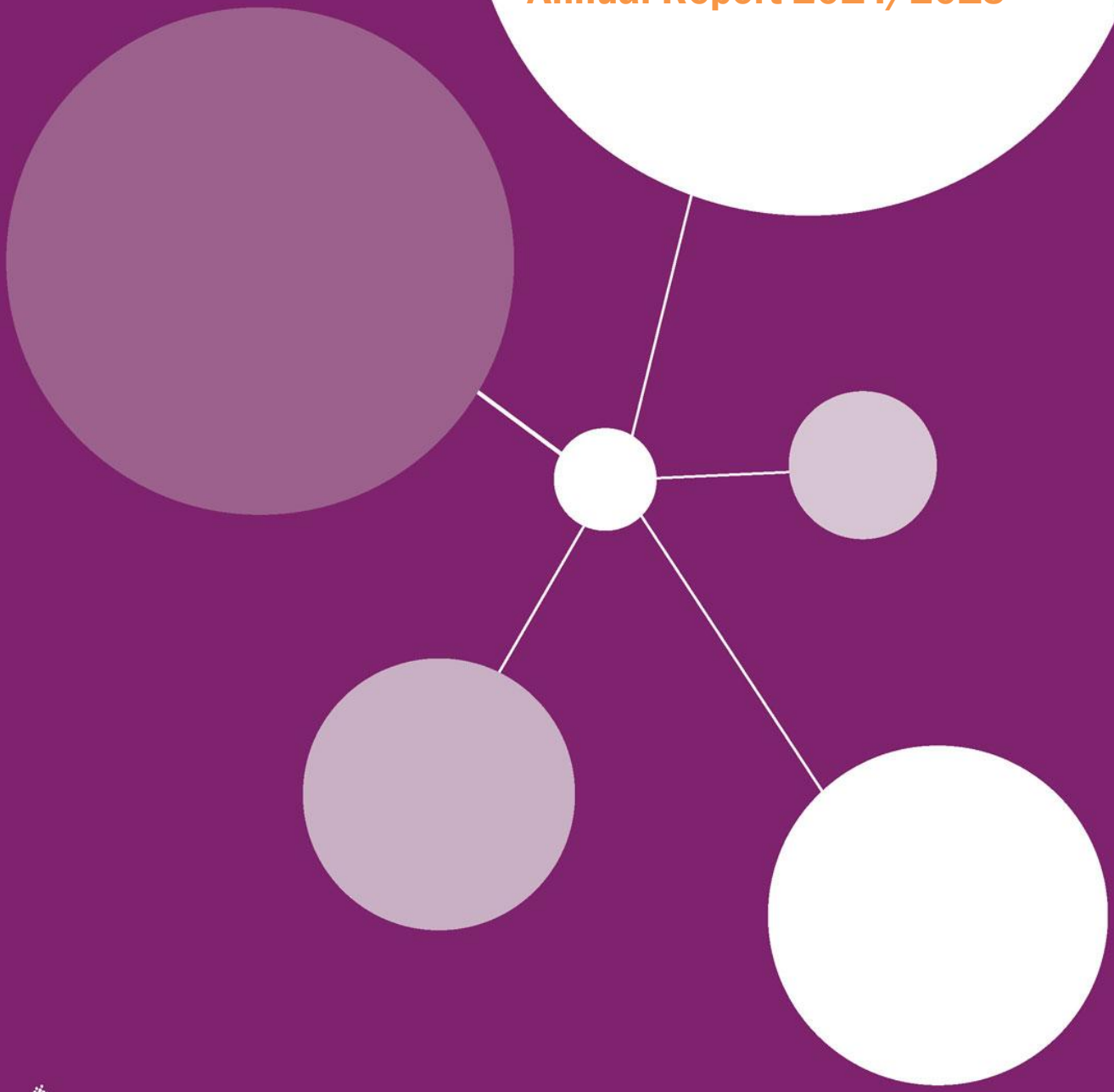
NCRI
National
Cancer
Research
Institute

NCRI Children's Cancer & Leukaemia Clinical Studies Group

Annual Report 2014/2015



Partners in cancer research

NCRI Children's Cancer & Leukaemia CSG Annual Report 2014/15

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

The CCL CSG has continued to have a high level of activity this year with 14 new studies opening (9 have closed). This has been reflected in a further increase in patients participating in interventional and non interventional cancer clinical trials.

Four paediatric studies were submitted to CTAAC this year two were funded, one endorsed (no funding requested) and a further study has been supported and final funding approval is awaited. None were deferred.

The CSG hosted a second Annual Trials Meeting which was very well attended and very positively reviewed.

There has been good progress on the strategic plan for the CSG (see Appendix 2A) with several outcomes achieved. A particular achievement has been the successful launch of the trainee membership within the CCL CSG subgroups.

2. Structure of the Group

As a result of the Progress Review in 2013, the CSG was asked to streamline and reduce the number of subgroups. Consequently the renal and hepatobiliary subgroups were withdrawn because of the very small numbers of studies within their portfolios. However representation of these important tumour sites will continue on the CSG, there is a study for Wilms tumour currently open across the UK and the next international liver study has been submitted for European funding. The rest of the group structure remains the same, with one change of Subgroup Chair: Dr Sara Stoneham has replaced Dr James Nicholson as Chair of the Germ Cell Tumour Subgroup. The CSG has supported the appointment of trainees to the subgroups. Financial support has been provided by the CCLG. Trainees are encouraged to actively contribute to the work if the CSG subgroups and asked to provide a short report annually to the CSG.

3. CSG & Subgroup strategies

Main CSG

The CSG strategy document (see Appendix 2A) describes the high number of aims of the group with timelines and leaders for each workstream identifed. An important focus has been the need to address gaps in the portfolio, not only for some tumour sites but also developing radiotherapy and surgical clinical trials. An important area is the development of clinical trials for children at the time of disease relapse and the CSG is actively supporting a GECIP application for funding for the development of genomic testing. There are a number of other themes within the strategy

document including increasing early phase activity and participation; raising the profile of the CSG; maximising output from clinical trials; strengthening UK wide and international working; further developing CSG structure and function and working more closely with patients and public.

Novel Agents Subgroup (Chair, Dr Darren Hargrave)

Dr Darren Hargrave took over as Subgroup chair in April 2015 following the excellent leadership of Prof Andrew Pearson and the group wish Andy well in his recent retirement. The portfolio of early clinical studies includes 17 currently open early clinical studies: 4 phase I, 7 phase I/II and 6 phase II. Of these, 70% are Pharma sponsored and 64% are phase I or I/II. Over the last year four early phase studies have been successfully completed and two have been presented at ASCO. There are 6 open pharmacology studies. It is expected that a further 4 phase I studies will open in 2015. Immunotherapy studies are increasing in the portfolio with on-going trials of Ipilimumab a CTLA4 antibody in childhood melanoma, the anti-GD2 monoclonal antibody in neuroblastoma and immunotherapy with CD19 gene modified EBV specific CTLs for high risk CD19+ ALL. The first UK paediatric study of an immune checkpoint inhibitor has opened targeting the PD-1 receptor has opened with a phase I study of Pembrolizumab with melanoma or PD-L1 positive relapsed/ refractory solid tumours (including CNS tumours) and a second phase I study targeting PDL-1 expected in 2015. A major strategic aim for the group this year has been to develop a paediatric precision medicine programme working with CRUK and an EU Horizon 2020 application.

Neuroblastoma Subgroup (Chair, Dr Kate Wheeler)

Achievements

- Funding of SIOPEN OMS; IL-2 continuous infusion; and amendments to SIOPEN High Risk Study and BEACON.
- SIOPEN HR Neuroblastoma trial – UK highest recruiter (with France) n=550 April 2015
- Current induction randomisation R3 will demonstrate the most effective induction regimen.
- Two open trials SIOPEN HR and LTI have enabled UK patients to receive immunotherapy with anti GD2 (currently only possible in a clinical trial setting). Trials aim to identify most effective method of administration with minimal toxicity
- UK Samples for tumour biology almost all now analysed at Newcastle NBL Reference Laboratory 2015
- Close links with SIOPEN the European Neuroblastoma group. Two SIOPEN meetings per year and regular telephone conference calls for the HR clinical trial national coordinators and for the SIOPEN executive group members. INRG and INRC projects have facilitated international/transatlantic collaborations.

Challenges

- Getting the R4 immunotherapy randomisation long term infusion antiGD2 +- IL2 open in all UK centres by end 2015
- Competition between European and American antiGD2 antibody anticipated end 2015
- Funding for research into tissue and radiological biological markers of prognostic significance
- Obtaining for the UK a system to register Low and Intermediate Risk patients and collect outcome data

- Clinical governance for autografts in NBL patients (NHS England reviewing process/QA for all autografts).

The general strategy for the next 3 years is to:

- Improve outcome for all Neuroblastoma patients
- Refine the prognostic significance of tissue and imaging biological markers and integrate them into stratification of treatment groups in clinical trials
- Define molecular targets in neuroblastoma

A more specific strategy for high risk and relapse patients is outlined in Appendix 2C.

Germ Cell Tumour (GCT) Subgroup (Chair, Dr Sara Stoneham)

The Subgroup continues to hold regular teleconference meetings to progress trial design and has held monthly conference calls with our US collaborators from COG. Dr Stoneham has been appointed as Chair, replacing Dr James Nicholson. Dr Mark Brougham has taken over the chair of SIG from Dr Juliet Hale. Dr Claire Thornton has stepped down and Dr Liz Hook has joined as our pathology expert.

Key achievements for the Subgroup this year are:

- Open trial: SIOP IC GCT II trial - recruiting on target - minor amendments accepted
- MaGIC collaboration: UK paed, UK testis, US COG paed, US GOG continued trial portfolio development as an international collaborative working group.
- Two publications from joint trial analysis from MaGIC database.
- COG science council approved trial for < 11years standard risk patients (AGCT 1531) where randomized between PEB vs JEB. Open to recruitment by end 2015 in US. Aim to decrease long term toxicity whilst maintaining excellent EFS and OS.

Central Nervous System (CNS) Subgroup (Chair, Dr Antony Michalski)

The CNS Tumour Subgroup has had an active and productive year. SIOP LGG2 study was completed internationally having accrued to target and data collection is ongoing. The HERBY study for high grade glioma recruited well and the UK was joint highest recruiter internationally. The SIOP CNS Germ Cell Tumour Study was rolled out and has now opened in most UK Centres and is accruing.

Most studies are developed and run internationally and the lag time to study conception to opening remains unacceptably long. Problems with international sponsorship of the PNET5 study for children with standard risk medulloblastoma meant that it had only opened in Germany and in one centre in France – it is expected to open in the UK this autumn. The study for high risk medulloblastoma is in development and that for young children with medulloblastoma is due to be finalised this year. The SIOP Ependymoma study is still not open due to sponsorship issues. For gliomas, BIOMEDE is due to open for children with diffuse intrinsic pontine glioma. There is no open study for high grade glioma as yet – any new study will probably involve novel agents and be run from a limited number of centres. The raft of studies for low grade gliomas remain in development and it is uncertain whether the UK will join all of these studies as there is the opportunity for collaborating with other international groups.

The bi-annual meeting of paediatric neuro-oncology was held in Singapore in June 2014 and the clear direction of travel is increasing molecular classification of tumours. This will result in a larger number of smaller subgroups and will be a challenge for future trial design.

Leukaemia Subgroup (Chair, Professor Ajay Vora)

The frontline ALL trial, UKALL 2011, is recruiting well to both randomisations but only 75% of screened patients are consenting to first randomisation and, of those, 58% to the second randomisation. Hence, there is concern about shortfall in recruitment to second randomisation requiring extension of recruitment to trial. We have agreed to register patients who do not consent to the first randomisation so that they are available for recruitment to the second randomisation. After a long delay, agreements are in place for the standard risk arm of IntReALL to open shortly. There is no news yet on when the HR arm of the study will open but the pharma-led Blinotumumab randomisation might go ahead prior to the full study being open. International Ph-pos ALL trial sponsored by BMS (CA180-372) has completed recruitment and an interim treatment guideline has been agreed until a new international trial opens in 2015/16. The UK-French front line AML protocol, MyeChild01 has been funded through CTAAC and will open autumn 2015. The case for inclusion of APL and DS-AML within MyeChild01 has so far not been accepted by CRCTU.

Discussions are on-going about a new International infant ALL trial to succeed Interfant 06 in 2015/16. The UK recruited a patient to the international phase II Blinotumumab study and has continuing access to the drug through the compassionate use and expanded access programmes. The LSG has agreed to support a MEK inhibitor study led by Professor Vormoor.

We have also agreed a chemotherapy free regimen for standard risk acute promyelocytic leukaemia as well as treatment recommendations for Myeloid-Leukaemia associated with Down syndrome and hope that data on these rare sub-groups can be collected through a registration only element to the front line AML study. We have agreed a plan for establishing a registry linked to biological studies for several rare haematological malignant disorders of childhood including Myelodysplasia, Fanconi Anaemia and other bone marrow failure syndromes.

4. Task groups/Working parties

There are no task groups or working parties within the CSG at present.

