GCT-07 Moving to a digital pathology supraregional germ cell tumour service

L. Browning[1,2], R. Colling[1,3], K. White[1], J. Rittscher[2,4], D. Roskell[1], H. Hemsworth[1], M. Soares[1], I.S.D. Roberts[1], D. Royston[1,5], G. Rees[1], G. Turner[1], E. Fryer[1], S. Roberts-Gant[1], D. Siiankoski[1], R.J. Bryant[3], A. Molyneux[6], A. Taibi[7], E. Johnson[6], A. Protheroe[8], M. Tuthill[8], M. Sullivan[9], C. Verrill[1,2,3,10]
[1]Department of Cellular Pathology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [2]Oxford NIHR Biomedical Research Centre, University of Oxford, Oxford, UK; [3]Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK; [4]Big Data Institute, University of Oxford, Oxford, UK; [5]Nuffield Department of Clinical and Laboratory Sciences, University of Oxford, Oxford, UK; [6]Department of Cellular Pathology, Milton Keynes University Hospital, Milton Keynes, UK; [7]Department of Cellular Pathology, Great Western Hospitals, Swindon, UK; [8]Department of Oncology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [9]Department of Surgery, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [10]Principal Investigator, Oxford PathLAKE

Background: Patients with testicular cancer in the UK are managed in supraregional networks serving a population of 2–4 million, seeing at least 100 new patients/year. Patient management includes the review of diagnostic glass slides from local sites for the supraregional MDT via postage of the original slides. The infrastructure to undertake this via a digital pathology platform was established across part of the Thames Valley network.
Methods: Philips slide scanners were deployed in 2018 (2 at Oxford (supraregional centre), 1 Milton Keynes and 1 Great Western Hospital Swindon). The service was evaluated as a traditional glass-slide based service in preparation for the switch to digital pathology.
Results: To calculate slide volumes, two specialist germ cell tumour pathologists reviewed 57 cases on glass slides from 6 centres (benign and malignant). The number of slides ranged from 3–75/case and mean reporting time was 18 minutes/case (range 7–49). Pathologists in Oxford validated digital reporting by creating a retrospective validation set. In March 2019, prospective validation and live digital reporting began with check of the glass slides before final pathology sign out. IT connectivity between image management systems in Oxford and Swindon was established in May 2019 such that cases scanned in Swindon could be viewed over the portal from Oxford. Digitising supraregional germ cell tumour services is feasible and brings potential benefits of efficiency, quality and libraries of images to build and test AI algorithms which may in the future support pathologists or generate new insights into tumour biology.

GCT-08 Ovarian and testicular malignant teratomas: A comparative pathological analysis

A.A. Hadjiconstanti[1], B.M.R. Mathew[1], C.A. Freeman[2], D.R. Arora[2], E.M. Lockley[1,3]
[1]Barts Cancer Institute, Queen Mary University of London, London, United Kingdom; [2]Department of Cellular Pathology, University College Hospital, London, United Kingdom; [3]Department of Oncology, University College Hospital, London, United Kingdom

Background: Malignant teratomas are a pathological germ cell tumour subtype. Ovarian teratomas are characterised by immature embryonic material which is graded for prognosis. In testicular teratomas, lymphovascular invasion (LVSI) rather than grade determines prognosis and the presence of in-situ lesions, also unique to testes, determines classification. Guidelines recommend BEP chemotherapy for women whereas testicular teratomas are considered chemoresistant and treated surgically. We are investigating whether the morphology of male and female teratomas explains these marked disparities.
Methods: Ovarian and testicular malignant teratomas diagnosed at UCLH from 2007–2019 were identified. Pathological reports were reviewed and morphological examination for grade, in-situ lesions and LVSI is ongoing. Immunohistochemistry for mismatch repair proteins, PDL-1, p53, CD4, CD8, as possible therapeutic targets, will be conducted on tissue microarray.
Results: 15 ovarian (median age 20; range 11–36) and 22 testicular (median age 29; range 14–42) malignant teratomas were identified. Review of pathological reports showed that all testicular cases were mixed germ cell tumours with only 4 containing immature elements, whilst all ovarian cases were pure immature teratomas. Ovarian cases were Grade 1: 46.6%, Grade 2: 40% and Grade 3: 13.3%. Grade was not assigned in any testicular tumours. In-situ lesions were identified in 20/22(90%) testicular tumours but were not reported in ovarian cases.54% of testicular cases were pT1, whilst 33% ovarian teratomas had metastasised, most commonly to the pelvic peritoneum.

