NCRI
National
Cancer
Research
Institute

NCRI
Head & Neck Cancer
Clinical Studies Group

Annual Report 2016-17

Partners in cancer research

NCRI Head & Neck Cancer CSG Annual Report 2016-17

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

The top three achievements in the year are outlined below:

1. The CSG has successfully operationalised the strategy that it developed early last year. An oral cancer study was successfully funded, as well as several oral health studies. Studies in the neoadjuvant setting and the surgical portfolio have also been developed and submitted for funding.
2. Recruitment into interventional trials reached its highest ever this year by a large margin, alongside a record increase in the number of trials that are open. The CSG has played a considerable role in setting up and recruiting into these trials.
3. The CSG membership underwent rejuvenation last year and the new membership has embedded well into the Group. The CSG allocated mentors and held a team building session specifically to help accelerate this process and to ensure that the newly formed CSG works well together. The Group has also engaged well with the Subspecialty Leads (SSLs) and instituted an annual meeting as well as four monthly updates and newsletters to keep dialogue open between the groups.

2. Structure of the Group

As mentioned above, the CSG membership was rejuvenated last year with seven new members: four oncologists, a medical oncologist, a nuclear medicine physician and a trials methodologist; they have embedded well into the Group. In addition, the Subgroups have been reviewed with a number of new members joining to increase the input into new trial development beyond the core Group. This has been in no small part due to an active strategy by the CSG which has included having a team building session, allocating mentors from the existing CSG members as well as having a welcoming and supportive environment.

3. CSG & Subgroup strategies

Main CSG

The CSG has progressed well towards operationalising and implementing the strategy developed in early 2016. The Group has already developed and obtained funding for a peri-operative oral adjuvant cancer trial, two studies in recurrent/metastatic disease and two oral health studies in oral xerostomia and osteoradionecrosis currently in set-up. The CSG has also operationalised and strengthened translational activities including developing standards and protocols for the

molecular stratification studies, developing a tissue collection study through setting up a head and neck GECIP and also developing capacity for molecular testing and molecularly-led trials (both through the work of Jackie James in Northern Ireland) and through the GeCIP 100,000 genome project. In the surgical field, the Liteform study has been funded and is in set-up, as is Lister and Valiant. An application has been submitted for a surgical trial examining tongue base mucosectomy.

Finally, work is continuing on developing a neo-adjuvant trial for laryngeal and hypopharyngeal cancers and several designs have been discussed and developed.

The CSG has also worked hard to embed its new members and develop strong links with the SSLs. Furthermore, the CSG has worked on continuing to strengthen the relationships with the EORTC and has had a leading role in the development of the Head and Neck Cancer International Group.

Thyroid Subgroup (Chair, Dr Kate Newbold)

The membership of the Thyroid Subgroup has changed over the last year with seven new members. This has balanced the spread of representation across the specialties involved with thyroid cancer management. However, the Subgroup is still looking for a member with nuclear medicine and radiology expertise and a consumer representative.

The Subgroup has been active in supporting NICE with expert statements for two reviews currently underway for systemic therapies in both differentiated and medullary thyroid cancer.

Research activity includes four academic studies, ELaTION, IoN, SEL-I-METRY and QaLM, and three pharma-led studies, EORTC 1209, Caprelsa and E7080-M000-213, open and recruiting at target rate. Two further studies are in set-up. The recent opening of SEL-I-METRY has been a significant achievement, led by Dr Jon Wadsley.

International collaborations are a priority and the first EORTC/ITOG (International Thyroid Oncology Group) trial investigating immunotherapy plus kinase inhibitor in advanced thyroid cancer is currently in development with involvement of the UK.

Areas identified for development include surgical research, management of high risk disease, molecular biomarkers and the role of TSH suppression. Trial proposals are in discussion for these areas with the target of protocol development by the next subgroup meeting in December.

Surgery & Localised Therapies Subgroup (Chair, Dr Jim McCaul)

The Surgery & Localised Therapies Subgroup is currently running and assisting in the running of interventional trials for head and neck premalignancy, oropharyngeal, hypopharyngeal and laryngeal cancer, and post-operative trials in oral cancer and mucositis and oral health trials. We continue to develop “window of opportunity” trials in all head and neck cancers treated primarily with surgery (AMG319 and INSPIRE are oral cavity only).

We have made significant progress in the following areas:

- Premalignancy: The LISTER trial (Lugols iodine visualisation for excision vs control) has now opened (currently in the feasibility phase) and is due to open in four centres. The SAVER trial of sodium valproate vs placebo for patients not suitable for surgical management has achieved funding from the Efficacy and Mechanism Evaluation programme and current efforts are around funding for placebo. Plans for a large

observational cohort study of patients with dysplasia and salivary cancer are underway with the Bristol head and neck 5000 trial team.

- Post-op trials in oral cancer: The Liteform trial (low level laser light therapy for patients with oral mucositis following adjuvant chemoradiotherapy or radiotherapy) has opened in a number of sites. The RaPTOR trial for medical therapy for osteoradionecrosis is again a placebo agent challenge for the Subgroup.

The Subgroup also has ongoing success with trials such as AMG-319 (TKI inhibitor vs control for all head and neck sites), PATHOS, PATHOS T, Best-of and ComPARE. We are supporting a new international commercial trial (INSPIRE – IRX therapeutics) which is currently undergoing UK ethics clearance.

Systemic Therapy & Radiotherapy Subgroup (Chair, Dr Professor Martin Forster)

The Systemic Therapy & Radiotherapy Subgroup had a change of leadership and refreshed membership in 2016. The existing trial portfolio has a healthy mix of early and late phase trials, and, following a strategy meeting earlier in 2016, a wave of new studies are in development. In locally advanced oropharyngeal disease, De-ESCALaTE successfully completed recruitment in low risk patients, with PATHOS ongoing. A proton therapy study is also being planned for this patient group. CompARE, a multi-arm phase III study, has opened for intermediate/high risk orophayngeal disease. In addition to earlier phase studies, ORCA2, BoHEMIaN and DARS have opened across broader disease sites. A multi-modality phase II/III study in high-risk hypopharnygeal/laryngeal cancers is being developed by a multi-centre consortium. NIMROD continues to recruit in patients not suitable for dual modality therapy, with the development of a future study in this setting under consideration. The AMG 319 windows study, exploring the impact of PI3Kδ inhibition in oral cavity cancers, is open and Wisteria, examining the chemo-potentiation effects of Wee1 inhibition including a pre-operative biological component, is in set-up. A larger phase II adjuvant study of nivolumab in oral cancer will be opening in late 2017. In recurrent disease, there are the EACH and POPPY studies evaluating immune checkpoint inhibition in combination with cetuximab or as monotherapy in patients of performance status 2 respectively.

