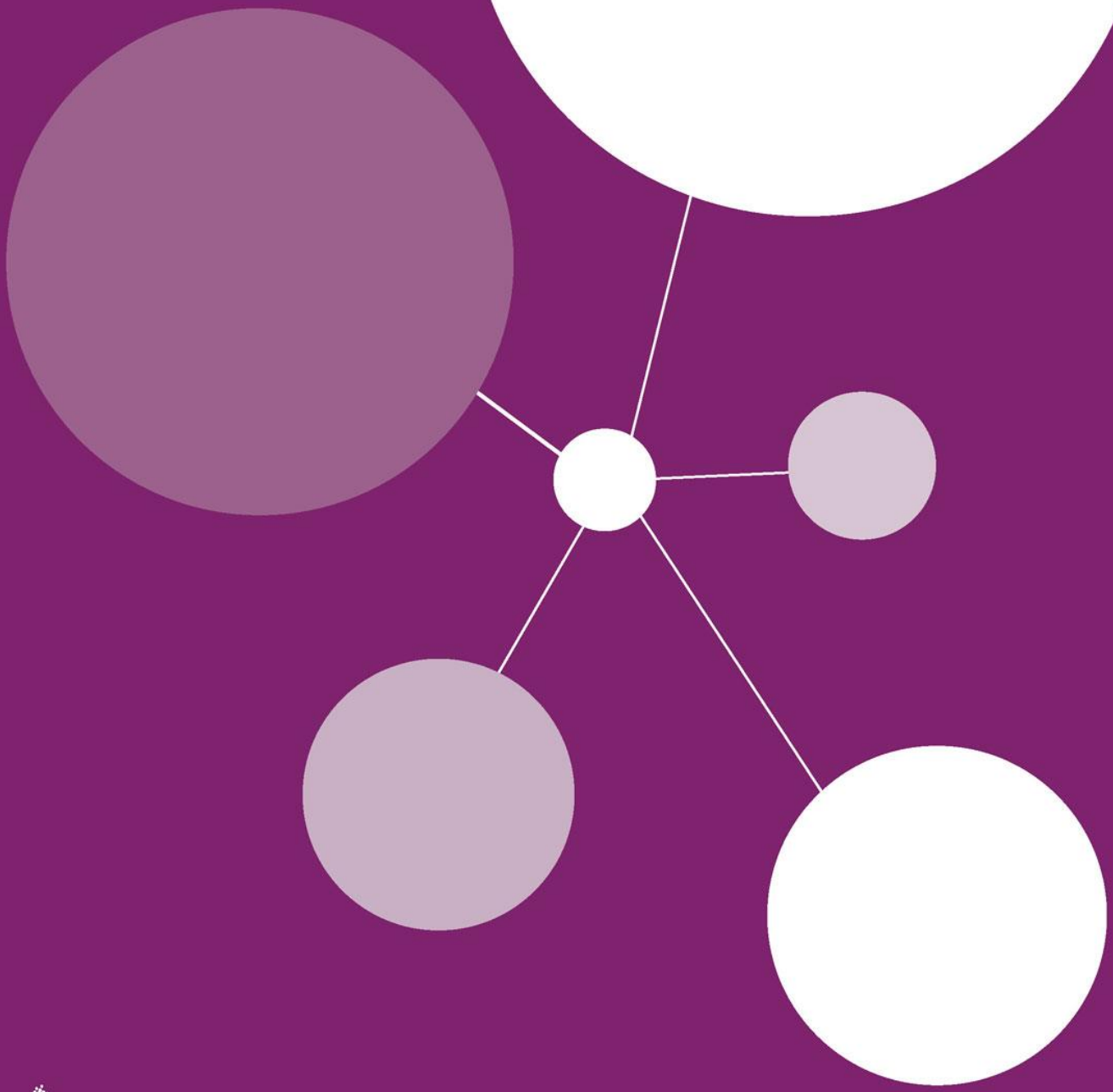
NCRI
National
Cancer
Research
Institute

NCRI Testis Cancer Clinical Studies Group

Annual Report 2015-16



Partners in cancer research

NCRI Testis Cancer CSG Annual Report 2015-16

1. Executive Summary (including top 3 achievements in the year)

The Testis Cancer CSG has seen numerous changes in the last year due to membership rotation and the completion of two successfully recruited stage 1 studies (111-BEP and TRISST). Two new studies have been approved and are due to open- TIGER - a randomised study in relapsing germ cell tumours following failure of conventional first line therapy and P3BEP - a randomised study of dose dense intensification in intermediate and poor prognosis untreated disease. The Group has endorsed the MaGIC collaborative proposals for the under 25 age group which should lead to a continuum of studies from the paediatric age group (>11 years) through to adulthood. The successful GeCIP application should ensure that germ cell tumour patients may benefit from new molecular techniques. The development of a new risk adapted study in good risk disease to include ovarian germ cell tumours as well as patients in the paediatric age group is well underway as are plans to look at strategies of remote follow up should mean that the Group remains in the forefront of study development and improvement in patient care in this rare cancer group. The focus of the group will concentrate on germ cell tumours including the female and extragonadal ones which have often not been clearly represented in studies, rather than just men with testicular cancer

2. Structure of the Group

There have been no new changes to structure but rotation of members within the Group has allowed for greater representation from urology (Mr Benjamin Thomas) to concentrate on minimally invasive strategies and those treating ovarian germ cell tumours (Dr Naveed Sarwar). The links with paediatric oncology/TYA have been strengthened by the co-opting of Dr Sara Stoneham with the translational aspects represented by Dr Matthew Murray. The Group continues to provide spaces for trainee members.

3. CSG & Subgroup strategies

Main CSG

- Design of new encompassing phase III study for good risk disease to include ovarian and paediatric cases.
- Open studies for patients untreated with poor prognosis and relapsed disease.

