age was 9.3 years (1.8–19.9 years). Most patients had an extragonadal tumour (63.6%) and yolk-sac was the main histological subtype (48.5%). About 60% were metastatic at diagnosis. Regarding the pre-HSCT disease status: 4 patients were in first remission, 12 in second remission, 8 in third remission or beyond and 9 had refractory disease. The main conditioning regimen was with Carboplatin, Etoposide and Melphalan (72.7%). Three patients died from transplant-related complications (9%). Fifteen patients (45.5%) had disease progression or relapse after HSCT and 14 of them died. Fifteen patients (45.5%) are alive in complete remission, with a median follow up of 4.9 years (1.1–17.4 years). None of the 9 patients who had refractory disease at the beginning of the conditioning regimen survived. The role of HSCT in the treatment of children with GCTs should be investigated in prospective trials.

Poor-Risk Tumour Patients

GCT-67 Long term follow-up of the MRC TE23 randomized phase II trial of intensive induction chemotherapy (CBOP/BEP) in poor prognosis germ cell tumours (GCT) (CRUK/05/014; ISRCTN53643604)

R.A. Huddart[1], F. Cafferty[2], J.D. White[3], J. Shamash[4], I. Hennig[5], M.H. Cullen[6], S.P. Stenning[2], for the TE23 Trial Management Group and Collaborators and the NCRI Testis Cancer Clinical Studies Group
[1]The Institute of Cancer Research and the Royal Marsden NHS Foundation Trust, Sutton, UK; [2]MRC Clinical Trials Unit at UCL, London, UK; [3]Beatson West of Scotland Cancer Centre, Glasgow, UK; [4]St Bartholomew's Hospital, London, UK; [5]Nottingham University Hospitals NHS Trust, Nottingham, UK; [6]University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

Background: Up to 50% of men with poor-prognosis nonseminomatous GCT die with standard BEP chemotherapy. An intensive regimen, CBOP/BEP (carboplatin, bleomycin, vincristine, cisplatin/BEP), met response targets in a phase II, multicentre, open-label, randomized trial. Here, we report long term outcomes and prognostic factors.
Methods: Patients with extracranial GCT and IGCCCG poor-prognosis features were randomised to 4xBEP or CBOP/BEP (2xCBOP, 2xBO, 3xBEP with bleomycin dose 15,000 iu). Low-dose, stabilising chemotherapy prior to entry was permitted. This analysis focuses on progression-free survival (PFS), overall survival (OS) and toxicity (all secondary outcomes), and exploratory analysis of prognostic factors and the impact of marker decline (as defined in GETUG13).
Results: 89 patients (43 CBOP/BEP) were randomised. After median 63 months follow-up, 3-year PFS is 55.7% (95% CI 39.7%, 69.0%) for CBOP/BEP arm, 38.7% (24.7%, 52.4%) for BEP (HR 0.59 (0.33, 1.06), $p = 0.079$). 3-year OS is 65.0% (48.8%, 77.2%) and 58.5% (43.0%, 71.2%), respectively (HR 0.79 (0.41, 1.52), $p = 0.49$). 12-month toxicity was affected by subsequent treatments, with no clear differences between arms. There was no grade ≥3 late toxicity in the CBOP/BEP arm. In multivariate models, use of pre-protocol chemotherapy was the only factor associated with poorer PFS (HR 2.09 (1.14, 3.81), $p = 0.017$). Mediastinal primary (HR 2.13 (1.02, 4.46), $p = 0.045$) and use of pre-protocol chemotherapy (HR 3.40 (1.74, 6.63), $p < 0.001$) were associated with poorer OS. In this study, use of low dose induction chemotherapy was associated with poorer outcomes. Further study in an international phase III trial is warranted.

GCT-68 Haematological neoplasms arising in patients with primary mediastinal nonseminomatous germ cell tumour are clonally related and represent secondary somatic malignant differentiation

J. Taylor[1], M. Donoghue[2], B.S. Taylor[2], O. Abdel-Wahab[1], D.R. Feldman[3]
[1]Leukemia Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, USA; [2]Center for Molecular Oncology, Memorial Sloan Kettering Cancer Center, New York, USA; [3]Genitourinary Oncology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, USA

Background: One in 17 patients with primary mediastinal germ cell tumour develops a haematological malignancy and the survival in such patients is poor. Intriguingly, the presence of isochromosome 12p, a clonal marker common to GCTs but absent in *de novo* myeloid neoplasms, has been demonstrated as shared across GCTs and myeloid neoplasms in such individuals. While these data suggest a clonal relationship between the two, the exact nature of the shared origin is unknown.
Methods: To trace the clonal evolution of these seemingly unrelated cancer types and identify recurrent genomic lesions in leukaemias present in GCT patients, we applied whole exome sequencing (WES), targeted genomic analyses, and/or RNA-seq to leukaemias, GCTs, and germline DNA in a series of patients with myeloid neoplasms and concurrent GCTs.
Results: We studied 12 patients with GCT and synchronously or metachronously occurring myeloid neoplasms (8 AML, 5 MDS/CMML, 2 histiocytic sarcoma (some had >1 haematologic malignancy)) with an average of 4 months between the two diagnoses. All were young men (median age 26 years) with PMGCT and nonseminomatous histology and a 3-month median survival from leukaemia diagnosis. In each case, at least one copy number alteration or coding mutation was shared across the GCT and hematopoietic neoplasm, demonstrating the shared origin of both lesions. The most common genomic alterations in leukaemias beyond i(12p) included mutations activating RAS-PI3K-AKT signalling or inactivating TP53. These data conclusively demonstrate that myeloid neoplasms developing in patients with PMGCT represent secondary somatic differentiation of cells that are present in the GCT.

Debate

GCT-69 Debate: This house believes that BEP should no longer be standard therapy for poor risk disease: Opposing view

C.J. Sweeney[1], D. Mazhar[2]
[1]Department of Medicine, Dana Farber Cancer Institute, Harvard Medical School, Boston, US; [2]Department of Oncology, Cambridge University Hospitals NHS Trust, Cambridge, UK

Background: Since the addition of etoposide and cisplatin to bleomycin in the 1980s, the BEP regimen has been the international standard for poor risk germ cell tumour (GCT). In this debate, we review the relevant data and detail the phase 3 trials that have failed against BEP. We also outline the strategies that have been more successful than changing current cytotoxic options in poor risk GCT,