Survivorship Subgroup (Chair, Professor Steven Thomas)

The remit of the Subgroup now includes epidemiology. Head and Neck 5000 is contributing to a range of collaborations - the link with the IARC has led to 1,000 participant's data being used in a genome-wide association study of oral cavity and oropharynx cancer. The most prominent finding overall and OPC meta-analyses was a strong association signal at 6p21.32 within the HLA class II region. Expansion of this collaboration is outlined in the strategy. H&N5000 is also part of the CRUK funded Integrative Cancer Epidemiology Programme (ICEP). This collaboration enables us to look at risk prediction and causality.

The portfolio has a number of NIHR funded trials currently in set-up including: A feasibility trial of pentoxifylline+tocopherol for the treatment of post-RT soft tissue fibrosis (trismus and dysphagia) in HNC survivors; a trial of Improving quality of life through the routine use of the Patient Concerns Inventory for head and neck cancer patients and a randomised controlled trial of the clinical and cost effectiveness of Low Level Laser in the management of Oral Mucositis in Head and Neck cancer irradiation. H&N5000 also contributes to a wide range of studies and analyses of patient related outcome measures. Five current Wellcome, CRUK, NIHR and MRC funded PhD fellowships and studentships linked to portfolio-based survivorship studies ensure the development of early career researchers in survivorship work.

4. Task groups/Working parties

There are no task groups or working parties

5. Patient recruitment summary for last 5 years

Patient recruitment into interventional trials is the highest that we have ever achieved. Recruitment into observational trials has started to increase following a significant dip after the completion of Head and Neck 5000. The second phase of Head and Neck 5000 is due to start in earnest and an increase in recruitment into observational trials is expected over the next year.

In the Head & Neck Cancer CSG portfolio, 11 trials closed to recruitment and 12 opened.

Table 1 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	2414	773	2374	681	24.9	7.2
2013/2014	2445	658	2415	602	25.4	6.3
2014/2015	1894	699	1888	654	19.8	6.9
2015/2016	527	641	527	631	5.54	6.63
2016/2017	841	1019	841	1004	8.84	10.55

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

Our CSG has had a main leadership role in the planning and founding of the Head and Neck Cancer International Group (HNCIG), which is a collaboration of 28 different national head and neck cancer research groups to develop harmonisation of protocols and collaboration. The CSG Chair is the founding Secretary of the HNCIG and several members of the CSG are members of the different committees. The Group has also participated in setting up a consensus radiotherapy QA document.

This Group has continued to strengthen its relationship with the EORTC head and neck group and this has resulted in the supporting of both the EORTC Best of trial and the PATHOS trial bilaterally. We continue to work with the oral health group to develop joint studies.

7. Funding applications in last year

The CSG has again had good success with its funding applications.

Table 2 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)			
Study	**Application type**	**CI**	**Outcome**
May 2016			
Biological sample collection for translational research within the Head and Neck cancer DARS and ART DECO radiotherapy trials	Sample collection	Dr Sheerang Bhide & Dr Mike Hubank	Not funded
Is ablative radioiodine Necessary for low risk differentiated thyroid cancer patients	Full application	Dr Ujjal Mallick	Funded

November 2016			
Optimizing immunotherapy for head and neck cancer	EMPA Outline	Professor Christian Ottensmeier	Invited to full
Accelerating the development, implementation and personalisation of combinatorial immunotherapeutic treatments for head and neck cancer (ADePT platform)	EMPA Outline	Professor Hisham Mehanna	Not invited to full
CRUK/11/043: De-ESCALaTE-HPV: Determination of Epidermal growth factor receptor-inhibitor (cetuximab) vs Standard Chemotherapy early and Late Toxicity Events in Human Papilloma Virus Positive oropharyngeal carcinoma	Full (Extension)	Professor Hisham Mehanna	Supported
Intergroup Study (EORTC-1420-HNCG-ROG) Phase III study assessing the "best of" radiotherapy compared to the "best of" surgery (trans-oral surgery (TOS)) in patients with T1-T2, N0 oropharyngeal carcinoma.	Full application	Professor Mererid Evans	Supported
The Efficacy and cost effectiveness of real time ultrasound Elastography in the investigation of Thyroid Nodules and the diagnosis of thyroid cancer - collection study (ELATION - Collect)	Sample Collection	Professor Hisham Mehanna	Not Supported
Other committees			
Study	**Committee & application type**	**CI**	**Outcome**
ECLIPSE study: Immunotherapy for post-operative oral cancer	BMS	Dr Joseph Sacco	Funded
POPPY: A randomised phase II trial to assess the efficacy and safety profile of pembrolizumab in patients of performance status 2 with recurrent or metastatic squamous cell carcinoma of the head and neck	MSD	Dr Martin Forster	Funded
EACH: Evaluating Avelumab in Combination with cetuximab in Head and Neck Cancer	Merck	Dr Martin Forster	Funded

8. Collaborative partnership studies with industry

The CSG has very good relationships with all major pharmaceutical companies including BMS, AstraZeneca and Merck. Industry has funded the fifth arm of the CompARE trial (AstraZeneca), the ECLIPSE trial in the post-operative setting (BMS) and the OPPY and EACH trials in the recurrent metastatic setting ((MSD and Merck respectively).

9. Impact of CSG activities

Internationally, the Group has led efforts to develop and establish a collective of national head and neck cancer clinical trials research groups. We have played a major part in negotiations and the CSG Chair is the founding Secretary of the HNC International Group.

The Group has provided considerable support to CRUK Clinical Research Committee in reviewing a large number of applications this year. The CSG has also participated in at least four NICE evaluations of technology, including the appraisal of nivolumab evaluationfor recurrent/metastatic disease.

The CSG and the UK also had significant participation in the Checkmate 141 study which recently reported in the New England Journal of Medicine showing benefit for the use of nivolumab in the recurrent/metastatic setting.

The Group's clinical trials fellowships have continued to expand, now encompassing several new areas including medical oncology, radiology and pathology. The result of this is that several fellows have developed their own studies and submitted them for funding. The fellowships are now being used as templates for other joint projects between the professional bodies in head and neck cancer in the UK.

10. Consumer involvement

The CSG currently only has one consumer member, Emma Kinloch, who has played a key role in the work of the Group including the development of new studies, contributing to the CSG's review of proposals seeking funding, development of patient information material and inputting into the future strategy of the CSG.