5. Patient recruitment summary for last 5 years

The CCL CSG has continued its excellent record of trial opening with 14 new studies opening within the past clear (9 closed). This has been reflected in a further increase in patients participating in interventional and non interventional cancer clinical trials.

There continues to be a steady stream of new trial proposals considered by the CSG. A particular challenge is that the majority of the trials are coordinated through one clinical trials unit (Birmingham CRCTU) and there is limited capacity to open new trials several times a year. New studies therefore have to be prioritised by the CSG at each meeting and inevitably there is a delay in progress for some of the studies. However this additional scrutiny is of value in further raising the standard clinical trials approved.

An important achievement has been the opening of 3 large clinical trials this year: MyeChild, for children with newly diagnosed acute myeloid leukaemia; EuroEwing 2012, for patients with newly diagnosed Ewing's Sarcoma; and ReCUur, a trial for children and young adults with recurrent Ewings sarcoma. Both the Ewing studies are international studies and with UK as the international sponsor.

The steady increase in the non interventional clinical trials reflects the recruitment to Early Phase and other Supportive Care studies within the portfolio.

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
2010/2011	721	314	455	314	-	-
2011/2012	1033	311	615	311	-	-

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	1077	491	632	483	-	-
2013/2014	1419	625	751	625	-	-
2014/2015	1605	643	795	643	-	-

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

There are strong links with the TYA CSG, and the CCL Chair recently contributed to the TYA strategy day. However there is an important distinction to be made between the two CSGs and this became clear at a recent event for the new network subspecialty leads. The CSG continues to have very strong links to the Children's Cancer and Leukaemia Group (CCLG) and it's Special Interest Groups (SIGs) where many new ideas and other developments within the CSG are shared. The CCLG support the attendance of trainees at CSG subgroup meetings.

A direct link has been made with the Psychosocial Oncology & Survivorship CSG and a representative from CTRad will present at the summer CCL CSG meeting. Many studies within the CSG portfolio are international are there strong ongoing links with several European International Study Groups (e.g. SIOPEN, SIOPEL, EpSSG, BFM) through which new trials are developed and sponsored internationally.

Members of the CSG are also working with CRUK in the launch of a 'Kids and Teens' campaign. This campaign is aiming to invest into research that will lead to a step change in care and improved outcomes for children and TYA with cancer.

7. Funding applications in last year

The CSG has continued to be successful in its applications for funding. There has been an extremely high number of trials submitted to the CSG for review and approval. The CSG therefore undertakes a process of prioritisation of studies at each meeting, identifying those studies that are to be taken forward by the CRCTU for each funding round. This process allows for a further scientific scrutiny of the studies and contributes to the high quality of studies submitted for funding.

Table 3 Funding submissions in the reporting year

Clinical Trials Advisory and Awards Committee (CTAAC)			
Study	**Application type**	**CI**	**Outcome**
July 2014			
A phase I/I dose schedule finding study of ch14.18/cho continuous infusion combined with subcutaneous Aldesleukin IL-2 in patients with primary refractory or relapsed neuroblastoma	Feasibility application *Amendment*	Dr Juliet Gray	Funded
November 2014			
High Risk Neuroblastoma Study 1 of SIOP - Europe	Full Application *Amendment*	Dr Martin Elliot	Endorsed
BEACON Trial Amendment: A randomized phase IIb trial of BEvACizumab added to Temozolomide ± IrinOtecan for children with refractory/relapsed Neuroblastoma	Feasibility Application *Amendment*	Professor Andrew Pearson	Funded
March 2015			
BIOMEDE: Biological Medicine for Diffuse Intrinsic Pontine Glioma (DIPG) Eradication	Full Application	Dr Darren Hargrave	Funded

8. Collaborative partnership studies with industry

Clinical trials are open or are in set-up with fourteen companies including; Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, BMS, Celgene, GSK, Hoffmann-La Roche-Genentech, Johnson & Johnson, Merck, Novartis and Pfizer. Collaborations with industry are progressing very well and the CSG continues to aim to rapidly open studies, recruit on target and submit high quality data. The Novel Agents Subgroup is aiming to develop additional collaborations with industry for the ECMC combinations alliance platform.

9. Impact of CSG activities

There are many studies within the recent portfolio that have had a direct impact on the care of patients. Examples include the use of minimal disease monitoring in guiding therapy for patients with acute lymphoblastic leukaemia; Reduction in treatment related toxicity and improvement in relapse outcome by the use of minimal disease monitoring in guiding therapy for patients with acute lymphoblastic leukaemia and significant improvement in outcome for TYA ALL patients by inclusion within a paediatric trial; the omission of doxorubicin for patients with stage II Wilms tumour; evidence that doxorubicin does not improve survival (but does increase toxicity) in

patients with high risk rhabodmyosarcoma and the use of dacarbazine in Hodgkins (replacing procarbazine, which has greater gonadotoxicity).

In neuroblastoma the results of the randomisation R1 in the high risk trial proved that high dose chemo using Bu Mel was better than CEM. Bu Mel is now the standard high dose conditioning treatment in an autologous setting for HR NBL in Europe and now the USA. The toxicity associated with anti GD 2 therapy is reduced when it is given as a long term infusion and the new randomisation R4 in the SIOPEN HR NBL trial is now only using the antibody in a long term setting (currently going through regulatory authorities to open in the UK).

The CSG continues to actively contribute to research strategy (NCIN workshop for late effects of therapy; CRUK Kids and Teens campaign and recently the PHE Cancer Taskforce). It also continues to regularly provide advice to CTAAC and the Population Research Committee for relevant applications and reports for NICE appraisals as required.

10. Consumer involvement

The CCL CSG is privileged to have two very active consumer representatives as members. Their contributions over the last year are detailed below:

Mr Chris Copland

Through membership of the Novel Agents' Subgroup, I have become involved with the Cancer Drugs Development Fund, participating in a working group and conference, both relating to the regulation of paediatric medicines for oncology. In connection with this, I participated in European Medicines Agency conference on *Better Medicines for Children* in London.

I have also joined the Trial Steering Committee of EuroEwing's Consortium and have been active in their PPI network. In addition, I recently joined the *Consequences of Cancer and its Treatment* Subgroup of the Psychosocial Oncology & Survivorship CSG.

I presented at the Childhood Cancer International conference in Valencia on PPI and, in the UK, have participated in meetings for patients / carers of the Childhood Cancer Leukaemia Group and Sarcoma UK. I gave a short presentation at the Consumer Liaison Group on the age of entry to adult trials. In terms of training, I attended a three day workshop on Cancer Biology and Targeted Treatments for Solid Tumours.

Other activities include being interviewed by Nuffield Council on Bioethics for report on ethics of children and clinical research and running in the Cambridge Half Marathon, in which I raised £1500 for *CRUK Kids and Teens.*

Mrs Danielle Horton Taylor

Mrs Horton Taylor has continued her work as a founder member of the Paediatric Oncology Reference Team (PORT), as part of that has reviewed the patient information sheets and consent forms for over 10 studies in the reporting year, and had meetings regarding upcoming trials. This year PORT had their second meeting at CR CTU (where the Children's Clinical Trials Team is located), where they devised templates for Patient Information Sheets for the various age groups.

With PORT, she engaged in consultations with the Chair of NREAP (National Research Ethics Advisory Panel) regarding assent issues in under 8s and young children, and also worked with the Nuffield Council on Bioethics to devise a case-study for assent in paediatric oncology, which is cited in their publication: Children and Clinical Research: Ethical Issues Box 6.3 Case study - young children with cancer (p160) and also Research Situation 1 in the Nuffield's shorter publication: Involving Children and Young People in Health Research - Getting it Right. She attended the launch of CRUK Kids & Teens campaign, and as part of this she presented at two Children's Cancer Events for CRUK. She has presented at the Children's Cancer Conference 2015 (in conjunction with Bethany's Wish and CCLG) and will present at the Childhood Cancer International Europe (formally ICCCPO) conference, speaking on Paed Onc and Patient Information Sheets and Clinical Trials issues, in May 2015. She has taken part in the two CRUK Big Thinks for the Grand Challenge (as well as the training day), and will sit on the Patient Panel of the CRUK Grand Challenge. She attended the NAEDI conference and separate meeting. Mrs Horton Taylor has also attended INVOLVE conference, the NCIN Cancer Outcomes Conference, the NCRI Conference (where she sits on the conference committee, and as a result also the Consumer Hub), the EMA conference on Better Medicines for Children , in addition to the Cancer Drug Development Forum Conference (previously known as BDA).

11. Open meetings/annual trials days/strategy days

The feedback from the annual trials day was extremely positive. The program was very full; on the positive side this reflected the high level of activity within the CSG, however it considerably restricted the time available for questions which was a concern to many of the participants. The program for the next meeting will be modified accordingly. Another request was that the trial day would include paediatric leukaemia trials. – this has been addressed and the next meeting will include reports from trials across the portfolio.

12. Progress towards achieving the CSG's 3 year strategy

Progress toward the 3 year strategy is described in the strategy document in Appendix 2A - many actions are completed and the timelines are clearly described. There has been particular success in the dissemination of the work of the CCL CSG through the annual trials day and the involvement of trainees within the subgroups.

13. Priorities and challenges for the forthcoming year

A priority for the CSG continues to be the implementation of the strategic plan with an emphasis on the development of precision medicine within paediatric cancer and a focus on clinical trials in surgery and radiotherapy.

There are relatively fewer children with brain tumours participating in clinical trials compared to other diagnostic groups. Many children have a poor outcome, both in terms of survival and quality of survival. Developing trials in this area is an important challenge for the CSG and the CNS Subgroup.

There is a need to develop stronger links with the CCL subspecialty leads across the UK to ensure equitable access for children with cancer to clinical trials within the new framework.

14. Concluding remarks

This has been another successful year for the CCL CSG and the group continues build on its previous achievements with strong links to other CSGs and the international research community. An important focus for next year will be to address gaps in the portfolio and focus the development of studies in patients for whom the progress is poor and for whom there are no current trials available.

15. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies

- A – Main CSG Strategy
- B – Novel Agents Subgroup Strategy
- C – Neuroblastoma Subgroup Strategy
- D – Germ Cell Tumour (GCT) Subgroup Strategy
- E – Central Nervous System (CNS) Subgroup Strategy
- F – Leukaemia Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous year

Dr Meriel Jenney (CCL CSG Chair)

Appendix 1

Membership of the CCL CSG

Name	Specialism	Location
Mr Christopher Copland	Consumer	York
Mrs Danielle Horton Taylor	Consumer	London
Dr Jane Beety	NIHR	London
Ms Karen Howe	Nurse	London
Dr John Moppett	Paediatric Haematologist	Bristol
Professor Ajay Vora	Paediatric Haematologist	Sheffield
Dr Amos Burke	Paediatric Oncologist	Cambridge
Dr Julia Chisholm	Paediatric Oncologist	London
Dr Martin Elliot	Paediatric Oncologist	Leeds
Dr Mark Gaze	Paediatric Oncologist	London
Dr Darren Hargrave	Paediatric Oncologist	London
Dr Lisa Howell	Paediatric Oncologist	Liverpool
Dr Meriel Jenney (Chair)	Paediatric Oncologist	Cardiff
Dr Pamela Kearns	Paediatric Oncologist	Birmingham
Dr Guy Makin	Paediatric Oncologist	Manchester
Dr Anthony Michalski	Paediatric Oncologist	London
Dr James Nicholson	Paediatric Oncologist	Cambridge
Dr Sara Stoneham	Paediatric Oncologist	London
Dr Kate Wheeler	Paediatric Oncologist	London
Dr Kieran McHugh	Radiologist	London
Professor Keith Wheatley	Statistician	Birmingham
Mr Ian Kamaly-Asl	Surgeon	Manchester

Membership of the Subgroups

Central Nervous System (CNS) Subgroup		
Name	**Specialism**	**Location**
Mr Neil Dickson	Brain Tumour Charity, Chair	Farnborough
Mr David Wicksman	Brain Tumour Charity	Farnborough
Dr Frank Saran	Clinical Oncologist	London
Dr Nicki Thorpe	Clinical Oncologist	Liverpool
Professor Steve Clifford	Paediatric Oncologist	Newcastle
Professor Richard Grundy	Paediatric Neurologist	Nottingham
Dr Darren Hargrave	Paediatric Oncologist	London
Professor Colin Kennedy	Paediatric Neurologist	Southampton
Dr Antony Michalski (Chair)	Paediatric Oncologist	London
Dr Andrew Peet	Paediatric Oncologist	Birmingham
Dr Sue Picton	Paediatric Oncologist	Leeds
Professor Barry Pizer	Paediatric Oncologist	Liverpool
Dr Heidi Traunecker	Paediatric Oncologist	Cardiff
Mr Connor Mallucci	Surgeon	Liverpool
Mette Jorgensen*		London
Patricia O'Hare*		