- Develop new strategies for follow-up that are non-clinic based both for patients with early disease and those who have completed systemic therapy.
- Develop standards for safe administration of chemotherapy for germ cell tumours, in particular bleomycin.

Quality of Life Subgroup

The main aim of the Quality of Life (QoL) Subgroup is to help develop follow up strategies that reduce the impact of the diagnosis of a germ cell tumour on a patient. This aim is supported by several strategies:

1. Reducing the burden of hospital based follow up.
2. Develop strategies to enhance patient fitness post chemotherapy.
3. Reduce the acute impact of chemotherapy on patients through de-escalation of treatment and improving supportive care.

4. Task groups/Working parties

Development of national guidelines for bleomycin to avoid pulmonary toxicity:
Through the CSG we have instigated a national survey of testicular cancer clinicians through survey monkey around practices concerning bleomycin delivery and pre-delivery tests. It was an opportunity to question practices around how bleomycin is given and knowledge around appropriateness of its use with certain conditions. The aim of the survey is an attempt to amalgamate clinical knowledge and generate some national guidance based on bleomycin delivery in this group of patients. The results once coordinated will be published along with some generated guidelines based on the survey. Both adult testicular cancer clinicians and TYA clinicians were surveyed. The results will be published in 2016.

Follow-up of testis cancer survivors:
A study exploring the use of remote follow-up of testis cancer patients after treatment is being developed through the Quality of Life Subgroup. We are collaborating with psychosocial experts from Oxford Brookes University including Eila Watson (who also sits on the Psychosocial Oncology & Survivorship CSG) and Mary Boulton. Following pilot interviews with patients and a survey of attitudes and opinions of testis cancer specialist nurses regarding follow-up, a randomised phase II/III study is now being developed comparing a model of remote vs standard hospital-based follow-up. The study will have quality of life, health economic and clinical end-points. The aim for the next year is to finalise the study protocol and submit for funding.

5. Patient recruitment summary for last 5 years

In the Testis Cancer CSG portfolio, 0 no. of trials closed to recruitment and 1 opened.