Emma has been a member of the Group since 2015 and is also a member of the patient and public advisory panel for radiotherapy research in cancer of the head and neck at Guy's and St Thomas's Hospital. Through her work running a head and neck support group in London and connections to other UK wide and international groups, current key patient feedback is fed into the work of the CSG. Her involvement with patient networks relating to rarer cancer types has led to collaboration of the set-up of a new UK wide network for salivary gland cancers with connections made through and supported by the CSG.

We are currently actively recruiting to the second vacant consumer post.

11. Open meetings/annual trials days/strategy days

Our strategy has been not to run an annual trials meeting due to the busy meetings calendar but instead undertake targeted updates within the different meetings in the UK. This year we have presented at the two main meetings of Head and neck cancer clinicians: the BAHNO Annual Scientific Meeting (the largest head and neck meeting in the UK) and the annual York head and neck cancer meeting.

12. Priorities and challenges for the forthcoming year

Priorities

1. To operationalise the thyroid cancer strategy and develop studies to achieve that.
2. Progress development of an observational study.
3. To develop a study for high risk locally advanced hypopharyngeal/laryngeal cancerSet.

Challenges

1. Development of the NRG group in the USA (amalgamation of three clinical trials study groups), attracting more industry collaboration due to its size and funding of infrastructure allocated specifically to head and neck cancer.
2. Lack of sufficient infrastructure in many centres to support clinical trials in head and neck cancer.

3. Obtaining funding for questions other than those examining immunotherapy, especially questions on existing therapies.

13. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies
- A – Main CSG Strategy
- B – Thyroid Subgroup Strategy
- C – Surgery & Localised Therapies Subgroup Strategy
- D – Systemic Therapy & Radiotherapy Subgroup Strategy
- E – Survivorship Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous year

Appendix 6 – Strengths & Weaknesses from the Head & Neck Cancer CSG 2016 Quinquennial Review (QQR)

Professor Hisham Mehanna (Head & Neck Cancer CSG Chair)

Appendix 1

Membership of the Head & Neck Cancer CSG

Name	Specialism	Location
Mr Oliver Dale*	Clinical Fellow	Gloucestershire
Ms Clare Schilling*	Clinical Fellow	London
Mr John Biddlestone*	Clinical Lecturer	Glasgow
Dr Olly Donnelly*	Clinical Oncologist	Southampton
Dr Stefano Fedele	Clinical Oncologist	London
Dr Bernie Foran	Clinical Oncologist	Sheffield
Dr Nachiappan Palaniappan	Clinical Oncologist	Cardiff
Dr Kate Newbold	Clinical Oncologist	London
Dr Ioanna Nixon	Clinical Oncologist	Edinburgh
Dr Stefano Schipani	Clinical Oncologist	Glasgow
Dr David Thomson	Clinical Oncologist	Manchester
Ms Emma Kinloch	Consumer	London
Dr Martin Forster	Medical Oncologist	London
Dr Joseph Sacco	Medical Oncologist	Liverpool
Dr Jacqueline James	Pathologist	Belfast
Dr Max Robinson	Pathologist	Newcastle
Dr Karwan Moutasim*	Pathologist	Southampton
Professor Stephen Porter	Professor of Oral Medicine	London
Dr Wai Lup Wong	Radiologist	Middlesex
Dr Christina Yap	Statistician	Birmingham
Mr Jagtar Dhanda*	Surgeon	Staffordshire
Dr Emma King	Surgeon	Southampton
Professor Jim McCaul	Surgeon	Glasgow
Professor Hisham Mehanna (Chair)	Surgeon	Birmingham
Mr Vinidh Paleri	Surgeon	Newcastle
Professor Steven Thomas	Surgeon	Bristol
Mr Stuart Winter	Surgeon	Oxford

* denotes trainee member

Membership of the Subgroups

Thyroid Subgroup		
Name	**Specialism**	**Location**
Dr Matt Beasley	Clinical Oncologist	Bristol
Dr Kate Garcez	Clinical Oncologist	Manchester
Dr Laura Moss	Clinical Oncologist	Cardiff
Dr Kate Newbold (Chair)	Clinical Oncologist	London
Dr Jon Wadsley	Clinical Oncologist	Sheffield
Dr Kristien Boeleart	Endocrinologist	Birmingham
Professor Mark Strachan	Endocrinologist	Edinburgh
Professor David Gonzalez de Castro	Genomic Medicine	Belfast
Dr Sarah Johnson	Pathologist	Newcastle
Dr David Poller	Pathologist	Portsmouth
Dr Sarah Brown	Statistician	Leeds
Mr Dae Kim	Surgeon	London
Mr Saba Balasubramanian	Surgeon	Sheffield

Surgery & Localised Therapy Subgroup		
Name	**Specialism**	**Location**
Mr Paul Nankivell*	Clinical Fellow	Birmingham
Mr Andrew Schache*	Clinical Fellow	Liverpool
Dr Mereid Evans	Clinical Oncologist	Cardiff
Mr Max Robinson	Pathologist	Newcastle
Professor Terry Jones	Surgeon	Liverpool
Mr Tas Kanatas	Surgeon	Leeds
Mr Mike Nugent	Surgeon	Sunderland
Dr Emma King	Surgeon	Southampton
Mr Jim Mccaul (Chair)	Surgeon	Glasgow
Professor Hisham Mehanna**	Surgeon	Birmingham
Mr Vin Paleri	Surgeon	Newcastle
Professor Richard Shaw**	Surgeon	Liverpool

Systemic Therapy & Radiotherapy Subgroup		
Name	**Specialism**	**Location**
Dr Martin Forster (Chair)	Medical Oncologist	London
Dr Bernie Foran	Clinical Oncologist	Sheffield
Dr Joe Sacco	Medical Oncologist	Liverpool
Dr Anthony Kong	Clinical Oncologist	Birmingham
Dr Shree Bhide	Clinical Oncologist	London
Dr Ketan Shah	Clinical Oncologist	Oxford
Dr Emma King	Surgeon	Southampton
Dr Kathy West	Molecular Path	Manchester
Professor Wim Oyen	Radiologist	Oxford
Dr Stefano Schipani	Clinical Oncologist	Glasgow

Survivorship Subgroup		
Name	**Specialism**	**Location**
Dr Cherith Semple	CNS	Ulster
Catriona Mayland	Palliative Care	Liverpool
Mrs Christine Allmark	Consumer	West Yorkshire
Professor Gerry Humphris	Psychologist	St Andrews
Dr Jo Patterson	Speech& language	Newcastle
Professor Mary Wells	Cancer Nurse	Stirling
Professor Steven Thomas (Chair)	Surgeon	Bristol

*denotes trainee member

**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

Head and Neck CSG Strategy: January 2016 – December 2018

This strategy timeline has been produced to define the Head and Neck Cancer Research Strategy Plan and its implementation and will be reviewed and updated at each CSG meeting (supported by All)
The document is composed of the following:

Page 2 – 7: NCRI Head and Neck CSG Strategy: plan of implementation, containing agreed strategic objectives (1- 7), specific actions, CSG leads and proposed deadlines.