Neuroblastoma Subgroup		
Name	**Specialism**	**Location**
Dr John Anderson	Paediatric Oncologist	London
Dr Penelope Brock**	Paediatric Oncologist	London
Dr Martin Elliott	Paediatric Oncologist	Leeds
Dr Mark Gaze	Paediatric Oncologist	London
Dr Juliet Gray	Paediatric Oncologist	Southampton
Dr Guy Makin	Paediatric Oncologist	Manchester
Dr Daniel Morgenstern**	Paediatric Oncologist	London
Professor Andy Pearson	Paediatric Oncologist	London
Dr Ramya Ramanujachar**	Paediatric Oncologist	Southampton
Professor Deborah Tweddle	Paediatric Oncologist	Newcastle
Dr Kate Wheeler (Chair)	Paediatric Oncologist	London
Mr Roly Squire	Paediatric Surgeon	Leeds
Professor Sue Burchill	Professor of paediatric & adolescent cancer research	Leeds
Professor Keith Wheatley	Statistician	Birmingham
Gail Halliday*		Newcastle
Sally George*		

* denotes trainee

**denotes non-core member

Leukaemia Subgroup		
Name	**Specialism**	**Location**
Mr Neil Ranasinghe**	Consumer	
Dr Anthony Moorman	Epidemiologist	Newcastle
Dr Brenda Gibson	Haematologist	Manchester
Dr Clare Rowntree	Haematologist	Cardiff
Dr Phil Ancliff**	Paediatric Haematologist	London
Dr Denise Bonney	Paediatric Haematologist	Manchester
Professor Nick Goulden**	Paediatric Haematologist	London
Dr Sarah Lawson**	Paediatric Haematologist	Birmingham
Dr John Moppett	Paediatric Haematologist	Bristol
Dr Anupama Rao	Paediatric Haematologist	London
Dr Sujith Samarasinghe**	Paediatric Haematologist	Newcastle
Professor Owen Smith	Paediatric Haematologist	Dublin
Professor Josef Vormoor	Paediatric Haematologist	Newcastle
Dr Rob Wynn	Paediatric Haematologist	Manchester
Professor Ajay Vora (Chair)	Paediatric Haematologist	Sheffield
Dr Donna Lancaster	Paediatric Oncologist	London
Dr David O'Connor*	Specialist trainee in haematology	West Midlands
Caroline Furness*		London

Novel Agents Subgroup		
Name	**Specialism**	**Location**
Professor Ajay Vora	Paediatric Haematologist	Sheffield
Dr Josef Vormoor	Paediatric Haematologist	Newcastle
Professor Steve Clifford	Paediatric Oncologist	Newcastle
Dr Martin Elliot	Paediatric Oncologist	Leeds
Dr Darren Hargrave (Chair)	Paediatric Oncologist	London
Professor Pam Kearns	Paediatric Oncologist	Birmingham
Dr Guy Makin	Paediatric Oncologist	Manchester
Dr Bruce Morland	Paediatric Oncologist	Birmingham
Dr Andrew Peet	Paediatric Oncologist	Birmingham
Dr Britta Vormoor*	Paediatric Oncologist	Newcastle
Dr Gareth Veal	Paediatric Pharmacologist	

Germ Cell Tumour (GCT) Subgroup		
Name	**Specialism**	**Location**
Dr Gail Horan	Clinical Oncologist	Cambridge
Dr Chris Barton*	Clinical Research Fellow	Liverpool
Dr Dan Stark	Medical Oncologist	Leeds
Dr Claire Thornton	Pathologist	Belfast
Mark Brougham	Paediatric Oncologist	Edinburgh
Dr Juliet Hale	Paediatric Oncologist	Newcastle
Dr James Hayden	Paediatric Oncologist	Liverpool
Dr Mathew Murray	Paediatric Oncologist	Cambridge
Dr James Nicholson	Paediatric Oncologist	Cambridge
Dr Anthony Penn	Paediatric Oncologist	Manchester
Dr Sara Stoneham (Chair)	Paediatric Oncologist	London
Mr Suren Arul	Surgeon	Birmingham

Appendix 2

CSG & Subgroup Strategies: A – Main CSG Strategy

Children's Cancer & Leukaemia CSG Strategy: September 2014 – June 2016

This strategy timeline has been produced to support the CCL Research Strategy Plan of Implementation (Draft v0.3 September 2014). It runs from September 2014 until June 2016, and will be reviewed and updated (by MJ, JB and SA) on a regular basis.
The document is composed of the following:

Page 2 – 5: NCRI CCL CSG Strategy: plan of implementation, containing agreed strategic objectives (1-6), specific actions, CSG leads and proposed deadlines.

Page 6 – 7: Overview of the entire strategy timeline, spread over two pages; September 2014 – July 2015 (Page 6) and August 2015 – June 2016 (Page 7).

Page 8 – 9: Strategic objectives 1a – 1e, spread over two pages; September 2014 – July 2015 (Page 8) and August 2015 – June 2016 (Page 9). Same information as shown in the pink boxes of the plan of implementation (pages 2 – 3) and pink arrows of the overview (pages 6 – 7).

Page 10 – 11: Strategic objectives 2, 3a – 3c, spread over two pages; September 2014 – July 2015 (Page 10) and August 2015 – June 2016 (Page 11). Same information as shown in the grey and teal boxes of the plan of implementation (pages 3 – 4) and the grey and teal arrows of the overview (pages 6 – 7).

Page 12 – 13: Strategic objectives 4, 5 & 6, spread over two pages; September 2014 – July 2015 (Page 12) and August 2015 – June 2016 (Page 13). Same information as shown in the orange, yellow and blue boxes of the plan of implementation (pages 4 – 5) and the orange, yellow and blue arrows of the overview (pages 6 – 7).

CCL strategy leads

AB	Amos Burke	JB	Jane Beety
AE	Angela Edgar	JC	Julia Chisholm
AM	Anthony Michalski	JN	James Nicholson
AP	Andy Pearson	KW	Kate Wheeler
AV	Ajay Vora	MG	Mark Gaze
CC	Chris Copland	MJ	Meriel Jenney
DH	Darren Hargrave	MMcC	Martin McCabe
DHT	Danielle Horton-Taylor	MP	Mark Powis
DR	Derek Roebuck	PK	Pamela Kearns
EL	Eileen Loucaides	SA	Seema Alexander
GM	Guy Makin	SS	Sara Stoneham

Strategic objective	Action	CSG Lead	Date	Outcomes
1a. Portfolio development (general)	Development of prioritisation process for the development and set up of studies that takes account of CRCTU and PTC capacity, available funding opportunities and clinical need Determine level of use of tissue bank samples for clinical research	AM/ KW/ AV/ AP/ SS DH with tissue banks	Dec 2014 Report 6-monthly	
1b. Portfolio development (local control)	CSG subgroups to identify potential surgical studies, to be coordinated across the CSG Engage with Royal College of Surgeons initiative to increase the number of surgeons receiving training in clinical trials, by encouraging paediatric surgeons to attend national training events Link with CTRad to expand RT studies in CCL portfolio, including establishing a research programme for proton beam therapy as this facility is established in the UK	Subgroup Chairs/ MJ MP (await report from surgical workshop) MG	Ongoing Oct 2015 Jun 2015	
1c. Portfolio development (cross cutting themes)	Identify leads within the CSG to link with the following cross cutting CSGs and advisory groups: •Psychosocial Oncology and Late Effects Special Interest Group (survivorship and late effects) •Palliative and Supportive Care •Primary Care •Screening, Prevention and Early Diagnosis (SPED) Advisory Group	LC to put on agenda TBD at next CSG mtg GM TBD at next CSG mtg TBD at next CSG mtg	 Jun 2015 Jun 2015 Jun 2015 Jun 2015	
1d. NCRI Teenage and Young Adult CSG (TYA CSG)	Establish regular contact with NCRI TYA CSG to work together to widen participation in research studies by young people, and share papers Discuss possibility of regular meetings/teleconferences with NCRI TYA CSG Agree most effective way of adult and paediatric groups working together, e.g. Hodgkins and Sarcoma Invite AE to CCL CSG	MJ/ SS/ JC MJ/ SS/ JC AB/ AE MJ/ LC	Apr 2015 (TYA Strategy Day) Apr 2015 Feb 2015 Nov 2014	 Check progress Complete

Strategic objective	Action	CSG Lead	Date	Outcomes
1e. National Cancer Intelligence Network (NCIN)	Establish clear link with NCIN Children Teenage and Young Adults Site Specific Clinical Reference Group (CTYA SSCRG) Explore with NCIN the development of relapse studies that use relapse data from national data sets	MJ/ MMcC DH/GM	Winter 2014 ?	Complete
2. Increasing early phase activity and participation	Increase the availability of early phase studies for patients at all PTCs by: •Agreeing a development plan so more PTCs are able to undertake and deliver early phase studies to time and target •Promoting and monitoring the referral of patients between centres so that more patients are considered for early phase studies •Developing an information portal for parents and patients to gain knowledge of early phase trials (website?) Address the Paediatric Investigation Plan issue through the MHRA MJ on MHRA Paediatric Medicines Group Develop plan for how to take forward research opportunities with: •New drugs which show activity in childhood cancers but have been withdrawn from development by pharmaceutical companies •Increasing predictive biomarker studies that are undertaken by more pre-screening to effectively target novel agents and increase response rates •Increasing number of pharmacodynamics biomarkers to increase understanding of drug interactions with targets	DH/ PK/ GM ? DHT/ CC AP/ PK/ MJ AP/PK	May 2015 ? 2016 Ongoing June 2015	MJ writing to DH/PK/GM for update
3a. Raising profile	Routine dissemination of results from studies through Annual Trials meetings and Annual Report Clarify links with CCLG Special Interest Groups, holding back to back meetings where appropriate Submission of abstracts to : •NCRI Cancer Conference •European Cancer Organisation (ECCO) •NCIN Conference •SIOP •BSH	MJ/ EL/ All AM/ KW/ AV/ AP/ SS All	Nov 2014 May 2015 June 2015 Ongoing	Complete Check next date

Strategic objective	Action	CSG Lead	Date	Outcomes
3b. Ensuring successful delivery of studies through integration with NIHR CRN: Cancer to engage with PTCs	Clarify position of UK and Ireland CCL Clinical Research Forum within the new NIHR CRN structures and implement appropriate reporting structures	AB (NSL)	Feb 2014	Cancer National Theme Group
	Work with PTCs in England to ensure they are able to provide equity of access to the clinical research portfolio for their patients	AB (NSL)	Ongoing	
	Monitor studies that are open at PTCs within England and facilitate the development of balanced local portfolio	AB (NSL)	Ongoing	
	Input into emerging processes within England fir Local Clinical Research Networks to improve delivery of studies to time and target	AB (NSL)	Ongoing	NIHR CRN Speciality Objective
	Continue to develop and monitor the shared care model for POSCUs so they can participate in suitable studies, including consideration of shared care model between PTCs	AB (NSL)/PK	Ongoing	
	Promote the need for PTC research staff to access work force development opportunities within their LCRN and region in England	RDMs via AB (NSL)	Ongoing	
	Facilitate agreement of a set of data items that PTCs agree to collect to benchmark their performance with each other, including supplying information about whether patients are eligible for studies	AB (NSL) /MMcC	Mar 2016	
	Monitor resources provided for PTC and POSCU research teams in England, and flag where difficulties are encountered to NIHR CRN CC	AB (NSL)	Ongoing	
	Contribute as far as possible to NIHR CRN: Cancer Speciality Objectives so they reflect what LCRNs need to deliver to ensure CCL patients can access the full portfolio of studies within England	AB (NSL)	2015, then annual	
3c. Maximise output from clinical trials	Establish working groups for studies within 6 weeks of funding award to facilitate swift set up, including representation from CI, CRCTU, NIHR CRN: Cancer	CI/CRCTU/AB	Winter 2014	Complete for MyeChild study - put in Annual Report
4. Strengthen UK wide and international working	Refine clear prioritisation process for international clinical trials to be submitted for funding to optimise the timing of applications	PK/ All	?	
	Define funding opportunities for travel to attend meetings with international partners	TBD	Ongoing	
	Target seventh EU funding (Horizon 2020) for international studies where appropriate	DH	Dec 2014	

Strategic objective	Action	CSG Lead	Date	Outcomes
5. CSG structure and function	Establish Renal Working Party	MP	Jun 2015	Complete
	Establish Hepatobiliary Working Party	DR	Jun 2015	Complete
	Consider case for Germ Cell Tumour Subgroup	JN/ EL/ MJ	Done	Complete
	Consider establishing Working Party to develop appropriate research studies for patients with retinoblastoma. Discuss with Sue Picton in order to liaise with Retinoblastoma Special Interest Group	AB/ MJ/ SP	Jun 2015	Complete
	Central Nervous System and Brain Subgroup to consider setting up Working Party if appropriate	AM	Jun 2015	Complete
	Agree mechanism and governance for co-opting trainee registrars onto the main CSG and subgroups, including: •Transparency •Role •Selection Process •Tenure Period •Funding through CCLG and Cancer Research UK	MJ/ MG	Done	Complete
6. Patient and Public Involvement and Impact	Increase the number of consumers involved in the Paediatric Oncology Reference Team (PORT) through advertising for membership via the CCLG and members clinics	All	Ongoing	
	Increase the number of children in less developed countries that participate in clinical trials	DHT/ CC/ PK with relevant CCLG SIG	Ongoing	