Table 1 Summary of patient recruitment by RCT/Non-RCT

Year	All subjects		Cancer patients only		% of cancer patients relative to incidence	
	Non-RCT	RCT	Non-RCT	RCT	Non-RCT	RCT
2011/2012	847	121	844	121	44.4	6.4

Table 2 Summary of patient recruitment by Interventional/Non-interventional

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2012/2013	1342	277	1335	259	59.8	12.4
2013/2014	1639	290	1495	290	67.0	13.0
2014/2015	1349	140	1269	140	56.9	6.3
2015/2016	752	20	686	20	30.73	0.90

The number of patients recruited in the last year has fallen – this was entirely predictable with the closure of two rapidly recruiting studies in stage 1 disease. The next two studies to open in poor prognosis and relapsed GCT should reverse this trend but a trial in early metastatic disease is required to reverse this trend more dramatically and this is in development.

6. Links to other CSGs, international groups and network subspecialty leads

Closer working with the Gynaecological Cancer CSG with presentation and endorsement of proposed metastatic good prognosis study to include ovarian germ cell tumours, and run such studies including the Gynaecological Cancer CSG, the TYA group and paediatric group (children oncology group, COG within the United States).

Provided data for management seminoma stage 1 relapsing post adjuvant carboplatin (international collaboration lead by Professor S Gillessen, Switzerland).

7. Funding applications in last year

Table 3 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)			
Study	**Application type**	**CI**	**Outcome**
July 2015 (CTAAC)			
None			
December 2015			
None			
Other committees			
Study	**Committee & application type**	**CI**	**Outcome**
Improving outcomes for children and young adults with extra cranial germ cell tumours 2015-2020	St Baldrick's Grant	Dr Matthew Murray	Successful
Genetic susceptibility and biomarkers of platinum-related toxicities 2014-2017	Josh Carrick foundation	Professor Robert Huddart	Successful
GAMMA – a phase 2 study in relapsed germ cell tumours	Orchid Cancer Appeal	Dr Jonathan Shamash	Successful
CarPET- PET scan response guided therapy of carboplatin AUC 10 in metastatic seminoma	Orchid Cancer appeal	Dr Jonathan Shamash	Successful

8. Collaborative partnership studies with industry

There are no current collaborations with industry this is mostly due to the fact that the perceived need for new drugs is low.

9. Impact of CSG activities

- GeCIP

Drs Protheroe, Verrill and Murray were successful in their application to Genomics England to lead on a Testicular Cancer GeCIP (Genomics England Clinical Interpretation Partnership). GeCIP is organised into disease specific and function-specific domains. This is UK-wide (not limited to England) and brings funders, researchers, NHS clinicians/healthcare professionals, trainees and potentially industrial partners together to enhance the value of this dataset for healthcare benefit. The GeCIP was launched on 27 June 2014.

The overall aim of the GeCIP is to create a thriving, sustainable environment for researchers and clinical (NHS) disease ex erts and trainees and a pre-competitive industrial consortium. This community will analyse and constantly refine the clinical interpretation of the 100,000 genomes dataset.

There are three overarching aims of GeCIP:

1. To optimise clinical data and sample collection, clinical reporting and data interpretation for return to clinicians and patients
2. To perform research to further improve our understanding of the implications of the findings for genomic medicine in the clinical setting
3. To provide a rich training environment for trainees both within the Genomics Education Programmes of Health Education England.

Our domain has brought together clinicians, scientists and lay members both in the UK and internationally with an aim to develop a programme of projects in which the Genomics data will provide a central resource to analyse outcomes with interpretable data. In the last year there have been no requests from CTAAC for comments nor any requests as part of the process of horizon scanning.

10. Consumer involvement

Both consumer representatives have been involved in discussions during CSG meetings. They have made suggestions about potential trials but have not been involved with trial development to date. There has been consumer involvement in educational activities related to testis cancer and raising awareness of the disease with plans to develop a national campaign to have a consistent testicular cancer awareness programme in all schools in the UK. It is proposed to seek greater involvement in the proposed study of strategies in follow up being developed by the Quality of Life subgroup.

11. Open meetings/annual trials days/strategy days

The NCRI Urological Annual Trials Meeting (January 2016) was well received and received excellent and very positive feedback.