Head and Neck Cancer CSG Members		Responsibility
HM	Hisham Mehanna	CSG Chair
ST	Steve Thomas	Survivorship Subgroup Chair
KN	Kate Newbold	Thyroid Subgroup Chair
JM	Jim McCaul	Surgery & Localised Therapies Subgroup Chair
KH	Kevin Harrington	Systemic & Radiotherapy Subgroup Chair
BF	Bernie Foran	Clinical Oncology
TGU	Teresa Guerrero-Urbano	Clinical Oncology
IN	Ioanna Nixon	Clinical Oncology
SS	Stefano Schipani	Clinical Oncology
MF	Martin Forster	Medical Oncology
SP	Stephen Porter	Oral Medicine
EK	Emma King	Surgical Studies
VP	Vin Paleri	Surgical Studies
SW	Stuart Winter	Surgical Studies
GT	Gareth Thomas	Pathology/Translational research lead
MR	Max Robinson	Pathology lead
JH	Jo Haviland	Statistics Lead
WLW	Wai Lup Wong	Radiology Lead
SF	Stefano Fedele	Oral Medicine Lead
ND	Nanita Dalal	NCRI Administrator
NK	Nicola Keat	NCRI, Head of Clinical Research Groups

Strategic objective	Action	CSG Lead	Date	Outcomes
Identify key research areas	Establish a set of priorities and set up studies taking into account the over subscription of oropharyngeal cancer studies, clinical need and the international scene. These areas are identified as follows: **Pre malignancy** Large observational trials **Laryngeal and hypopharyngeal cancers** Michigan protocol for primary CRT Immunomodulatory studies for post op high risk patients **Oral cancers** Immunomodulatory studies for post op high risk patients **Surgery** Functional outcomes of surgery versus radiotherapy in early supraglottic cancer. Window of opportunity trials **Oral health** Radio protectives and treatment for oral fibrosis and xerostomia and osteoradionecrosis **Translational** Developing standard protocols and studies for molecular stratification of patients in trials Imaging studies predicting treatment response and guiding extent of treatment. Develop studies for improved surveillance and detection of recurrence using combinations of imaging and molecular markers, eg circulating DNA **Thyroid** Molecular profiling Better surveillance Immunomodulatory therapies	ALL	Strategy day 26 January 2016. Progress review 6 monthly at CSG meetings	

Strategic objective	Action	CSG Lead	Date	Update
2a Portfolio development. Observational studies	Develop a new large observational study in oral and laryngeal pre-malignancy building on: a. Expertise developed in Head and Neck 5000 b. Allowing and enabling nested studies c. Developing core outcomes set d. Incorporating genomics and epigenomics e. Incorporating health economics	ST	Dec 2016	Still exploring study in dysplasia
2b Portfolio development. Neoadjuvant setting	Examine feasibilty of study validating the Michigan protocol for chemoradiosensitivity in laryngeal and hypopharyngeal cancers to include: a. Imaging (PET CT) and genomic markers of response b. May incorporate additional treatments c. Need pre-clinical work with patient reps and incorporation of feasibility study	VP/IN	Dec 2016	Working group established and designed study application in Q4 2017
2c Portfolio development. Post-Operative setting	Escalation of treatment for high risk post-operative patients. For example with addition of immunomodulatory agent in addition to post-operative CRT or RT	MF/Sacco/SS	Dec 2016	Study funded and protocol being written
2d Portfolio development. Surgical studies	Study looking at functional outcomes and quality of life for patients with T1/T2 N0 supraglottic cancer having surgery versus radiotherapy Study to assess efficacy of transoral mucosectomy for occult primary Development of window of opportunity trials	VP/SW HM	Dec 2016 Dec 2016	Discontinued Application submitted. Now being resubmitted 2 studies opened and platform study planned

Strategic objective	Action	CSG Lead	Date	Outcomes
2e Oral Health Following treatment	Studies comparing different radioprotective agents to prevent and/or reduce: a. Fibrosis post radiotherapy b. Xerostomia post radiotherapy c. Osteoradionecrosis Both studies should incorporate the development of biomarkers for development of sequelae to treatment	SP / SF	Dec 2016	Sudies funded and in set up on xerostomia and osteoradionecrosis
2f Thyroid	Develop international collaborations further to increase patient recruitment Develop molecular biology driven studies with improved risk stratification Explore immunomodulatory therapies for thyroid Develop studies on follow up and detection of recurrence and tissue collections	KN and All thyroid subgroup DP	Ongoing July 2017 Ongoing Dec 2016	Ongoing Ongoing Study designed and application submitted
2g Imaging and biomarkers studies	Develop standards and capacity for molecular testing and molecular led trials. Develop a sample/tissue/assays collection study. Develop imaging studies both to predict response to treatment eg in the neo adjuvant setting and to guide treatment.	GT/MR MR, GT & KM WLW SS	Ongoing Dec 2016 Dec 2016	Strategy put in place Tissue study developed – submitted Standards being developed

Strategic objective	Action	CSG Lead	Date	Updates
3 Improving external communication and collaboration 3a Ensuring successful delivery of studies through working with NIHR CRN: Cancer	CSG members to commit to delivering studies developed by the CSG	All	Ongoing	Ongoing for all
	Interaction with CRN Subspecialty Leads to determine placement of new studies and address barriers to actively recruiting patients	All	Ongoing	
	Monitor recruitment to portfolio studies, esp those developed by the CSG to ensure delivery to time and target	All	Ongoing	
	Contribute as far as possible to NIHR CRN: Cancer Speciality Objectives so they reflect what LCRNs need to deliver to ensure head and neck cancer patients can access the full portfolio of studies within UK	All	Ongoing	
	Utilise patient power to pressurise hospitals into taking on trials	EK	Ongoing	
	Work to ensure research and clinical trials are core to NHS and continue to push for ring fenced time for trials and research in job plans.	HM/All	Ongoing	
	Work to address impediments to clinical trials in head and neck cancer through liaising with CRN cancer on areas needing increased capacity such at RTQA, Pharmacy and Radiology Review.	All	Ongoing	Increased number of trials opened in hospitals