Key – for page 6 onwards

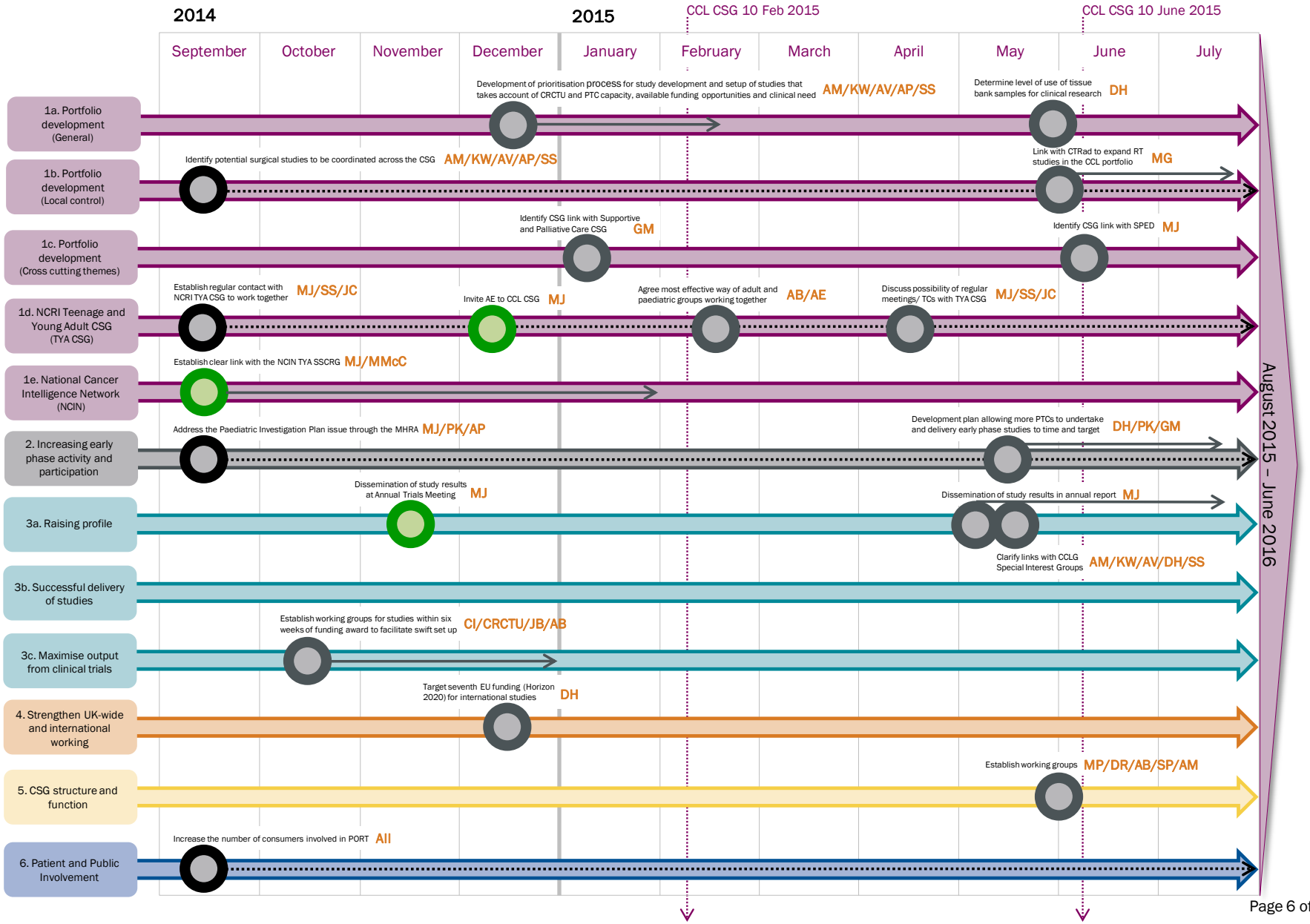
Proposed start date – TBC for objective 3b

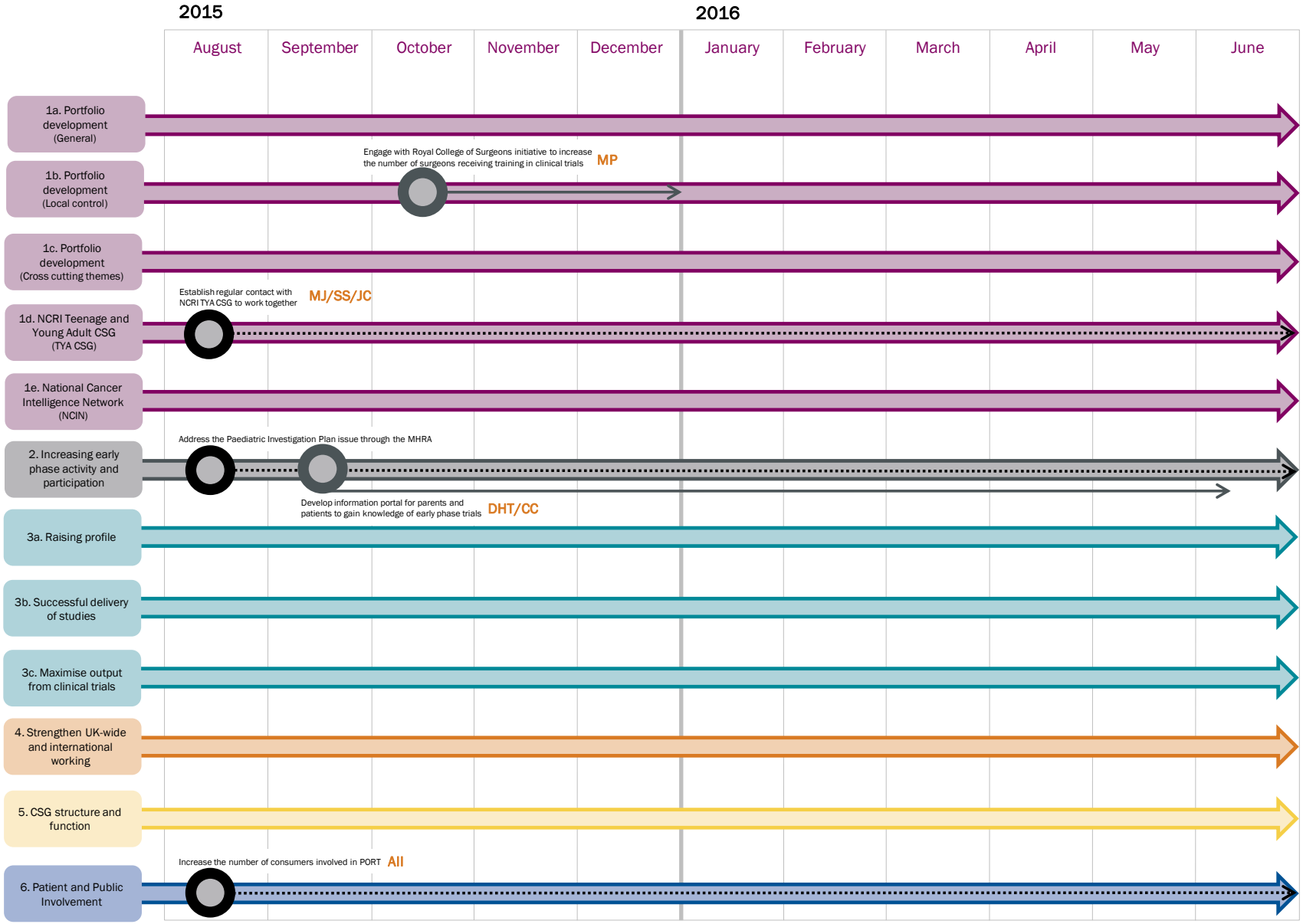
Proposed end date

Recurrent activity

XX CSG lead

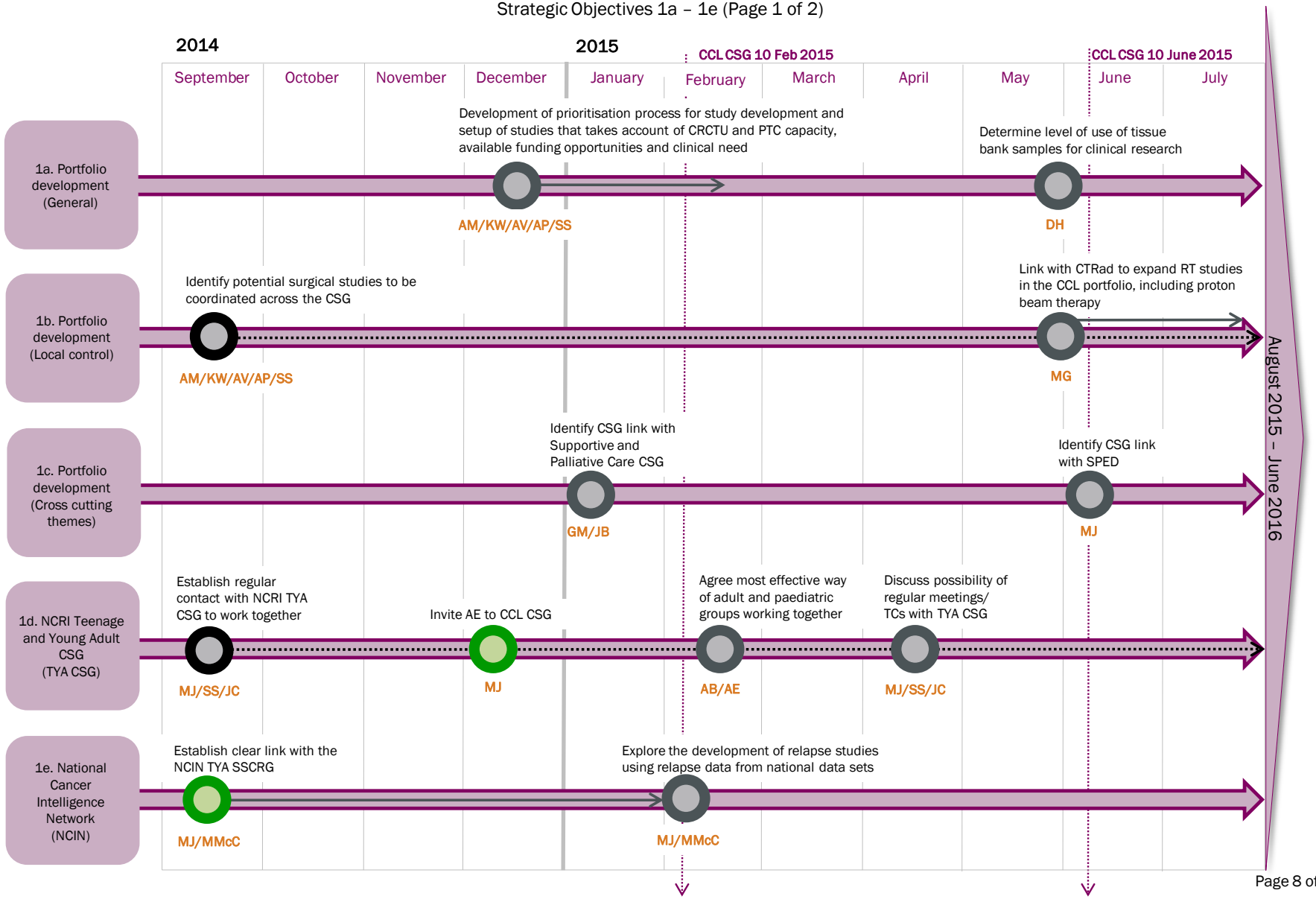
CSG meeting


2014
2015
CCL CSG 10 Feb 2015
CCL CSG 10 June 2015
September
October
November
December
January
February
March
April
May
June
July
1a. Portfolio development (General)
1b. Portfolio development (Local control)
1c. Portfolio development (Cross cutting themes)
1d. NCRI Teenage and Young Adult CSG (TYA CSG)
1e. National Cancer Intelligence Network (NCIN)
2. Increasing early phase activity and participation
3a. Raising profile
3b. Successful delivery of studies
3c. Maximise output from clinical trials
4. Strengthen UK-wide and international working
5. CSG structure and function
6. Patient and Public Involvement
Development of prioritisation process for study development and setup of studies that takes account of CRCTU and PTC capacity, available funding opportunities and clinical need AM/KW/AV/AP/SS
Determine level of use of tissue bank samples for clinical research DH
Identify potential surgical studies to be coordinated across the CSG AM/KW/AV/AP/SS
Link with CTRad to expand RT studies in the CCL portfolio MG
Identify CSG link with Supportive and Palliative Care CSG GM
Identify CSG link with SPED MJ
Establish regular contact with NCRI TYA CSG to work together MJ/SS/JC
Invite AE to CCL CSG MJ
Agree most effective way of adult and paediatric groups working together AB/AE
Discuss possibility of regular meetings/ TCs with TYA CSG MJ/SS/JC
Establish clear link with the NCIN TYA SSCRG MJ/MMcC
Address the Paediatric Investigation Plan issue through the MHRA MJ/PK/AP
Development plan allowing more PTCs to undertake and delivery early phase studies to time and target DH/PK/GM
Dissemination of study results at Annual Trials Meeting MJ
Dissemination of study results in annual report MJ
Clarify links with CCLG Special Interest Groups AM/KW/AV/DH/SS
Establish working groups for studies within six weeks of funding award to facilitate swift set up CI/CRCTU/JB/AB
Target seventh EU funding (Horizon 2020) for international studies DH
Establish working groups MP/DR/AB/SP/AM
Increase the number of consumers involved in PORT All
August 2015 – June 2016


