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.
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.

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.

Methods: We performed a pooled *post hoc* analysis on paediatric CS I GCT patients enrolled in 3 prospective trials: INT-0097 (phase II), INT-0106 (phase III), and AGCT0132 (phase III). Pathology was centrally reviewed. Patient demographics, pT stage, serum tumour markers, margin status, histology, relapse, and survival were compiled. Cox regression analyses were used to identify predictors of outcomes.
Results: 88 patients were identified with histological data available. Most patients were pT1-2 stage. Yolk-sac tumour was present in 75%, while 16% had embryonal carcinoma and 9% had choriocarcinoma. When evaluable, lymphovascular invasion (LVI) was present in 36/66 (55%) of patients. Over a median follow-up of 5.0 years, no patients died and 24 patients (27%) relapsed (median relapse-free survival not reached). Predictors of relapse included presence of choriocarcinoma (HR 4.3, p = 0.004), embryonal carcinoma (HR 3.8, p = 0.002), pT3 stage (HR 6.9, p = 0.027), and age ≥12 years (HR 3.1, p = 0.011). LVI (HR 2.4, p = 0.072), serum tumour markers, and dominant tumour size did not reach significance. Paediatric CS I GCT patients exhibit remarkable 5-year survival. Using combined data from multiple prospective trials, our study identifies clinicopathological features that predict relapse and potentially inform personalized treatment for these patients.

GCT-36 Carboplatin AUC10 monotherapy for metastatic seminoma – an updated multicentre review of outcomes in 216 patients

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Background: The standard-of-care for good prognosis metastatic seminoma includes radiotherapy in stage 2 disease, and in more advanced disease combination cisplatin-based chemotherapy. Long-term and short-term morbidity of cisplatin-based chemotherapy for young men with germ-cell-tumours is increasingly recognised and alternate strategies have been sought to retain cure rate and improve on toxicity and burden of treatment. Previous reports of Carboplatin AUC10 have explored safety and deliverability in early-phase studies. This current study reports on the outcomes of 216 patients treated at two UK referral centres utilising single-agent carboplatin AUC10.
Methods: We performed a retrospective analysis of patients treated for IGCCCG good prognosis metastatic seminoma with carboplatin AUC10 monotherapy in St Bartholomew's Hospital and Mount Vernon Hospital, London. We identified 216 cases. Patient characteristics and outcomes were reviewed.
Results: In the 216 treated patients, the median follow up is 56 months. 75 patients had stage IIa disease and 141 had stage 2b and above including 3 mediastinal seminomas. The 2-year progression-free survival is 96.5% with a 3-year overall survival rate of 99.3%. The disease-specific survival at 3-years is 100%. Seven cancer relapses occurred and 3 deaths from unrelated diseases. In univariate analysis, age >38 y was significant (p = 0.032) as a predictor for relapse. Of the 7 relapses, 5 were salvaged with further chemotherapy ± surgery and remain progression-free. Carboplatin AUC10 in this large cohort has a low-risk of failure, and the efficacy observed is comparable to results seen with established combination chemotherapy regimens.

GCT-37 The effect of lowering haematological cut-offs for treatment and blood product support on the deliverability of carboplatin AUC10 in metastatic seminoma

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Background: The standard-of-care for good prognosis metastatic seminoma includes radiotherapy in stage 2 disease, and combination cisplatin-based chemotherapy in more advanced disease. Long and short-term morbidity of cisplatin-based chemotherapy for young men with germ cell tumours is increasingly recognised and alternate strategies have been sought to retain cure rate and reduce toxicity. Previously reported studies of carboplatin AUC10 monotherapy have described its efficacy [1]. This study reports on the toxicity and deliverability of this regimen.
Material and methods: We performed a retrospective analysis of patients treated for IGCCCG good prognosis metastatic seminoma in St Bartholomew's Hospital, London, UK in the last 2 years (since our protocol changed to allow treatment if platelets >75 and neutrophils >0.5). We identified 33 patients who received a total of 105 cycles of carboplatin AUC10 and analysed toxicity data including need for blood product support. Cut-offs for blood product support were platelet <10 and haemoglobin <70 (lower than previous cut-offs).
Preliminary results: There was one admission for febrile neutropenia and one admission for non-neutropenic fevers; 3% of patients were admitted for neutropenic fever throughout treatment. A total of 8 transfusions of blood products (3 red cells and 5 platelets) were required; 6 of 33 patients (18%) required blood products. 16 cycles (15%) were delayed by >48 hours to enable haematological recovery. There were no treatment-related deaths. In summary, carboplatin monotherapy is associated with low rates of neutropenic fever compared to cisplatin-based chemotherapy, and new treatment cut-offs have reduced delays [1].

Reference

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GCT-38 Which germinomas/dysgerminomas should be treated with chemotherapy? Is any patient high-risk?

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Background: Germinomas are considered good responders to chemotherapy. The majority of protocols in the literature stratify patients according to risk group to treat as low-, intermediate- or high-risk.
Methods: Our First Brazilian National Protocol started in 1991 and 3 different protocols were proposed after that. The last patient from the