Strategic objective	Action	CSG Lead	Date	Update
3b Raising awareness and profile	Regular dissemination of study recruitment activity and outcomes through newsletters, annual meetings and Annual Report and submission of meeting abstracts Restart dedicated annual NCRI Head & Neck cancer trials meeting Communications about new studies with CRN subspecialty leads Engage with Make Sense campaign and other patient group campaigns to raise awareness of clinical trials	ALL Clinical Trials fellows Clinical Trials fellows EK	Ongoing 2016 After each CSG meeting Ongoing	Ongoing Ongoing
3c Maximise outputs from clinical trials	Improve adoption of results of trials into clinical practice through: a. Engaging early with TMGs of closing trials b. Engaging with NICE c. Engaging with professional bodies d. Engaging with commissioners	WLW	Ongoing	
4 Improving the UK head and neck phase I capability	Continue to develop Network of phase I centres through: a. Identifying funding sources b. Developing joint meetings and protocols c. Badging phase I studies	HM	Ongoing	CR UK Accelerator bid being planned

Strategic objective	Action	CSG Lead	Date	Outcomes
5 Enhancing international collaborations	Continue to engage early with strategic co-operative groups such as EORTC and GORTEC to develop joint studies Engage fully with HNC Inter Group to help increase the collaborations and harmonisation	JMC HM	Ongoing Ongoing	Ongoing Strong engagement CSG Chair is secretary
6. Develop new Pis and ensure succession planning	I. Mentor new CSG members and outside Principal Investigators (Pis) to help them develop studies. II. Continue to develop and expand the Clinical Trials Fellowship a. Develop a Fellowship in thyroid oncology and thyroid surgery	All	Ongoing	Ongoing
7. CSG structure and function	Renewal of membership with commitment of members to develop trials and to deliver studies developed by CSG – especially subgroups Development of new PIs and trainees Formalise open resource for harmonisation and sharing of protocols and core datasets for tissue collection and RTQA Ensure Pis of all new trials and of existing trials are asked regarding their willingness to allow open access to their protocols. Failure to do so would result in lack of support by CSG Adoption of efficient designs where at all possible Closer co-operation and integration of thyroid subgroup into the main Head and Neck CSG	All All GT GT/HM All KN	Ongoing	Ongoing Ongoing Ongoing Ongoing

B – Thyroid Subgroup Strategy

Research targets

1. To coordinate molecular pathology studies through the Subgroup.
2. To develop a multi-centre trial for high risk differentiated thyroid cancer.
3. To investigate the role of TSH suppression in differentiated thyroid cancer.
4. To open a surgical trial aimed at reducing the risk of post thyroidectomy hypoparathyroidism utilizing *N*ear *I*nfrared *F*luorescence (NIRF) Imaging.
5. To develop and open trial for systemic targeted therapy for anaplastic thyroid cancer.

C – Surgery & Localised Therapies Subgroup Strategy

Our contribution toward the strategic aims of the Head & Neck CSG specifically include interventional trials for laryngeal and hypopharyngeal cancer, premalignancy trials, post-operative trials in oral cancer and mucositis and oral health trials. We are currently working on planning and/or implementing these proposals and studies.

D – Systemic Therapy & Radiotherapy Subgroup Strategy

Aims

1. To continue to recruit efficiently into current portfolio of open studies, as outlined below
2. To open studies currently in set up, as outlined below.
3. To progress studies in development, as outlined below, including:
    - A randomised study in locally advanced hypopharyngeal/laryngeal cancer, possibly exploring a chemo-selection strategy but also incorporating immune checkpoint inhibition.
    - A study to evaluate the use of proton beam therapy in head and neck cancers.
    - Immunotherapy studies for rarer head and neck cancers such as recurrent salivary gland and nasopharyngeal cancers.
4. To begin to consider new trial designs for areas of unmet need where there are no studies currently/imminently recruiting including further collaboration with international groups for rarer tumour types.

E – Survivorship Subgroup Strategy

Strategy

Head and Neck 5000 is a major part of a new collaboration is now extended with a successful US NIH grant RO1 DE025712 to look at the role of germline and somatic DNA mutations in oral and oropharyngeal cancers. This work has begun and will continue over the next five years.