12. Priorities and challenges for the forthcoming year

1. Set up a phase III study in good prognosis disease – this is likely to be the largest recruiting study and is in an advanced stage of development with expected submission for funding in September 2016.This study should help cement cross CSG working with the Gynaecological Cancer CSG and paediatrics.
2. Develop a Quality of Life/long term follow up study to assess the value of remote follow up both at a patient preference level and at an economic level.
3. Develop the interface with urology – the areas for potential collaboration include the value of delaying orchidectomy in patients with small incidental lesions where the risk of cancer appears low and we are currently collating a data base in this area. The introduction of minimally invasive surgery for RPLND in particular robotic techniques is an area for CSG involvement in the future.

13. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies
A – Main CSG Strategy
B – Quality of Life Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous year

Dr Jonathan Shamash (Testis Cancer CSG chair)

Appendix 1

Membership of the Testis Cancer CSG

Name	Specialism	Location
Mr Stephen Francis Thomas	Consumer	Cardiff
Mr Vincent Wolverson	Consumer	Norwich
Dr Linda Evans	Medical Oncologist	Sheffield
Professor Johnathan Joffe	Medical Oncologist	Huddersfield
Dr Danish Mazhar	Medical Oncologist	Cambridge
Dr Andrew Protheroe	Medical Oncologist	Oxford
Dr Alison Reid	Medical Oncologist	Surrey
Dr Naveed Sarwar	Medical Oncologist	London
Dr Jonathan Shamash (Chair)	Medical Oncologist	London
Professor Nick Stuart	Medical Oncologist	Gwynedd
Dr Matthew Wheater	Medical Oncologist	Southampton
Dr Benjamin Fairfax*	Medical Oncology Trainee	Oxford
Dr Hayley McKenzie*	Medical Oncology Trainee	Southampton
Mrs Sue Brand	Nurse	Bristol
Dr Sara Stoneham	Paediatric Oncologist	London
Dr Matthew Murray	Paediatric Oncologist and Translational Scientist	Cambridge
Dr Clare Verrill	Pathologist	Oxford
Dr Tom Maishman	Statistician	Southampton
Mr Benjamin Thomas	Urologist	Cambridge

*denotes trainee member

Membership of the Subgroups

Quality of Life (QoL) Subgroup		
Name	**Specialism**	**Location**
Dr Jenny Harrington	Clinical Fellow	Cambridge
Dr Rob Huddart	Clinical Oncologist	London
Mr James Ashton	Consumer	
Dr Ed Wilson	Health Economist	Cambridge
Dr Danish Mazhar (Chair)	Medical Oncologist	Cambridge
Dr Dan Stark	Medical Oncologist	Leeds
Professor Nick Stuart	Medical Oncologist	Gwynedd
Dr Jeff White	Medical Oncologist	Glasgow
Mrs Sue Brand	Nurse	Bristol
Ms Nicola Thomson	Nurse	Glasgow
Dr Sara Stoneham	Paediatric Oncologist	London

*denotes trainee member
**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

The strategy of the Testis Cancer CSG has been evolving over the last year. This has been driven by several core principles:

1. The realisation that germ cell tumours although predominantly occurring in young adult males also occur in the paediatric age group, in women and that although histologically similar their response to treatment may vary and that there may be a lot to be learnt from understanding these differences.
2. There is a need for a large randomised phase III study in patients with good risk metastatic disease where risk stratification based on histology may allow de-escalation of therapy and that this may require global collaboration.
3. Studies need to be carried out in patient with good outcomes (>90% cure rate) as well as those whose prognosis is less favourable and these studies should include female germ cell tumours (in view of their common histology and under representation in randomised studies).

To this end, we have established closer links with the Gynaecological Cancer CSG, the paediatric oncology groups both here and within the United States (CCL CSG and COG) seeking and getting their support in such studies.

Within this approach, we wish to look at novel tumour markers (micro RNA in particular - especially in those patients who do not produce classical tumour markers). Such markers may have potential to pick up early relapse as well as reducing the reliance on imaging, particularly in post treatment residual masses.