2015
2016
August
September
October
November
December
January
February
March
April
May
June
1a. Portfolio development (General)
1b. Portfolio development (Local control)
Engage with Royal College of Surgeons initiative to increase the number of surgeons receiving training in clinical trials
MP
1c. Portfolio development (Cross cutting themes)
1d. NCRI Teenage and Young Adult CSG (TYA CSG)
Establish regular contact with NCRI TYA CSG to work together
MJ/SS/JC
1e. National Cancer Intelligence Network (NCIN)
2. Increasing early phase activity and participation
Address the Paediatric Investigation Plan issue through the MHRA
Develop information portal for parents and patients to gain knowledge of early phase trials
DHT/CC
3a. Raising profile
3b. Successful delivery of studies
3c. Maximise output from clinical trials
4. Strengthen UK-wide and international working
5. CSG structure and function
6. Patient and Public Involvement
Increase the number of consumers involved in PORT
All

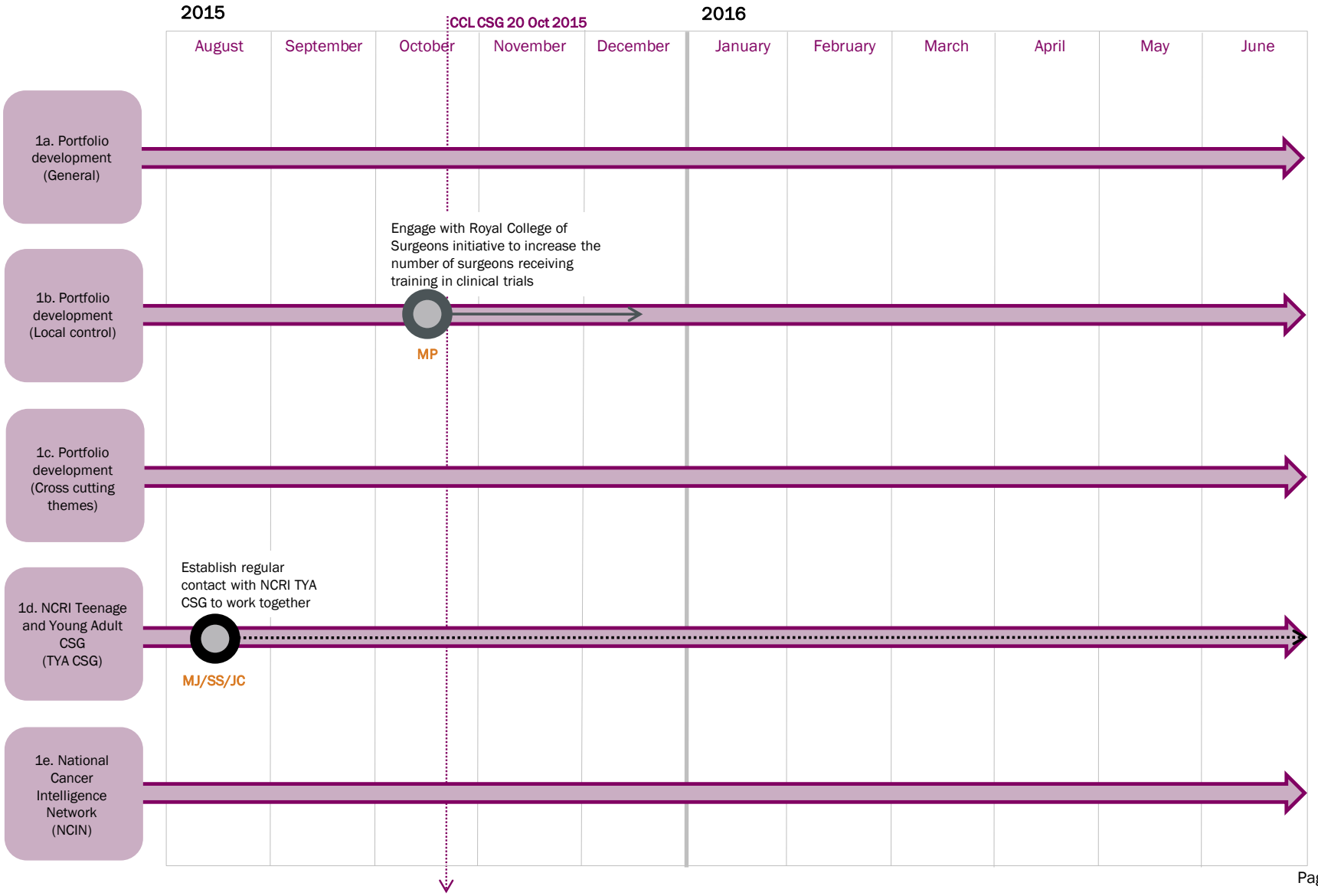
Children's Cancer & Leukaemia CSG Strategy: September 2014 – June 2016

Strategic Objectives 1a – 1e (Page 1 of 2)



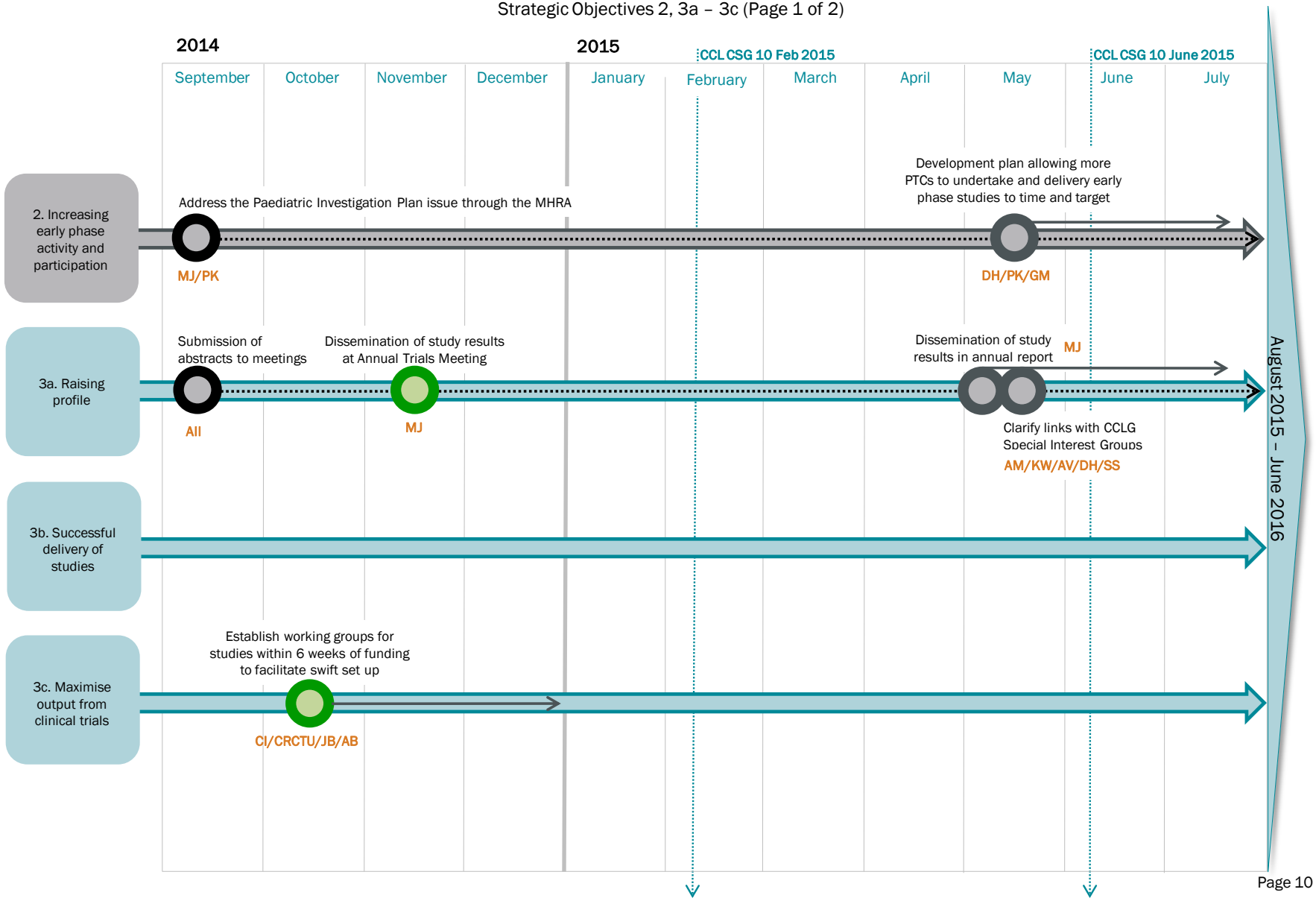
Children's Cancer & Leukaemia CSG Strategy: September 2014 – June 2016

Strategic Objectives 1a – 1e (Page 2 of 2)



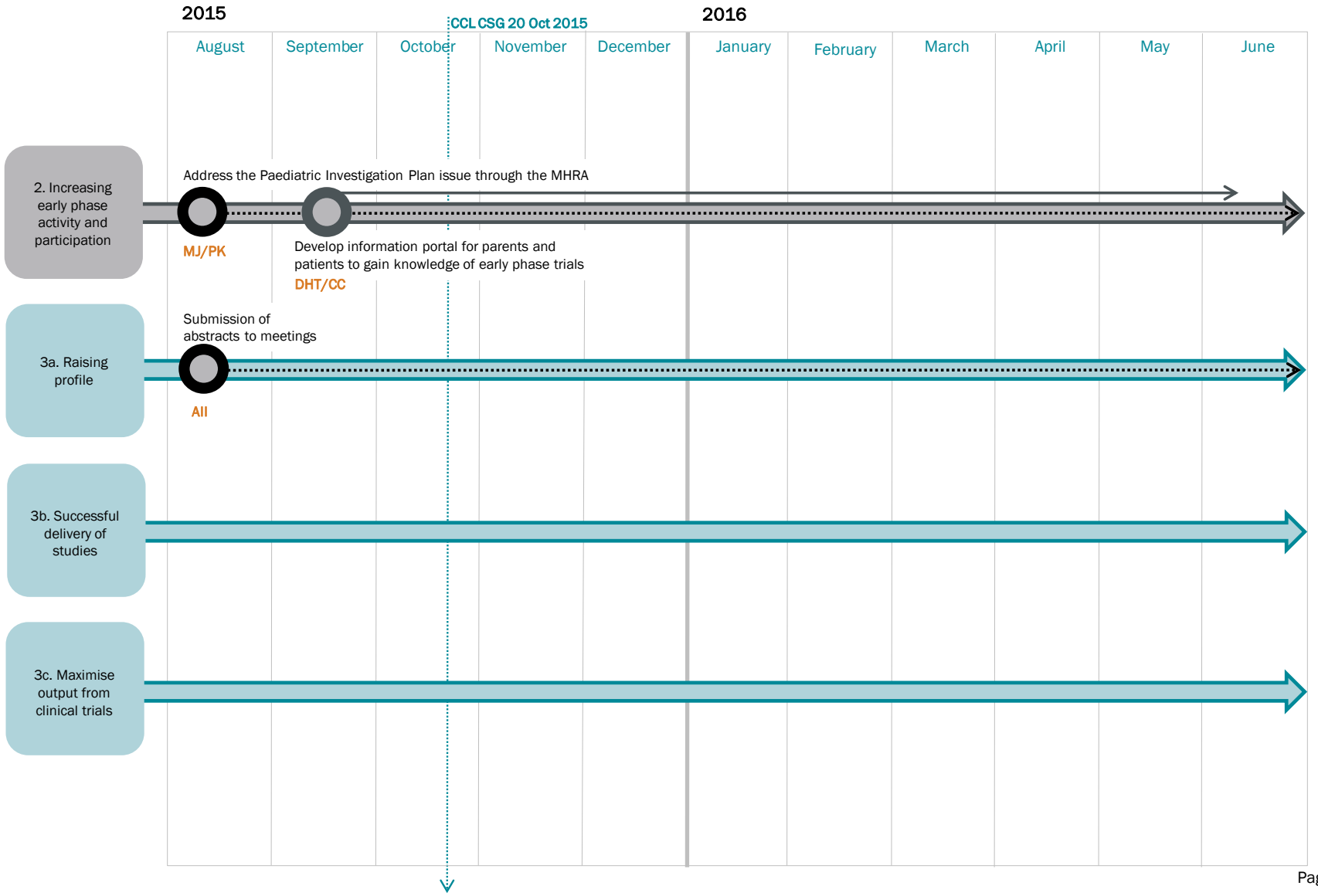
Children's Cancer & Leukaemia CSG Strategy: September 2014 – June 2016

