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

[1] Shamash J. *et al.* A phase II study of carboplatin AUC-10 guided by positron emission tomography–defined metabolic response in metastatic seminoma. *European Journal of Cancer*. July 2019; 115: 128–135.

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

3rd (GCT-2008 protocol) was admitted 18 months ago. No patients with CNS as primary site of GCT disease were included.
Results: From 120 patients with pure germinoma component, 109 were female, 9 testicular, 107 ovarian, 1 sacrococcygeal, 2 mediastinal and 1 retroperitoneal. Increased AFP was seen in 10 of 83 patients with this information, BHCG 33/88, LDH 46/76. For the entire group 10 y OS was 94.8%. According with staging 47 Stage (S)-I, 18 S-II, 46 S-III, 9 S-IV (10 y OS with no statistical significance). Ovarian cases were 107, 42 S-I, 17 S-II, 41 S-III and 7 S-IV. Non-metastatic 81 (10 y OS 96.2%), 20 lymph node metastases (94.7%) and 6 other (liver, lung or both; 10 y OS 100%). S-I+II were 59 patients (10 y OS 96.5%) and 48 S-III+IV (95.7%). No statistical significance was found for age (< or > 11 years), increased LDH, alpha-fetoprotein or BHCG. Our data suggests that no patient should be treated as high-risk. Complementary analysis should be done among S-II and S-III to define which patients should receive chemotherapy and which should be classified as low-risk and receive no chemotherapy.

Clinical Trials and Updates II

GCT-39 Outcome of children with malignant germ cell tumours by response status at the end of induction chemotherapy

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Background: The management of paediatric malignant germ-cell-tumours (MGCTs) includes induction therapy with 3–4 cycles cisplatin/etoposide/bleomycin (PEb). The current practice recommends 2–3 cycles of PEb (total 6 cycles) as consolidation therapy if response is not complete at end-of-induction (EOI), different to that used in adult patients who receive a standard number of cycles. No evidence exists supporting a PEb consolidation phase in paediatric MGCT patients.
Methods: We retrospectively reviewed all patients enrolled in a phase III, single-arm trial for low-risk and intermediate-risk MGCTs (AGCT0132). All patients received 3 PEb cycles and underwent response assessment at EOI. Complete response (CR) was defined as negative tumour-markers and no viable residual lesion. Patients in CR received no further chemotherapy. Patients not in CR received 3 additional PEb cycles as consolidation. Event-free survival (EFS) and overall survival (OS) was calculated using Kaplan-Meier method.
Results: Among 210 patients enrolled, 193 patients had CR at EOI, and their post-induction 4 yr-EFS and OS was 93% and 99%. Fifteen patients were not in CR at EOI and received additional chemotherapy; their 4 yr-EFS and OS was 51% and 60%, respectively. Children with MGCTs with partial response after EOI had inferior outcomes despite additional cycles of PEb chemotherapy. Consolidation is therefore of unclear benefit. Although our results are limited by small sample size and lack of comparator, we propose that paediatric MGCT patients who fail to achieve a CR after standard induction chemotherapy should receive a salvage regimen with different agents rather than consolidation with more cycles of the same chemotherapy.

GCT-40 Alpha-fetoprotein (AFP) as a predictor of outcome for children with germ cell tumours: A report from the Malignant Germ Cell International Consortium (MaGIC)

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Background: Several studies describe the correlation between unsatisfactory tumour marker decline and poor prognosis in adult patients treated for germ-cell-tumours (GCTs). In paediatric patients data is limited. We retrospectively analyzed data collected from paediatric patients treated on Children's Oncology Group (COG) Protocol AGCT0132 to determine whether a relationship exists between AFP decline and outcome.
Methods: One hundred and thirty-one patients with GCTs enrolled on Children's Oncology Group Protocol AGCT0132 were eligible for analysis of AFP decline. Serum AFP half-life was calculated from levels collected post-operatively, as a baseline, and after the start of chemotherapy, excluding values in the first 7 days of chemotherapy to accommodate unpredictable increases in the initial days of treatment. AFP decline was defined as automatically satisfactory (AFP normalized within the first two AFP measures following the start of chemotherapy), calculated satisfactory (AFP half-life $\leq$7 days following the start of chemotherapy), and unsatisfactory.
Results: The 3-year cumulative incidence of relapse (CI-R) was 11% (95% confidence interval - CI: 6.0–18%) for patients with satisfactory decline and 38% (95% CI: 13–64%) for unsatisfactory decline ($p = 0.006$). In stratified analyses, this effect was limited to patients $\geq$11 y and standard-risk (SR2) disease ($p = 0.004$ and $p = 0.007$, respectively). Three-year overall-survival for patients with satisfactory versus unsatisfactory decline was not statistically significant. This study is the first to show association between AFP decline and CI-R in paediatric patients. Although no association between marker decline and outcome was shown, recognition of patients at high-risk of relapse may allow early therapy intensification and impact future clinical trial design.

GCT-41 Outcomes of the use of carboplatin in the treatment of paediatric malignant germ cell tumours (GCTs) in the UK – Experience from GCII and GCIII trials

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