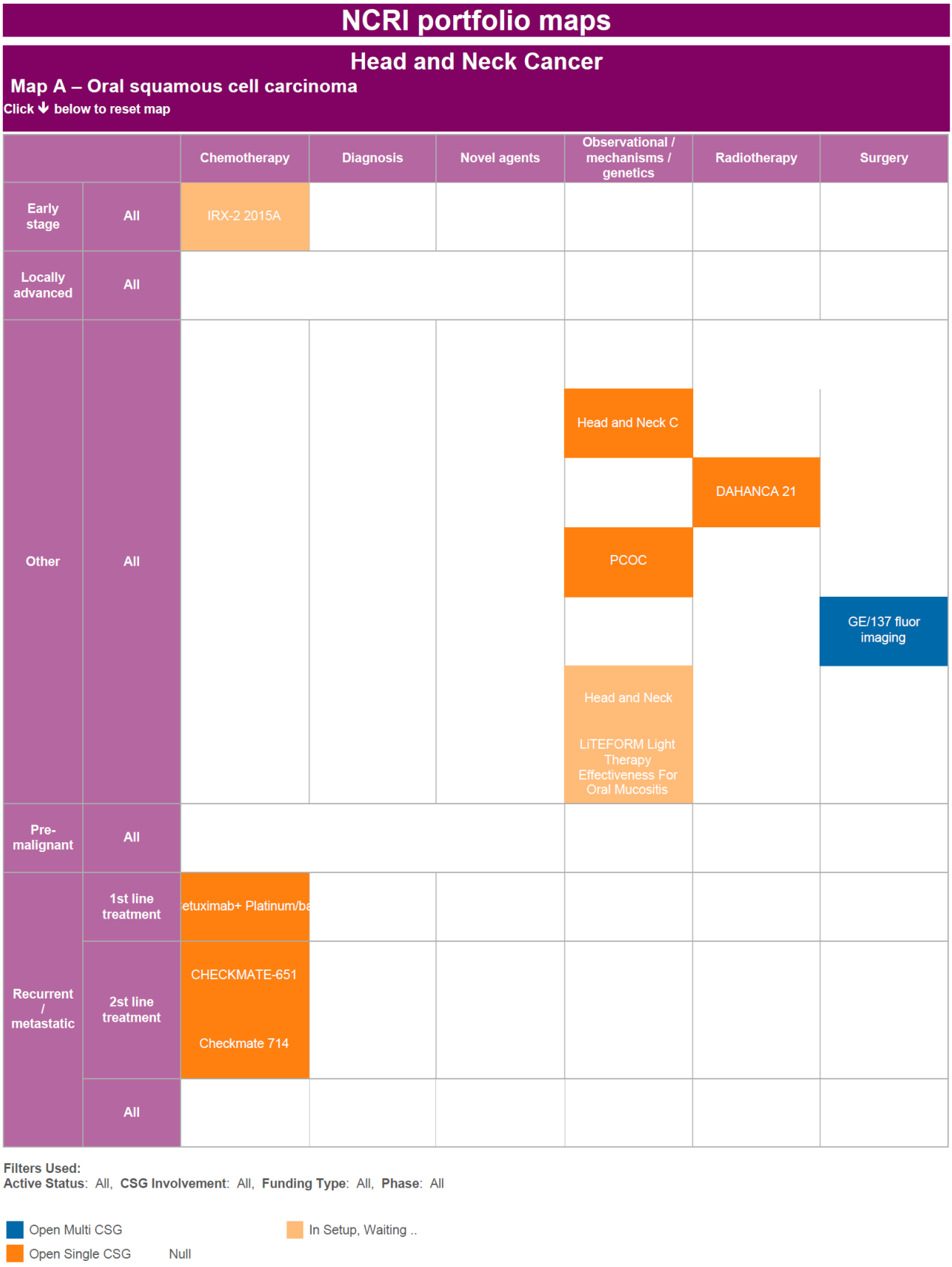
A second major collaboration with H&N5000 is with the CRUK funded Integrative Cancer Epidemiology Programme (ICEP). This collaboration has enabled us to look at risk prediction and causality. Using a combination of these hypothesis-generating methodology including genome-wide and epigenome-wide association studies (GWAS and EWAS, respectively), comprehensive literature text mining, epigenetic phenotype predictors and MR analyses (hypothesis-free, two-sample and two-step-two-sample MR), this project will aim to establish and appraise robust causal pathways associated with head and neck cancer incidence and progression. We plan to use epigenetic signatures to objectively predict exposure to risk factors for oropharyngeal cancer incidence and progression and to assess whether the causal pathway between a risk factor and oropharyngeal cancer development is mediated by DNA methylation using a Mendelian randomization (MR) approach and assess concordance between blood, saliva and tumour-based methylation signals.

Other streams of activity with ICEP include the investigation of the observational association between alcohol and smoking behaviours and outcomes using H&N5000. Identifying epigenetic and molecular signatures of tobacco and alcohol exposure in this population, establishing whether they predict outcomes and to try to develop a risk score which predicts HNC outcomes up to three years after diagnosis. MR is being used to quantify the causal effect of vitamin D on HNC risk and progression using (HN5000) to investigate the casual effect of vitamin D on three year recurrence or survival. ICEP provides opportunities for collaborative PhD fellowships, NIHR clinical training and has opened the issues of the need for a biorepository for head and neck cancer. Via ICEP, we are exploring other cohorts such as an UK Biobank.

H&N5000 is now in the three year follow-up and a range of collaborations related to the Survivorship Subgroup can be seen on the website http://www.headandneck5000.org.uk/.

Appendix 3

Portfolio maps



NCRI portfolio maps

Head and Neck Cancer

Map B – Pharynx-larynx squamous cell carcinoma

Click ↓ below to reset map

		Chemotherapy	Diagnosis	Novel agents	Observational / mechanisms / genetics	Quality of life	Radiotherapy	Surgery
Early stage	All							
Locally advanced	1st line treatment							
	2st line treatment							
	HPV-				Bohemian (Prompts)			
	HPV+			A Cancer Resear				
	HPV+/-	tuximab+ Platinum/			RAPPER			
Other	Other				PCOC Biological Magnetic Resonance Head and Neck		DAHANCA 21	
Pre-diagnosis	All							
Recurrent / metastatic	2st line treatment	CHECKMATE-651 Checkmate 714						

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

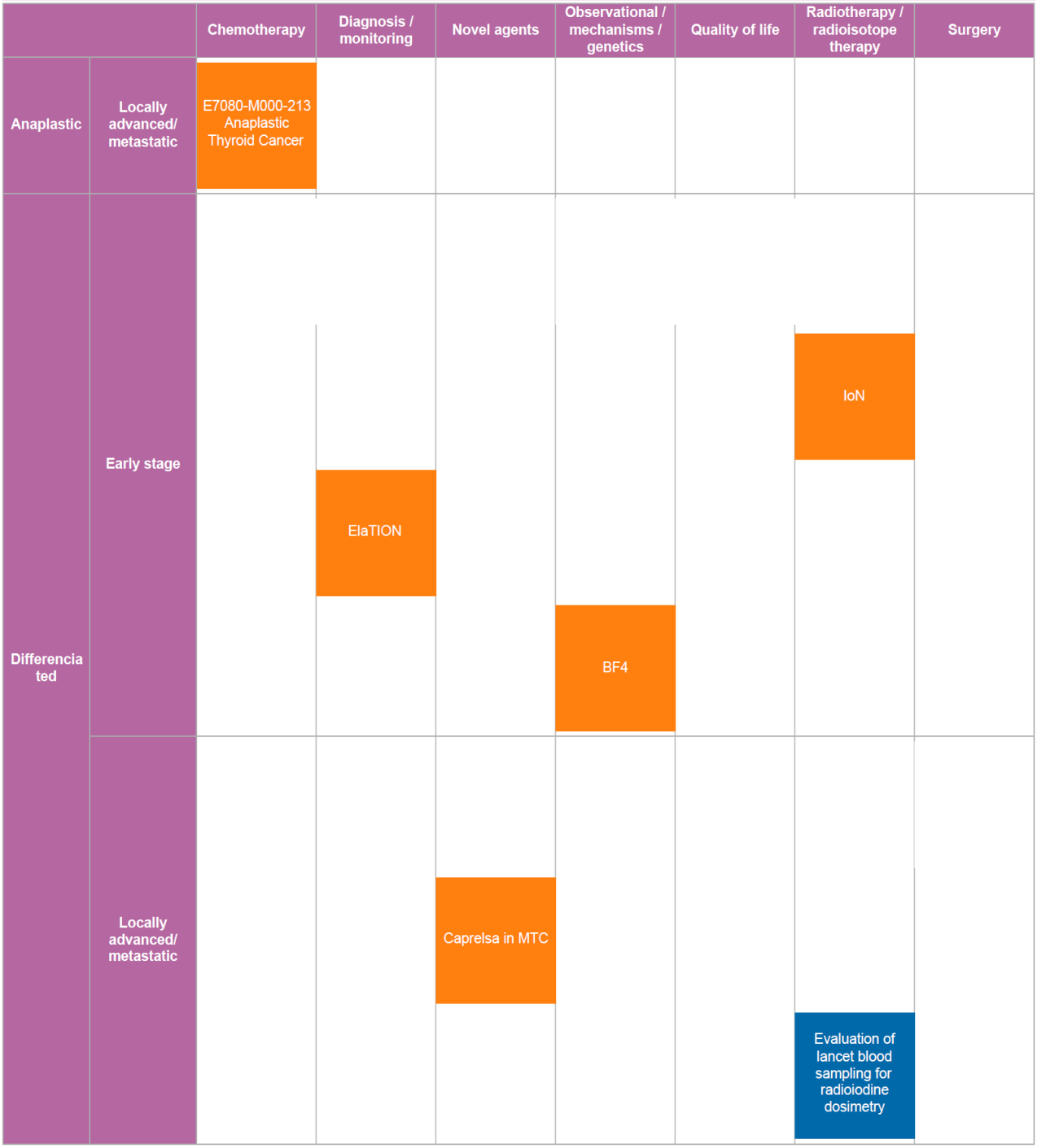
Open Multi CSG
Open Single CSG
Null
In Setup, HRA Ap..
In Setup, Waiting ..