In stage 1 disease, the aim to improve risk stratification based on histological features of the primary tumour remains an important factor. The recent publication by Gilbert et al suggests that a new prognostic marker CXCL12 helps refine the role of embryonal cancer in stratifying stage 1 patients and thereby allowing the more selective use of adjuvant therapy.

B – Quality of Life Subgroup Strategy

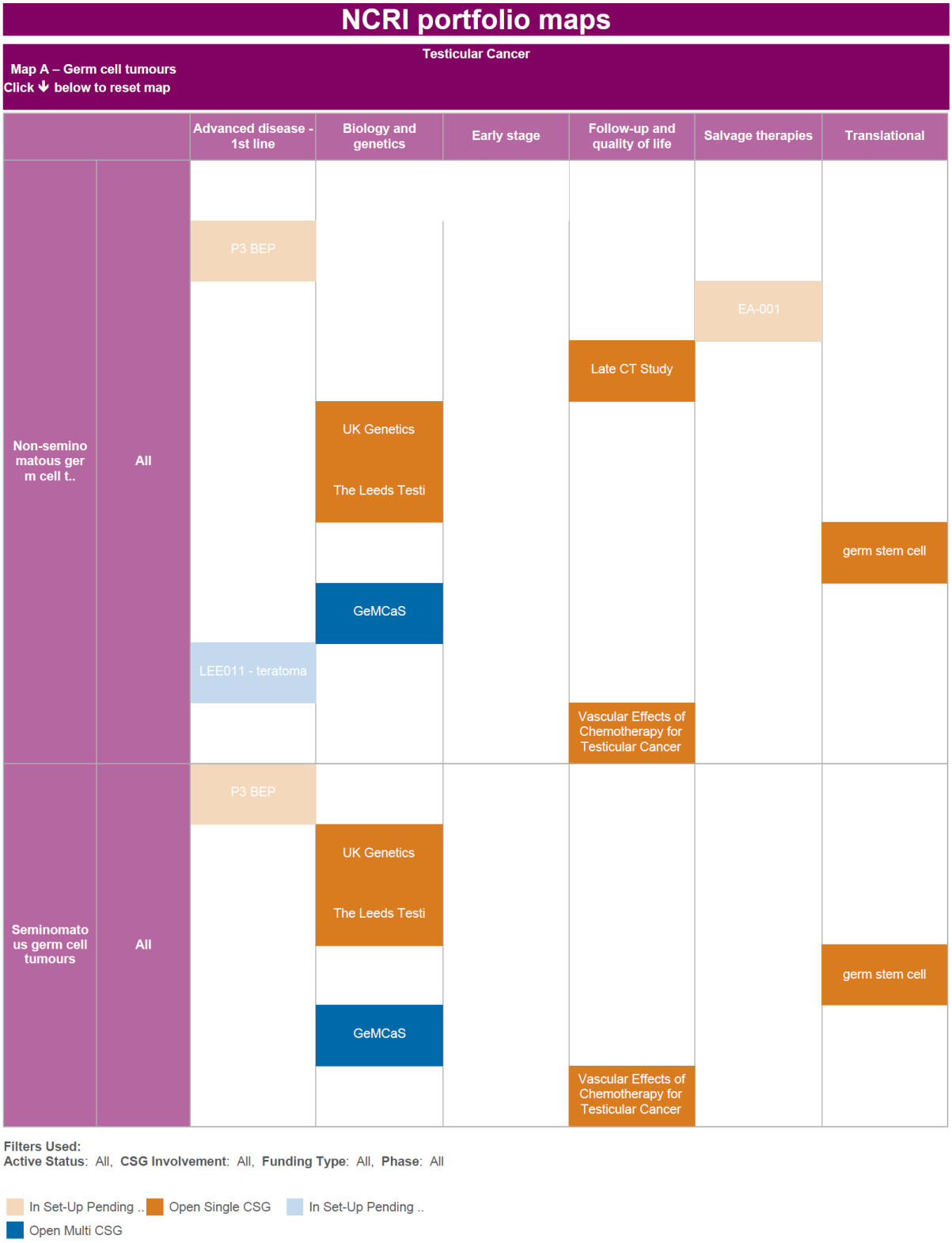
The success of the ReStart pilot study to evaluate a rehabilitation programme for patients with germ cell tumours which demonstrated that exercise had a favourable effect on global functioning a larger study in this area which the Testis Cancer CSG will be keen to take forward. The question of remote follow up using email/text/telephone rather than traditional face-to-face outpatient clinic has time and cost implications for patients and the NHS as a whole. The QoL Subgroup has had several meetings to address how this is best taken forward, a randomised phase III study is proposed.