Clinical Trials and Updates I

GCT-09 111-A single arm, phase 3 trial evaluating one cycle of BEP as adjuvant chemotherapy in high-risk, stage 1 non-seminomatous or combined germ cell tumours of the testis (NSGCTT)

M. Cullen[1], R. Huddart[2,3], J. Joffe[4], D. Gardiner[5], L. Maynard[5], P. Hutton[1], D. Mazhar[6], J. Shamash[7], M. Wheater[8], J. White[9], A. Goubar[5], N. Porta[5], S. Witts[5], R. Lewis[5], E. Hall[5], on behalf of the 111 Trial Management Group
[1]University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; [2]The Institute Of Cancer Research, London, UK; [3]The Royal Marsden NHS Foundation Trust, London, UK; [4]The Leeds Teaching Hospitals NHS Trust, Leeds, UK; [5]Clinical Trials and Statistics Unit at The Institute of Cancer Research, London, UK; [6]Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; [7]Barts Health NHS Trust, London, UK; [8]University Hospital Southampton NHS Foundation Trust, Southampton, UK; [9]Beatson West of Scotland Cancer Centre, NHS Greater Glasgow and Clyde, Glasgow, UK

Background: Standard adjuvant treatment in the UK for high-risk stage one non-seminomatous germ cell tumours of the testis (NSGCTT) is two cycles of bleomycin, etoposide (360 mg/m^2) and cisplatin ($BE_{360}P$) chemotherapy. The 111 trial investigates whether one cycle of $BE_{500}P$ achieves similar recurrence rates.
Methods: 246 patients with vascular invasion positive, stage one NSGCTT or combined seminoma+NSGCTT were centrally registered in a single arm prospective study. Intervention: One cycle of bleomycin 30000 IU d1,8,15, etoposide 165 mg/m^2 d1-3 and cisplatin 50 mg/m^2 d1-2, plus antibacterial and GCSF prophylaxis. Outcome measurements and statistical analysis: The primary endpoint was two-year malignant recurrence, aiming to exclude a rate of 5% or greater. Participants had regular imaging and tumour marker assessment for five years.
Results: Median follow-up is 49 months (IQR 37–60). Ten patients had rising tumour markers at baseline and were excluded. Four patients had malignant recurrences at 6, 7, 13, and 27 months; all received second line chemotherapy and surgery; three remain recurrence-free at five years. Two-year recurrence rate was 1.3% (95% CI: 0.3–3.7%). Three additional patients developed non-malignant recurrences with teratoma differentiated in retroperitoneal nodes, rendered disease-free post-surgery. Grade 3–4 adverse events occurred in 41% participants (neutropenia 32%, febrile neutropenia 7%). $BE_{500}P$ is safe and the two-year recurrence rate is consistent with that seen following

two $BE_{360}P$ cycles. 111 is the largest prospective trial investigating adjuvant $BE_{500}P$ x1 in high-risk stage one NSGCTT. The adoption of $BE_{500}P$ x1 as standard would reduce overall exposure to chemotherapy in this young population.

GCT-10 Outcomes of adolescent males with extracranial metastatic germ cell tumours compared with children and young adults: A report from the Malignant Germ Cell Tumour International Consortium (MaGIC) group

F. Shaikh[1], D. Stark[2], H. Dang[3], C. Xia[3], M. Krailo[3], S. Stenning[4], F. Pashankar[5], C. Rodriguez-Galindo[6], T. Olson[7], S. Depani[8], S. Stoneham[9], J. Nicholson[10], M. Murray[10], J. Amatruda[11], D. Billmire[12], A. Fonseca[1], A. Lindsay Frazier[13]
[1]The Hospital for Sick Children, University of Toronto; [2]Leeds Institute of Cancer and Pathology; [3]Children's Oncology Group; [4]Medical Research Council Clinical Trials Unit at University College London; [5]Yale Cancer Center; [6]St Jude's Children's Cancer Hospital; [7]Aflac Cancer Centre, Children's Healthcare of Atlanta, Emory University; [8]University of Birmingham; [9]Children's and Young Persons Cancer Services, University College London Hospital Trusts; [10]Cambridge University Hospitals NHS Foundation Trust; [11]University of Texas Southwestern Medical Center and Children's Medical Center Dallas; [12]Riley Hospital for Children; [13]Dana-Farber Cancer Institute

Background: Adolescents with extracranial malignant germ cell tumours (GCTs) are often treated on the same regimens developed for children, but more closely resemble the clinical characteristics of young adult patients. We sought to determine whether event-free survival (EFS) for adolescents with GCTs was more like that of children or young adults.
Methods: We assembled an individual patient database of eleven GCT trials: eight conducted by paediatric cooperative groups and three by an adult group. We selected male patients aged 0–30 years treated with platinum-based chemotherapy for metastatic, nonseminomatous malignant GCTs of the testis, retroperitoneum, or mediastinum. We categorized age-group as children (0 to <11 years), adolescents (11 to <18 years), or young adults (18 to <30 years). We compared EFS and adjusted for calculated IGCCCG risk-group using Cox proportional hazards analysis.
Results: 593 patients met inclusion criteria, of whom 90 were children, 109 were adolescents, and 394 were young adults. The 5-year EFS for adolescents (72%; CI = 62–79%) was significantly lower than for children (90%; CI = 81–95%, p = 0.003) or young adults (88%; CI = 84–91%, p < 0.001). Risk-group was significantly associated with EFS in the adolescent age-group (p = 0.002). In a Cox multivariable analysis, the difference between adolescents and children remained significant (HR = 0.30, p = 0.001), but the difference between adolescents and young adults did not (HR 0.66, p = 0.114). EFS for adolescent patients with extracranial metastatic GCTs was similar to young adults but significantly worse than children. This finding may have important implications for how adolescent patients are treated.