Strategic Objectives 2, 3a – 3c (Page 1 of 2)



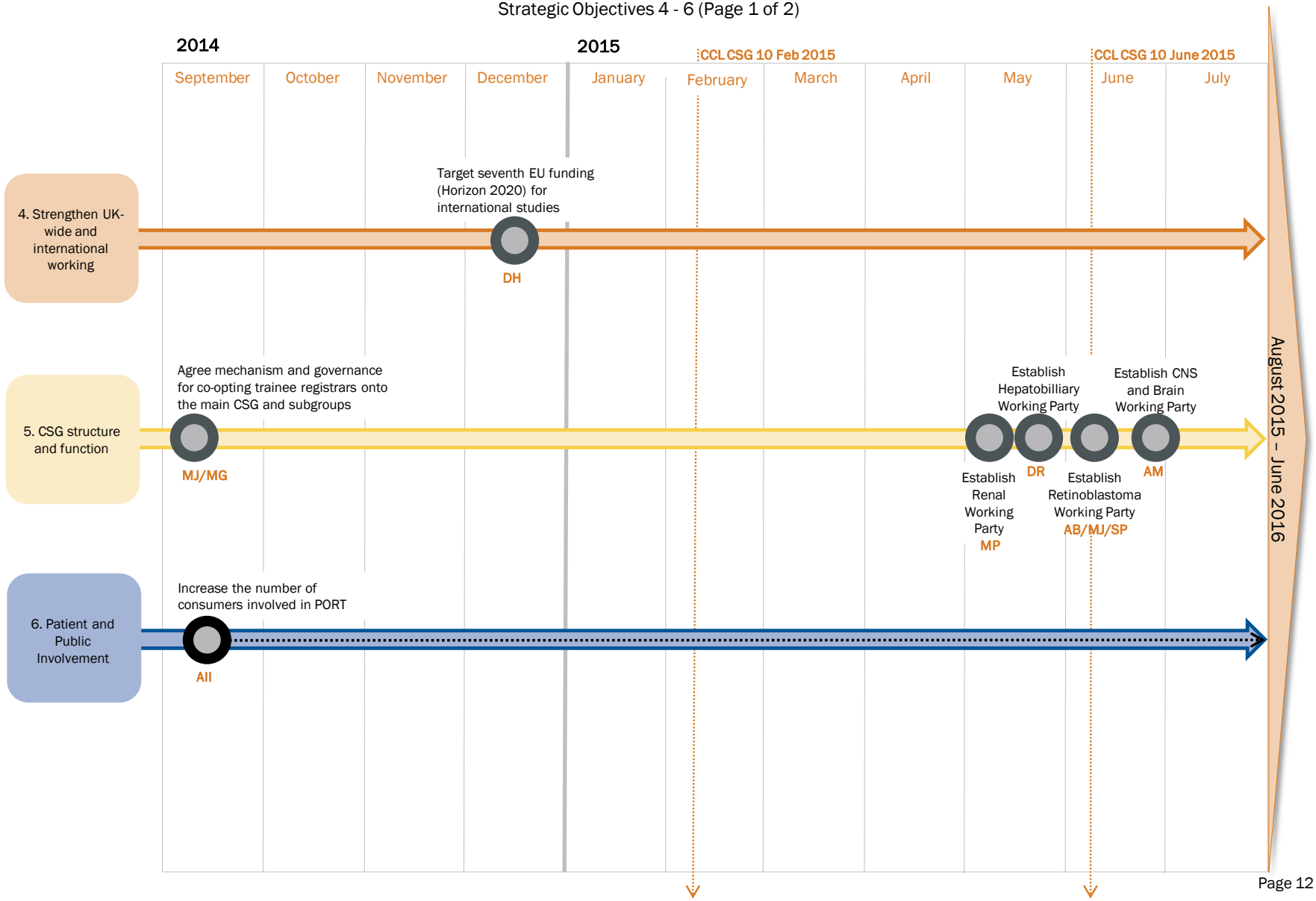
Children's Cancer & Leukaemia CSG Strategy: September 2014 – June 2016

Strategic Objectives 2, 3a – 3c (Page 2 of 2)



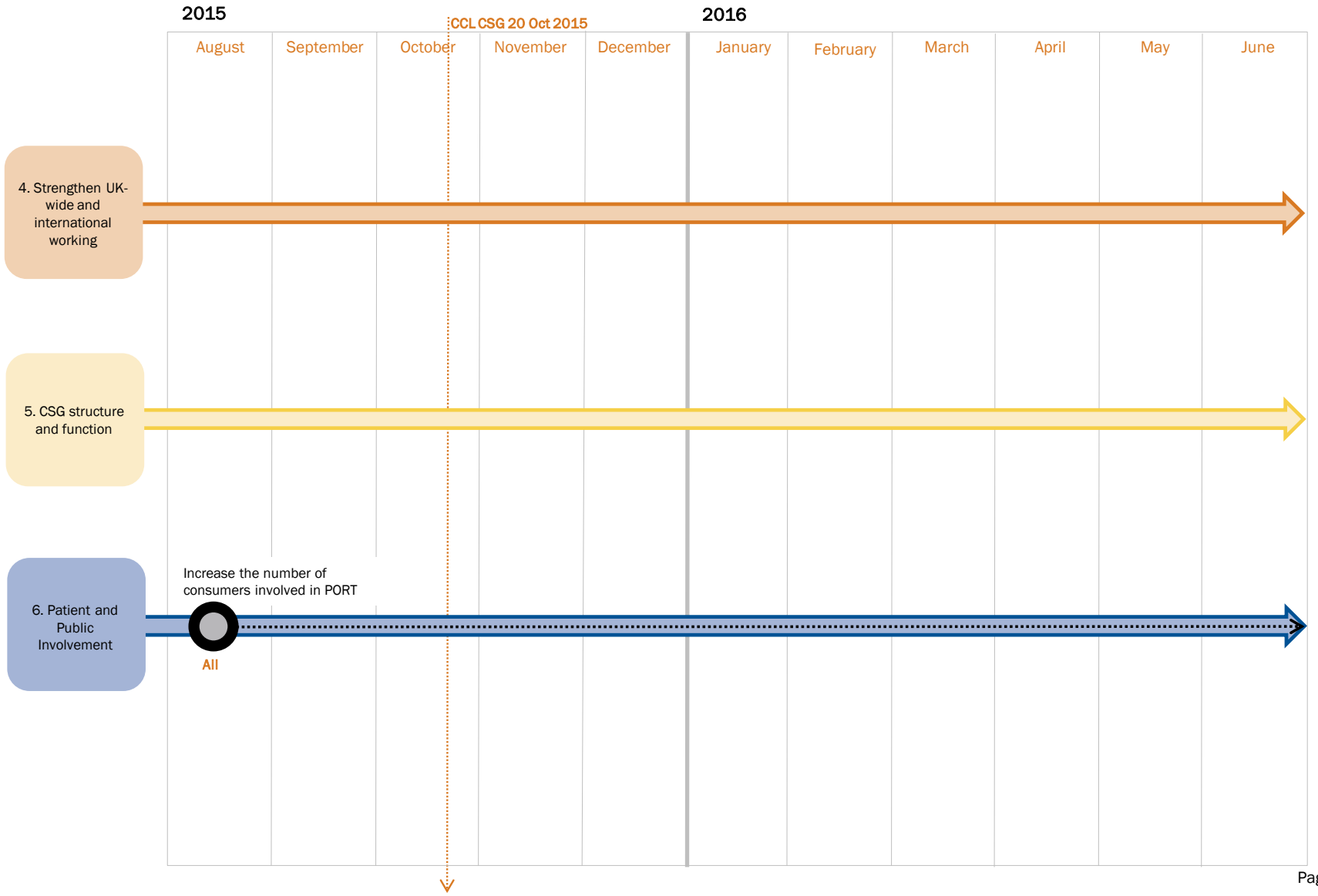
Children's Cancer & Leukaemia CSG Strategy: September 2014 – June 2016

Strategic Objectives 4 - 6 (Page 1 of 2)



Children's Cancer & Leukaemia CSG Strategy: September 2014 – June 2016

Strategic Objectives 4 - 6 (Page 2 of 2)



B – Novel Agents Subgroup Strategy

The main aim of the Novel Agents Subgroup is:

To develop biologically driven trials of novel therapies for childhood cancer based on the best scientific rationale and to provide trial access to as many patients as possible regardless of disease type or geographical location.

To try and achieve this aim the current strategic objectives are:

- To continue to increase the portfolio generally and consider how to provide better novel therapy access to underrepresented tumour entities by working with academics, industry and regulatory partners.
- To work closely with the pharmacology group in developing integrated and standalone PK studies to better understand the use of both existing and novel drug treatments in childhood cancer.
- Work with the Paediatric ECMC network to improve access to novel therapies and to consider the development of regional geographical early phase networks.
- Work with the main CSG to develop a Paediatric Stratified Medicine programme to allow the possible delivery of precision medicine studies in childhood cancer. Will include links to the NHS 100,000 Genome Medicine and CRUK Stratified medicine programmes.
- Continue and promote strong patient, public involvement in relation to subgroups activities and discussions with industry and regulatory partners.

C – Neuroblastoma Subgroup Strategy

Key aim: To improve event free and overall survival for all Neuroblastoma patients

Diagnosis, staging, risk stratification

Refine the prognostic significance of tissue and imaging biological markers and integrate them into stratification of treatment groups in clinical trials:

- Finalise analysis in current HR study of data linking biological markers, and radiology specifically mIBG scans 2016
- Evaluate FDG PET and mIBG PET
- Undertake an international retrospective study of ALK mutation testing and next generation sequencing for selected genes from banked DNA samples from patients treated on the high risk Neuroblastoma trial

Define molecular targets in NBL

Introduce molecular targeted treatments upfront into ultra-high risk and relapsed patient studies

- To continue to increase the portfolio of molecularly driven early phase trials for patients with relapsed neuroblastoma in conjunction with the NCRI New Agents Group.

High Risk NBL

Continue to enrol all eligible UK patients in the SIOPEN HR trial.

Work with the European group to develop the next HR trial for 2017.

Induction chemotherapy

Continue enrolling into R3 to evaluate the best induction regimen

Local therapy

Establish evidence for current local therapy in HR NBL, radiotherapy dose and extent of field and timing and extent of surgical excision of primary tumour

Immunotherapy

Define and refine Immunotherapy administration to maximise effectiveness and minimise toxicity

- Get the R4 in HR NBL 1 open in the UK and in all centres by 2015 Q3
- Open the Phase 1b trial of zoledronate and IL-2 combined with ch14.18 anti-GD2 antibody 2015
- Facilitate data collection and analysis re immunotherapy in HR study and LTI study 2017

Surveillance

Monitor off treatment HR patients with imaging and molecular monitoring and link with clinical data to better understand patterns of relapse:

- Set up a randomised maintenance treatment study with biomarker monitoring alongside maybe including DFMO 2016

Refractory disease

Get SIOPEN Veritas clinical trial open in the UK by 2016.

Relapsed disease

To better understand the biology and clinical characteristics of relapsed Neuroblastoma:

- Continue recruitment into BEACON study and get amendment through UK regulatory process for additional third randomisation with TOTEM 2015
- Await outcome of a grant application for a national retrospective genetic and Epidemiological study of relapsed Neuroblastoma 2015

Low and Intermediate Risk NBL

Facilitate registration and collection of toxicity and outcome data for these Neuroblastoma patients who are not currently treated within a clinical trial as unable to get the SIOPEN LINES trial open in the UK in 2012:

- Participate in the PICORET study, a Horizon 2020 project that is comparing outcome in comparable patients treated within and without a clinical trial. Await grant application 2015 Q4 and if favourable participate
- Achieve UK participation in the SIOPEN spinal cord compression study 2015/6
- Plan for involvement in next low and intermediate risk NBL trial if it involves further randomisations

D – Germ Cell Tumour (GCT) Subgroup Strategy

Strategic aims of the GCT Subgroup are:

1. Joint UK:US trial for all patients with GCT aged 0-25 years; stratified by risk and age.
2. Continue excellent recruitment to SIOP IC GCT II
3. Amend recently CTAAC funded Acc BEP for high risk patients to include patients < 16 years and to allow inclusion of female patients.
4. Secure funding for biological and PROMS as add on studies for AGCT 1531
5. Further analyses of MaGIC database: focusing on TYA outcomes; immature teratoma and dysgerminoma. Use this evidence to inform new trial design strata.
6. Development of evidence based guidelines/update guidelines on CCLG website whilst awaiting trial development.