The Subgroup has been active in supporting the role of testicular salvage and recently presented data suggests that not all patients with testicular lesions require orchidectomies. The suggestion is that small non-vascular lesions may be candidates for excision or in those less than 5mm for a period of observation. These findings are being validated by looking at a similar cohort in Oxford

The appointment of a robotic urological surgeon to the Subgroup this year is a response to the demand, particularly from consumers, for more minimally invasive surgery in those requiring retroperitoneal surgery where the significant morbidity of the open procedure is appreciated.

Appendix 3

Portfolio maps



Appendix 4

Publications in the reporting year

Patterns of relapse in patients with clinical stage I testicular cancer managed with active surveillance
Kollmannsberger C, Tandstad T, Bedard PL, Cohn-Cedermark G, Chung PW, Jewett MA, Powles T, Warde PR, Daneshmand S, Protheroe A, Tyldesley S, Black PC, Chi K, So AI, Moore MJ, Nichols CR. J Clin Oncol. 2015 Jan 1;33(1):51-7.

Defining a New Prognostic Index for Stage I Nonseminomatous Germ Cell Tumors Using CXCL12 Expression and Proportion of Embryonal Carcinoma
Gilbert DC, Al-Saadi R, Thway K, Chandler I, Berney D, Gabe R, Stenning SP, Sweet J, Huddart R, Shipley JM. Clin Cancer Res. 2016 Mar 1;22(5):1265-73. doi: 10.1158/1078-0432.CCR-15-1186. Epub 2015 Oct 9.PMID: 26453693

Handling and reporting of orchidectomy specimens with testicular cancer: areas of consensus and variation among 25 experts and 225 European pathologists
Berney DM, Algaba F, Amin M, Delahunt B, Compérat E, Epstein JI, Humphrey P, Idrees M, Lopez-Beltran A, Magi-Galluzzi C, Mikuz G, Montironi R, Oliva E, Srigley J, Reuter VE, Trpkov K, Ulbright TM, Varma M, Verrill C, Young RH, Zhou M, Egevad L. Histopathology. 2015 Sep;67(3):313-24. doi: 10.1111/his.12657. Epub 2015 Mar 17. PMID: 25619976

Revised risk classification for pediatric extracranial germ cell tumors based on 25 years of clinical trial data from the United Kingdom and United States
Frazier AL, Hale JP, Rodriguez-Galindo C, Dang H, Olson T, Murray MJ, Amatruda JF, Thornton C, Arul GS, Billmire D, Shaikh F, Pashankar F, Stoneham S, Krailo M, Nicholson JC. J Clin Oncol. 2015 Jan 10;33(2):195-201. doi: 10.1200/JCO.2014.58.3369. Epub 2014 Dec 1. PMID: 25452439

Is adjuvant chemotherapy indicated in ovarian immature teratomas? A combined data analysis from the Malignant Germ Cell Tumor International Collaborative
Pashankar F, Hale JP, Dang H, Krailo M, Brady WE, Rodriguez-Galindo C, Nicholson JC, Murray MJ, Bilmire DF, Stoneham S, Arul GS, Olson TA, Stark D, Shaikh F, Amatruda JF, Covens A, Gershenson DM, Frazier AL. Cancer. 2016 Jan 15;122(2):230-7. doi: 10.1002/cncr.29732. Epub 2015 Oct 20. PMID: 26485622

Appendix 5

Major international presentations in the reporting year

There were no international presentations during this reporting year.