GCT-11 Site of extranodal metastasis impacts survival in patients with testicular germ cell tumours

N. Singla MD[1,*], H.D. Patel MD, MPH[2,*], R.A. Ghandour MD[1], Y. Freifeld MD[1], S.L. Woldu MD[1], P.M. Pierorazio MD[2], A. Bagrodia MD[1]
[1]Department of Urology, University of Texas Southwestern, Dallas, TX, USA; [2]The James Buchanan Brady Urological Institute and Department of Urology, Johns Hopkins University School of Medicine, Baltimore, MD, USA
*Co-First Authors

Background: We systematically evaluated the impact of the location and burden of extranodal testicular germ cell tumour (TGCT) metastases on survival using a large, nationally representative population-based cancer registry.
Methods: Men with stage III TGCT captured by the Surveillance, Epidemiology, and End Results registry from 2010–2015 with distant extranodal metastases were identified. Clinicopathological information were collected, and patients were subdivided based on specific organ site(s) of metastatic involvement (lung, liver, bone, and/or brain). Kaplan–Meier analysis and multivariable Cox regression were used to evaluate cancer-specific survival (CSS), and model performance was assessed using Harrell's C-statistic.
Results: 969 patients with stage III TGCT were included, with predominantly nonseminomatous histology (84%). Most patients (91%) had pulmonary metastases, while 20%, 10%, and 10% had liver, bone, and brain metastases, respectively. Over a median follow-up of 21 months, 19% of men died of TGCT. When grouped by primary site of metastasis, patients with more than one extrapulmonary metastasis exhibited the worst CSS (HR 4.27 (95% CI 2.60–7.00), vs. isolated pulmonary involvement, p < 0.01). Among patients with isolated extrapulmonary involvement, those with brain metastases had the poorest survival (HR 3.24 (95% CI 1.98–5.28), p < 0.01), followed by liver (HR 2.29 (95% CI 1.56–3.35), p < 0.01) and bone (HR 1.97 (95% CI 1.11–3.50), p = 0.02). Multivariable Harrell's C-statistic was 0.71. Site of metastatic involvement impacts survival outcomes in patients with TGCT, which may reflect both the aggressive biology and challenging treatment of these tumours. Further incorporation of organotropism into current prognostic models for metastatic TGCT warrants attention.

GCT-12 Pattern of events in children, adolescents and young adults with testicular germ cell tumour (TGCT): The MAKEI-experience

M. Heimbrodt[1], P. Hillebrand[1], S. Schönberger[1], D.T. Schneider[2], C. Teske[1], I. Leuschner[3], C. Vokuhl[3], D. Harms[3], U. Göbel[4], G. Calaminus[1]
[1]Department of Paediatric Hematology and Oncology, University of Bonn, Bonn, Germany; [2]Clinic of Paediatrics, Municipal Hospital, Dortmund, Germany; [3]Paediatric Tumour Registry, Dept. of Paediatric Pathology, University of Kiel, Kiel, Germany; [4]Coordination Center for Clinical Studies, ESPED Surveillance Unit, University Düsseldorf Germany

Supported by the German Cancer Aid and the Barbara and Hubertus Trettner foundation.

Background: TGCT comprise children, adolescents and young adults. Outcome is excellent in young boys, whereas in adolescents this is dependent on stage and tumour composition.
Methods: Between 1st January 1996 and 31st of March 2017, 1895 patients with GCT were treated according to consecutive MAKEI protocols. 375 patients had TGCT: 89 teratoma, Lugano stage I, 286 malignant GCT who presented with stage Lugano I: 154, Lugano II: 102 and Lugano III: 30.
Results: In teratoma patients no events occured. In 286 malignant TGCT, 28 events occured. 8/28 died of disease (DOD) at first treatment. 7/8 who died had choriocarcinoma (CHC). The other events were: 18 relapses, one progression, one second malignancy. 16/18 relapsed were adolescents. 16/18 patients had mixed malignant histologies at primary diagnosis. Events in Lugano I were one secondary tumour and 4 relapses, 2 after watch and wait and 2 after platinum-based chemotherapy. All of them could by salvaged by additional platinum-based chemotherapy. In Lugano II/III, all patients received platinum-based chemotherapy at initial treatment. In Lugano II, 11 events were reported, two DOD in first therapy and 9 relapses. 8 of them could be salvaged by surgery, platinum-based or another