E – Central Nervous System (CNS) Subgroup Strategy

The CNS Subgroup Strategy is to:

- Recruit to open studies
- Open PNET 5. SIOP Eependymoma and Biomede
- Complete development of studies for young children with medulloblastoma, high risk medulloblastoma
- With collaborators, continue to develop studies for gliomas and rare tumours
- Ensure QoS questions are asked in all trials, where appropriate. More specifically the QoS strategy, with regard to clinical studies, is to:
    - Demonstrate that on-line collection of PROMs is feasible in UK and SIOP studies of brain tumours, starting with national and international aspects of PNET5
    - Move forwards in establishing a sustainable and affordable way of enabling on-line PROMs to be collected in future studies
    - Use this method to obtain QoS data in future SIOP-E and CCL studies and in UK children receiving PBT
- Secure funding to explore the potential of on-line reports generated from on-line PROMs as an intervention to improve the QoL of children receiving out-patient care for brain tumours.
- Focus on aspects of imaging, namely:
    - Implement updated SIOPE imaging and functional imaging guidelines into clinical trials
    - Work with CR CTU and wider SIOPE group to develop databases which can incorporate imaging for central radiological review and quantitative analysis
    - Continue development of multi-centre functional imaging protocols – in particular perfusion imaging

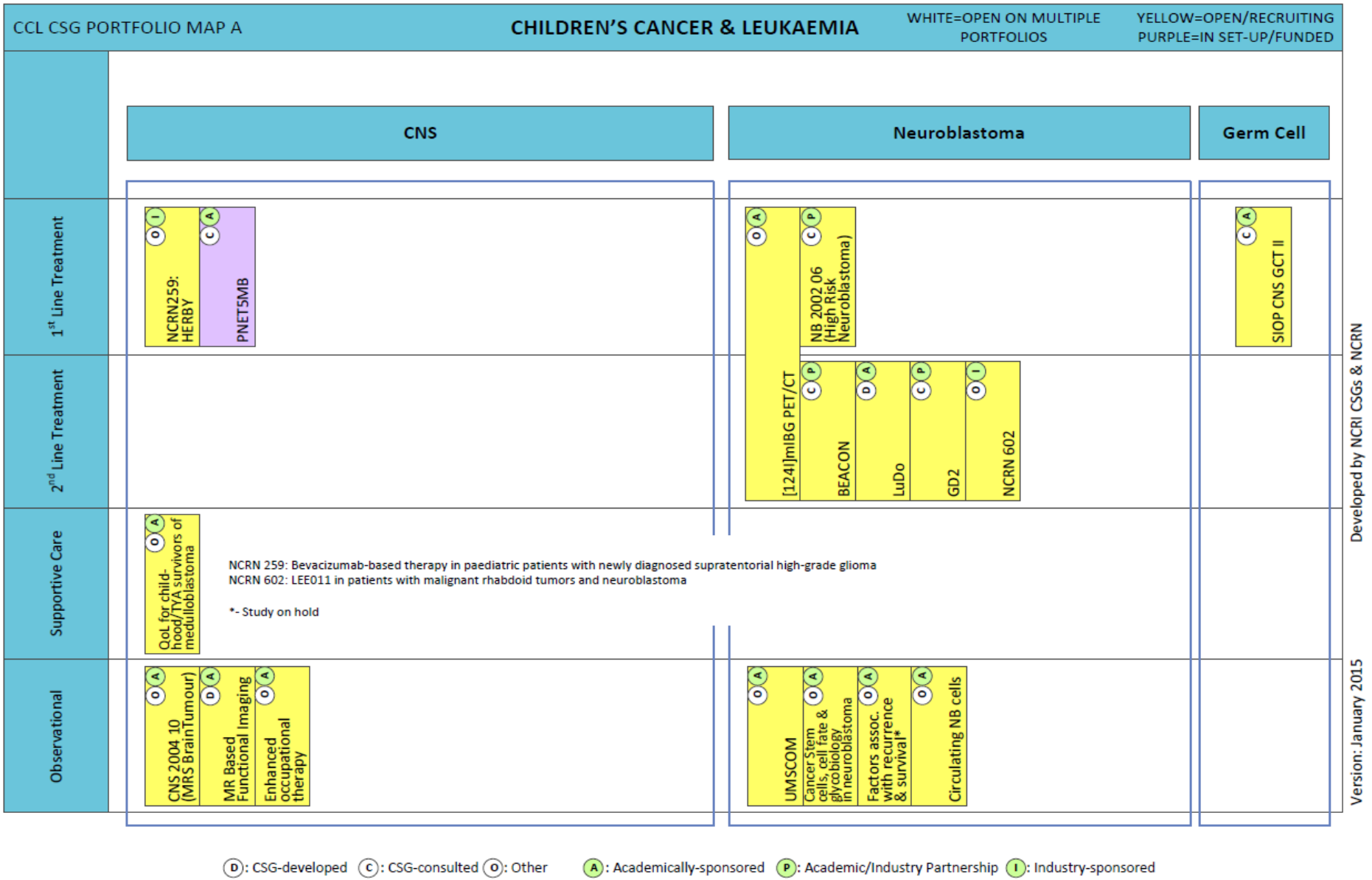
F – Leukaemia Subgroup Strategy

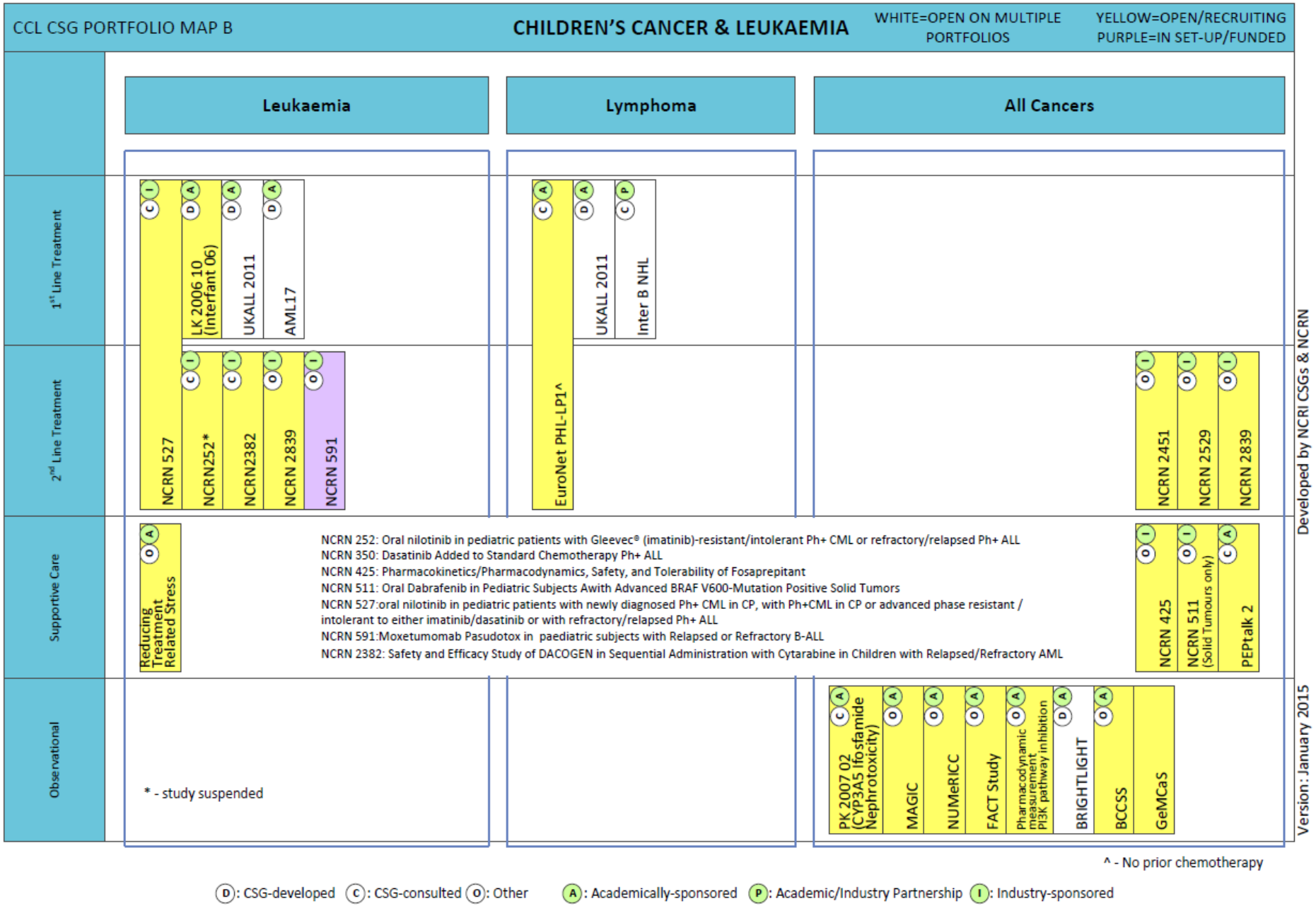
The strategy for the Leukaemia Subgroup is outlined below:

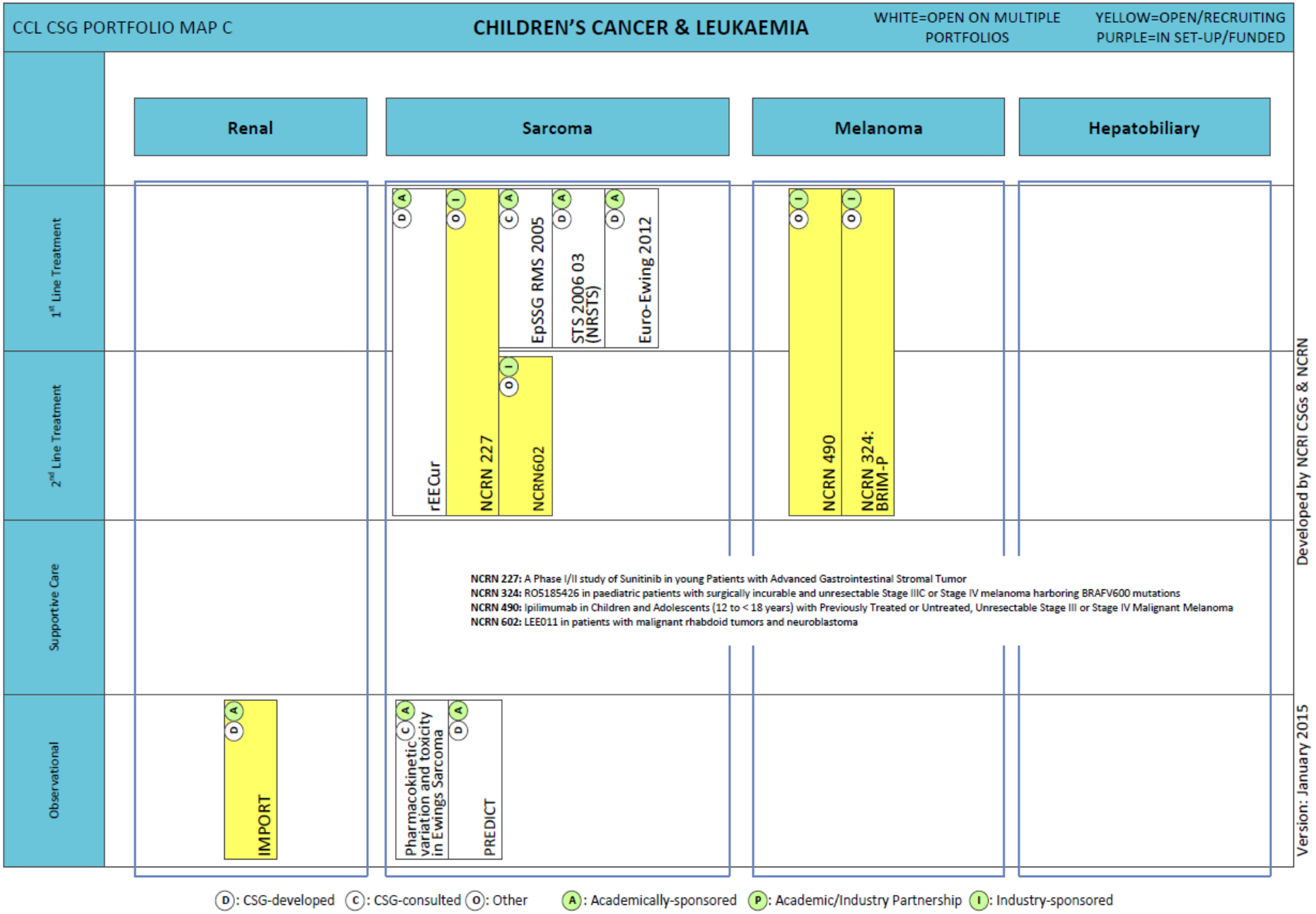
1) Improve recruitment to second randomisation of UKALL 2011 by allowing registration only entry.
2) Agree international trials for Ph-pos and infant ALL.
3) Open MyeChild this year.
4) Open registries with linked biological sample collection and studies for APL, DS-AML, CML and MDS.
5) Liaise with new agents group to increase portfolio of phase I and II leukaemia trials testing immune based and targeted agents.