NCRI portfolio maps

Head and Neck Cancer

Map C – Thyroid-specific cancer

Click ↓ below to reset map



Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

Open Multi CSG
Open Single CSG

NCRI portfolio maps

Head and Neck Cancer

Map D – Cross-cutting: early stage, locally advanced, recurrent / metastatic

Click ↓ below to reset map

		Chemotherapy	Diagnosis	Novel agents	Observational / mechanisms / genetics	Radiotherapy	Surgery
Early stage	All	WISTERIA: WEE1 inhibitor with Cisplatin and Radiotherapy					
Locally advanced	All	WISTERIA: WEE1 inhibitor with Cisplatin and Radiotherapy					
	HPV-						
	HPV+				Links betw.HPV		
	HPV+/-	NIMRAD ORCA/2			RAPPER VoxTox	INSIGHT NIMRAD ORCA/2	
Recurrent / metastatic	1st line treatment						
	2st line treatment						
	All	WISTERIA: WEE1 inhibitor with Cisplatin and Radiotherapy				MEDI combo	

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

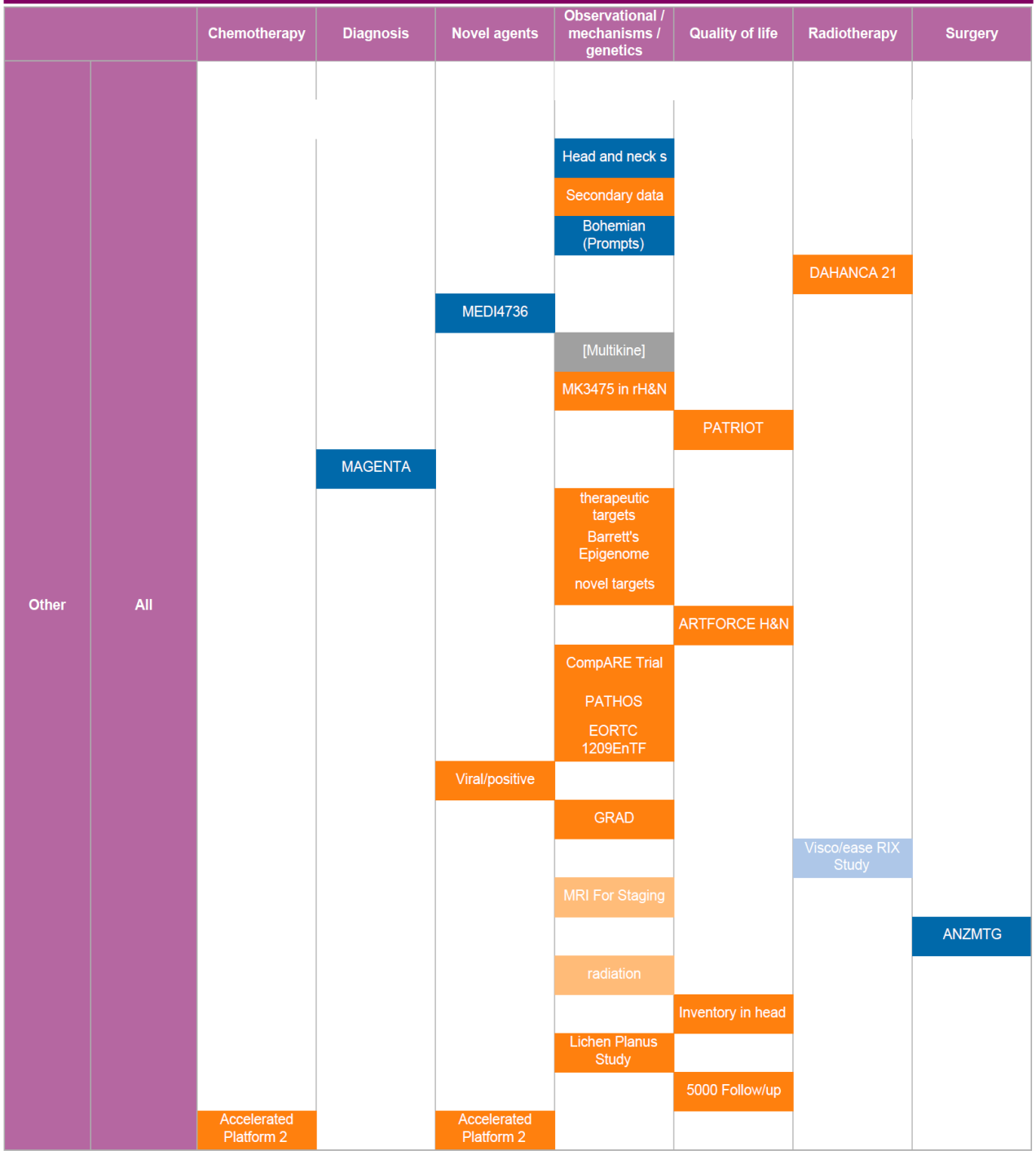
Open Multi CSG
Open Single CSG
In Setup, HRA Ap..
Null

NCRI portfolio maps

Head and Neck Cancer

Map E – Cross-cutting: other

Click ↓ below to reset map



Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

Open Multi CSG
Open Single CSG
Null
In Setup, HRA Ap..
In Setup, Waiting ..
In Setup, Waiting ..
Suspended Single..

