view

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Background: Ovarian immature teratomas (IT) are rare and account for 1% of ovarian tumours. They are treated by paediatric and adult oncologists with very different treatment approaches. Standard of care for adult women is postoperative chemotherapy, except for FIGO stage IA, grade 1, whereas in children, surgery alone is recommended regardless of stage or grade. The question of chemotherapy or not remains unanswered and a randomized clinical trial is not feasible due to the rarity of ovarian IT. In this debate, we will address why we think there is no place for chemotherapy in management of ovarian IT.
Methods: A literature review was conducted to identify studies addressing the outcome of ovarian IT.
Results: A pooled analyses from the Malignant Germ Cell International Consortium (MaGIC), compared 2 adult and 2 paediatric clinical trial data. Ninety of the 98 paediatric patients were treated with surgery alone, whereas all 81 adults received postoperative chemotherapy. Despite difference in management, there were striking similarities in the results with 5-year EFS and OS of 91% and 99% for the paediatric cohort and 87% and 93% for the adult cohort [1]. A recent multicentre cohort study from the UK reported on 42 patients with ovarian IT (15 <18 years and 33 ≥18 years). Nine patients received chemotherapy (3 pre-operatively and 6 post-operatively) and 33 patients had surgery only. There was no difference in relapse between the groups. Interestingly, they found little evidence of radiological response in patients who received pre-operative chemotherapy [2].
Disclaimer: Please note that the views expressed in this abstract, and during the debate *per se*, may not necessarily reflect the views and beliefs of those individuals proposing and/or opposing the motion.

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GCT-32 Debate: This house believes that there is no place for chemotherapy in the management of immature teratoma: Opposing view

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Background: Ovarian germ cell tumours (OGCT) are rare tumours arising in young women. These tumours include several subtypes sharing in general good prognosis but sensitivity/dependency to chemotherapy can be variable.
Methods: Comprehensive literature review.
Results: The question of adjuvant chemotherapy in pure ovarian immature teratoma (IT) remains unsolved to date and illustrates differences in management between paediatric and adult oncologists. Because of the rarity of IT, this question has never been addressed through randomised trials. Standard of care for adult women with ovarian IT is postoperative platinum-based chemotherapy for all patients except FIGO stage IA, grade 1 tumours, whereas paediatric series concluded that surgery alone is curative for completely resected ovarian IT, regardless of grade. Moreover, the role of chemotherapy in incompletely resected tumours and its impact on the rate of relapse needs to be better assessed. Chemosensitivity of IT is a matter of debate. The development of a prognostic score may help to make appropriate risk-based decisions about therapy in this disease, in order to increase

the cure rate in patients with a poor prognosis and to decrease toxicity in patients with a low risk of relapse. A trend is emerging to avoid chemotherapy in totally resected (of any grade) and grade 1 (any stage) ovarian IT. For grade 2 and 3 incompletely resected ITs, the ideal strategy remains controversial; adjuvant chemotherapy remains the recommendation in current international guidelines. This emphasizes the urgent need for cooperation between adult and paediatric teams.
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Stage I and Good-Risk Tumour Patients – Rationale for Reducing Therapy

GCT-33 Rational trial design for stage I nonseminomatous germ cell tumour (NSGCT) patients

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Background: Prognosis of adult stage 1 germ cell tumours (GCTs) is excellent with expected survival rates approaching 100%. Despite this, controversy exists over optimal treatment strategies with the focus on minimising treatment burden and treatment toxicity. As such, 'classic' clinical trial designs such as randomised trials based on survival or progression free survival may not address these issues. This presentation will discuss recent stage 1 trial designs [1].
Methods: The UK have recently completed two stage 1 GCT trials ('111' and TRISST) based on novel trial designs which will inform future rational trial design.
Results: The single-arm phase III '111' trial (245 patients) [2] assessed efficacy of single-cycle adjuvant BEP chemotherapy in stage 1 NSGCT at high-risk of relapse. It excluded >5% recurrence rate, as robust data from 2 BEP cycles showed recurrence rate of <2% and pre-trial consensus was that recurrence ≤5% would be acceptable. A formal randomised trial would have require >800 patients and not been feasible. The trial demonstated 2-year recurrence rate of 1.3% with upper confidence limits less than 5%. The TRISST trial [3] examined role of MRI and follow-up intensity for stage 1 seminoma and used the stage at recurrence as primary endpoint, aiming to exclude a defined increase in the development of stage IIC disease. PROVINCE is in trial development and will test a novel prognostic index integrating the CXCL12 biomarker. In summary, when survival is excellent, clinically relevant questions need novel/imaginative clinical trial design.

References

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GCT-34 Rational treatment reductions for good-risk metastatic seminoma patients

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Background: Metastatic seminoma is very treatable – rapid durable responses to chemotherapy are consistently reported. For metastatic, high-volume disease, therapy with combination chemotherapy (cisplatin and etoposide with/without bleomycin) should be used. For lower-volume disease (clinical stage 2A/2B), either chemotherapy or radiotherapy with/without limited chemotherapy are acceptable. Historically, a number of randomised trials have compared combination chemotherapy to single agent carboplatin but increased relapse rates were seen and such therapy discarded.
Methods: Studies of escalated doses of carboplatin monotherapy (area-under-the-curve – AUC-10) given every 3 weeks were explored in metastatic IGCCC good-risk patients.
Results: AUC 10 carboplatin monotherapy is feasible with similar outcomes to combination chemotherapy in such patients. Anaemia and thrombocytopenia appeared more commonly whilst other side effects were less. Developing strategies to test this as a replacement for combination treatment will rely on patient-reported-outcome-measures (PROMs) – in particular, many trials have underestimated the risk of long-term oto- and neuro-toxicity, as well as quality-of-life reduction during therapy. For low-volume disease, particularly clinical stage 2A – further reduction in treatment intensity with the use of primary retroperitoneal lymph-node dissection with additional limited chemotherapy may be possible. The presence of residual masses post-therapy has always created a problem with follow-up: PET-CT has a limited role in assessing the likelihood of cancer – but alternatives, such as monitoring of circulating microRNA, may prove more attractive. Dysgerminoma – the ovarian equivalent of seminoma – lends itself to the same potential opportunities and should be included in any attempts at treatment de-escalation.

GCT-35 Clinicopathologic predictors of outcomes in children with stage I germ cell tumours: A pooled *post hoc* analysis of trials from the Children's Oncology Group

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Background: Patients with clinical stage I (CS I: cN0M0) germ cell tumours (GCT) exhibit favourable oncological outcomes. While prognostic features can help inform treatment in adults with CS I GCT, we lack reliable means to predict relapse among paediatric patients. We sought to identify predictors of relapse in children with CS I GCT.