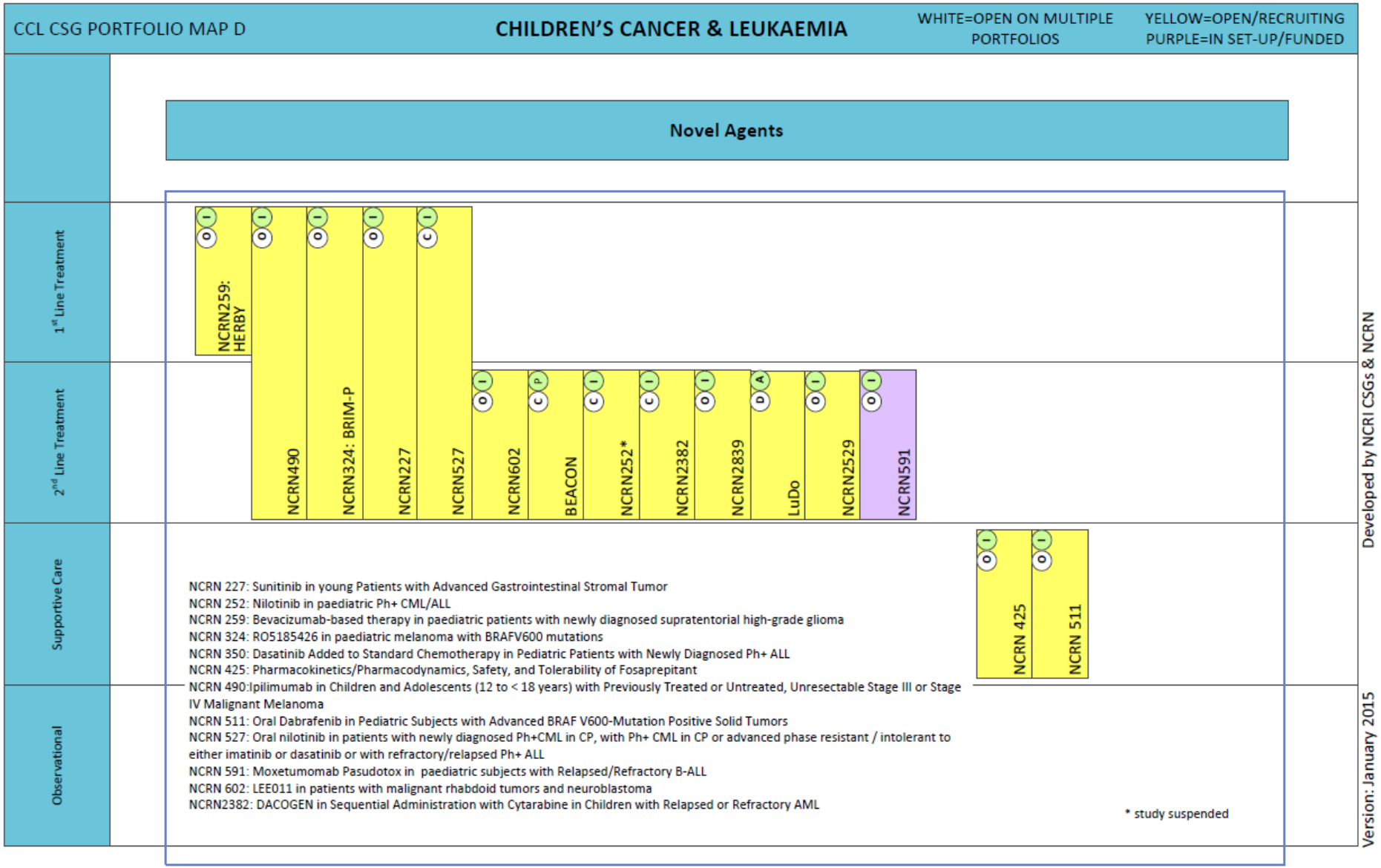
Appendix 3

Portfolio maps




CCL CSG PORTFOLIO MAP B
CHILDREN'S CANCER & LEUKAEMIA
WHITE=OPEN ON MULTIPLE PORTFOLIOS
YELLOW=OPEN/RECRUITING
PURPLE=IN SET-UP/FUNDED
Leukaemia
Lymphoma
All Cancers
1st Line Treatment
2nd Line Treatment
Supportive Care
Observational
NCRN 527
LK 2006 10 (Interfant 06)
UKALL 2011
AML17
NCRN252*
NCRN2382
NCRN 2839
NCRN 591
EuroNet PHL-LP1^
UKALL 2011
Inter B NHL
NCRN 2451
NCRN 2529
NCRN 2839
Reducing Treatment Related Stress
NCRN 425
NCRN 511 (Solid Tumours only)
PEPtalk 2
PK 2007 02 (CYP3A5 Ifosfamide Nephrotoxicity)
MAGIC
NUMeRICC
FACT Study
Pharmacodynamic measurement PI3K pathway inhibition
BRIGHTLIGHT
BCCSS
GeMCaS
NCRN 252: Oral nilotinib in pediatric patients with Gleevec® (imatinib)-resistant/intolerant Ph+ CML or refractory/relapsed Ph+ ALL
NCRN 350: Dasatinib Added to Standard Chemotherapy Ph+ ALL
NCRN 425: Pharmacokinetics/Pharmacodynamics, Safety, and Tolerability of Fosaprepitant
NCRN 511: Oral Dabrafenib in Pediatric Subjects Awith Advanced BRAF V600-Mutation Positive Solid Tumors
NCRN 527:oral nilotinib in pediatric patients with newly diagnosed Ph+ CML in CP, with Ph+CML in CP or advanced phase resistant / intolerant to either imatinib/dasatinib or with refractory/relapsed Ph+ ALL
NCRN 591:Moxetumomab Pasudotox in paediatric subjects with Relapsed or Refractory B-ALL
NCRN 2382: Safety and Efficacy Study of DACOGEN in Sequential Administration with Cytarabine in Children with Relapsed/Refractory AML
* - study suspended
^ - No prior chemotherapy
(D): CSG-developed (C): CSG-consulted (O): Other
(A): Academically-sponsored (P): Academic/Industry Partnership (I): Industry-sponsored
Developed by NCRI CSGs & NCRN
Version: January 2015


CCL CSG PORTFOLIO MAP C
CHILDREN'S CANCER & LEUKAEMIA
WHITE=OPEN ON MULTIPLE PORTFOLIOS
YELLOW=OPEN/RECRUITING
PURPLE=IN SET-UP/FUNDED
Renal
Sarcoma
Melanoma
Hepatobiliary
1st Line Treatment
2nd Line Treatment
Supportive Care
Observational
rEECur
NCRN 227
NCRN602
EpSSG RMS 2005
STS 2006 03 (NRSTS)
Euro-Ewing 2012
NCRN 490
NCRN 324: BRIM-P
IMPORT
Pharmacokinetic variation and toxicity in Ewings Sarcoma
PREDICT
NCRN 227: A Phase I/II study of Sunitinib in young Patients with Advanced Gastrointestinal Stromal Tumor
NCRN 324: RO5185426 in paediatric patients with surgically incurable and unresectable Stage IIIC or Stage IV melanoma harboring BRAFV600 mutations
NCRN 490: Ipilimumab in Children and Adolescents (12 to < 18 years) with Previously Treated or Untreated, Unresectable Stage III or Stage IV Malignant Melanoma
NCRN 602: LEE011 in patients with malignant rhabdoid tumors and neuroblastoma
Developed by NCRI CSGs & NCRN
Version: January 2015
(D): CSG-developed (C): CSG-consulted (O): Other (A): Academically-sponsored (P): Academic/Industry Partnership (I): Industry-sponsored


CCL CSG PORTFOLIO MAP D
CHILDREN'S CANCER & LEUKAEMIA
WHITE=OPEN ON MULTIPLE PORTFOLIOS
YELLOW=OPEN/RECRUITING
PURPLE=IN SET-UP/FUNDED
Novel Agents
1st Line Treatment
2nd Line Treatment
Supportive Care
Observational
NCRN259: HERBY
NCRN490
NCRN324: BRIM-P
NCRN227
NCRN527
NCRN602
BEACON
NCRN252*
NCRN2382
NCRN2839
LuDo
NCRN2529
NCRN591
NCRN 425
NCRN 511
NCRN 227: Sunitinib in young Patients with Advanced Gastrointestinal Stromal Tumor
NCRN 252: Nilotinib in paediatric Ph+ CML/ALL
NCRN 259: Bevacizumab-based therapy in paediatric patients with newly diagnosed supratentorial high-grade glioma
NCRN 324: RO5185426 in paediatric melanoma with BRAFV600 mutations
NCRN 350: Dasatinib Added to Standard Chemotherapy in Pediatric Patients with Newly Diagnosed Ph+ ALL
NCRN 425: Pharmacokinetics/Pharmacodynamics, Safety, and Tolerability of Fosaprepitant
NCRN 490:Ipilimumab in Children and Adolescents (12 to < 18 years) with Previously Treated or Untreated, Unresectable Stage III or Stage IV Malignant Melanoma
NCRN 511: Oral Dabrafenib in Pediatric Subjects with Advanced BRAF V600-Mutation Positive Solid Tumors
NCRN 527: Oral nilotinib in patients with newly diagnosed Ph+CML in CP, with Ph+ CML in CP or advanced phase resistant / intolerant to either imatinib or dasatinib or with refractory/relapsed Ph+ ALL
NCRN 591: Moxetumomab Pasudotox in paediatric subjects with Relapsed/Refractory B-ALL
NCRN 602: LEE011 in patients with malignant rhabdoid tumors and neuroblastoma
NCRN2382: DACOGEN in Sequential Administration with Cytarabine in Children with Relapsed or Refractory AML
* study suspended
Developed by NCRI CSGs & NCRN
Version: January 2015
(D): CSG-developed (C): CSG-consulted (O): Other (A): Academically-sponsored (P): Academic/Industry Partnership (I): Industry-sponsored

Appendix 4

Publications in the reporting year

UKALL 2003

Vora A, Goulden N, Mitchell C, Hancock J, Hough R, Rowntree C et al. Augmented post-remission therapy for a minimal residual disease-defined high-risk subgroup of children and young people with clinical standard-risk and intermediate-risk acute lymphoblastic leukaemia (UKALL 2003): a randomised controlled trial. *Lancet Oncol* 2014 July;15(8):809-18.

Patrick K, Wade R, Goulden N, Mitchell C, Moorman AV, Rowntree C et al. Outcome for children and young people with Early T-cell precursor acute lymphoblastic leukaemia treated on a contemporary protocol, UKALL 2003. *Br J Haematol* 2014 April 8.

O'Connor D, Bate J, Wade R, Clack R, Dhir S, Hough R et al. Infection-related mortality in children with acute lymphoblastic leukemia: a retrospective analysis of infectious deaths on UKALL 2003. *Blood* 2014 June 5.

Patrick K, Wade R, Goulden N, Rowntree C, Hough R, Moorman AV et al. Outcome of Down syndrome associated acute lymphoblastic leukaemia treated on a contemporary protocol. *Br J Haematol* 2014 May;165(4):552-5.

Patrick K, Vora A. Update on biology and treatment of T-cell acute lymphoblastic leukaemia. *Curr Opin Pediatr* 2015;27(1):44-49.

Buitenkamp TD, Izraeli S, Zimmermann M et al. Acute lymphoblastic leukemia in children with Down syndrome: a retrospective analysis from the Ponte di Legno study group. *Blood* 2014;123(1):70-77.

Russell LJ, Enshaei A, Jones L et al. IGH@ Translocations Are Prevalent in Teenagers and Young Adults With Acute Lymphoblastic Leukemia and Are Associated With a Poor Outcome. *J Clin Oncol* 2014.

Lennard L, Cartwright CS, Wade R, Vora A. Thiopurine dose intensity and treatment outcome in childhood lymphoblastic leukaemia: the influence of thiopurine methyltransferase pharmacogenetics. *Br J Haematol* 2014.

Mitchell C, Goulden N, Vora A. MRD stratification for paediatric ALL. *Lancet Oncol* 2014;15(10):e415-e416.

Moorman AV, Enshaei A, Schwab C et al. A novel integrated cytogenetic and genomic classification refines risk stratification in pediatric acute lymphoblastic leukemia. *Blood* 2014;124(9):1434-1444.

SIOP CNS GCT II

Stoneham S, Hale JP, Rodriguez-Galindo C, Dang H, Olson T, Murray M, Amatruda J, Thornton C, Arul S, Billmire D, Krailo M, Stark D, Covens A, Hurteau J, Stenning S, Nicholson JC, Gershenson

D, Frazier L. Adolescents and Young Adults with a “Rare” Cancer: Getting Past Semantics to Optimal Care for Patients With Germ Cell Tumors. *Oncologist* 2014;19:1–4

Frazier L, Hale JP, Rodriguez-Galindo C, Dang H, Olson T, Murray M, Amatruda JF, Thornton C, Arul S, Billmire D, Shaikh F, Pashankar F, Stoneham S, Krailo M, Nicholson JC. Revised Risk Classification for Pediatric Extracranial Germ Cell Tumors Based on 25 Years of Clinical Trial Data from the United Kingdom and United States. *J Clin Oncol*. 2015, Jan 10;33(2):195-201 (epub 2014, 10.1200/JCO.2014.58.3369

Appendix 5

Major international presentations in the reporting year

There were no major international presentations in the reporting year.