Appendix 4

Publications in the reporting year

Study	Reference
ORCA-2	Forster MD, Mendes R, Harrington K, Guerrero Urbano T, Baines H, Spanswick V, Ensell L, Hartley J, Adeleke S, Gougis P, Leader D, McDowell C, Lopes A, Teague J, Forsyth S, Beare S (ASCO 2016), A phase I study of olaparib in addition to cisplatin-based concurrent chemoradiotherapy for patients with high risk locally advanced squamous cell carcinoma of the head and neck.
	Patritumab or placebo plus cetuximab and platinum-based therapy in squamous cell carcinoma of the head and neck Harrington K, Forster MD, Dillon M, Grove L, Adeleke S, Chen S, Diamond J, Hannus H, Cooper K, Greenberg J (ASCO 2016) Patritumab (P) or placebo (PBO) plus cetuximab (C) and platinum-based therapy in squamous cell carcinoma of the head and neck (SCCHN): a phase 2 study.
PATRIOT	Dillon M, Ellis S, Grove L, McLellan L, Clack G, Smith S, Laude J, Viney Z, Adeleke S, Lazaridis G, Spicer J, Forster MD, Harrington K (ASCO 2016), A phase I study to assess the tolerability, safety and biological effects of a specific ataxia telangiectasia and Rad3-related (ATR) inhibitor (AZD6738) as a single agent and in combination with palliative radiation therapy in patients with solid tumours.
SEL-I-METRY	Wadsley J, Gregory R, Flux G, Newbold K, Du Y, Moss L, Hall A, Flanagan L, Brown SR. SELIMETRY-a multicentre I-131 dosimetry trial: a clinical perspective.Br J Radiol. 2017. May;90(1073):20160637.

Appendix 5

Major international presentations in the reporting year

Study	Conference details
LIHNCS Trial (Lugol's Iodine in the Surgical Management of Oral and Oropharyngeal Cancer)	Poster presentation ASCO, Chicago June 2017
A Phase I multicenter dose-escalation study of AZD6738 ATR inhibitor monotherapy in advanced solid tumors (PATRIOT Part A): Preliminary results	Poster presentation AACR, Washington 2017
ORCA2 Trial (A phase I study of olaparib in addition to cisplatin-based concurrent chemoradiotherapy for patients with high risk locally advanced squamous cell carcinoma of the head and neck)	Poster presentation ASCO, Chicago June 2016
PATERNOSTER Trail Patritumab or placebo plus cetuximab and platinum-based therapy in squamous cell carcinoma of the head and neck: a phase 2 study	Poster presentation ASCO, Chicago June 2016
A phase I study to assess the tolerability, safety and biological effects of a specific ataxia telangiectasia and Rad3-related (ATR) inhibitor (AZD6738) as a single agent and in combination with palliative radiation therapy in patients with solid tumours	Poster presentation ASCO, Chicago June 2016
Patritumab + Cetuximab + Platinum-Based Therapy in Squamous Cell Carcinoma of the Head and Neck (SCCHN): A Multicenter, Open-label, Phase-1b Study	Poster Presentation ECHNO, September 2016

Appendix 6

Strengths & weaknesses from the 2016 Head & Neck Cancer CSG Quinquennial Review (QQR)

The Panel thanked the CSG team for the documentation provided, the informative presentation, which covered a number of aspects not included in the written documentation, and the openness with which they had engaged in discussions. The Panel Chair noted that the Group has a tremendous Chair and it is a compliment to him that the CSG has made such progress since its last review. The Group are also to be congratulated on the leadership shown by the subgroup chairs and the way they are mutually supportive of each other and their Chair. The presenting team demonstrated a cohesion and togetherness, which impressed the Review Panel. The Chair has built a strong team that clearly works well together and a Group, which is inclusive, engages the wider research community and is supportive of young researchers and seeks to involve them in the Group's activities. He is highly commended for this. The CSG has strong consumer involvement at all areas of the Group's activities. There is mutual respect and support between the consumers and clinicians, with consumers feeling respected, valued and supported. The Group has a strong multidisciplinary attitude and is to be congratulated on the successful inclusion of thyroid cancer within its remit. The subgroup structure is working well and is productive. The Panel are supportive of the Group's wish to retain its current subgroup structure, which is underpinned by a sound rationale.

The portfolio has breadth and balance and the portfolio maps are well used to demonstrate this breadth and identify gaps in the portfolio. The Group has clear ideas how these gaps can be filled. Since the last review the number of trials and recruitment have grown exponentially, with the CSG being the fourth highest recruiter during 2011/12. For a rare cancer this is particularly noteworthy and the CSG are to be congratulated on their success. The Group has a good publication record and good links with CTRad and the BI CSG. It is collaborating well with the EORTC and DHANCA and is actively engaged in the International Rare Cancer Initiative. International links are beginning to be extended. The Group has addressed all the issues raised at the last review.

Whilst acknowledging the undoubted progress and success of the Group the Panel identified a number of suggestions, which the CSG should consider.

The CSG needs to:

The Group has clearly been successful with its opportunistic approach to doing trials but should begin to move to a more strategic approach. The portfolio maps will assist them in doing this. Particular attention needs to be paid to developing strategies for recurrent and/or metastatic disease and HPV-ve patients. The Panel has provided some suggestions as to how the Group might move forward in these areas.

Consideration should be given to various ways in which the Group might raise its profile, celebrate its successes and promote additional recruitment e.g. through regular annual/biannual trials meetings, slide presentations at trial launches and at research network meetings. The Project Officers may be able to assist with these activities. The Group are encouraged to develop some guidelines outlining the expected time frame from recruitment of last patient to preparation of the final manuscript in order to ensure timely publication of trial results.

International links should be extended where possible and international funding of studies explored. The Panel were impressed by the quality assurance of RT and encourage such an approach to be extended to surgery and chemotherapy. Greater engagement with the Gynae and Palliative Care CSGs is encouraged, as is a round table discussion with other cancer sites where HPV plays a role in tumour development.

The NCRI needs to:

There were no specific issues for the NCRI.