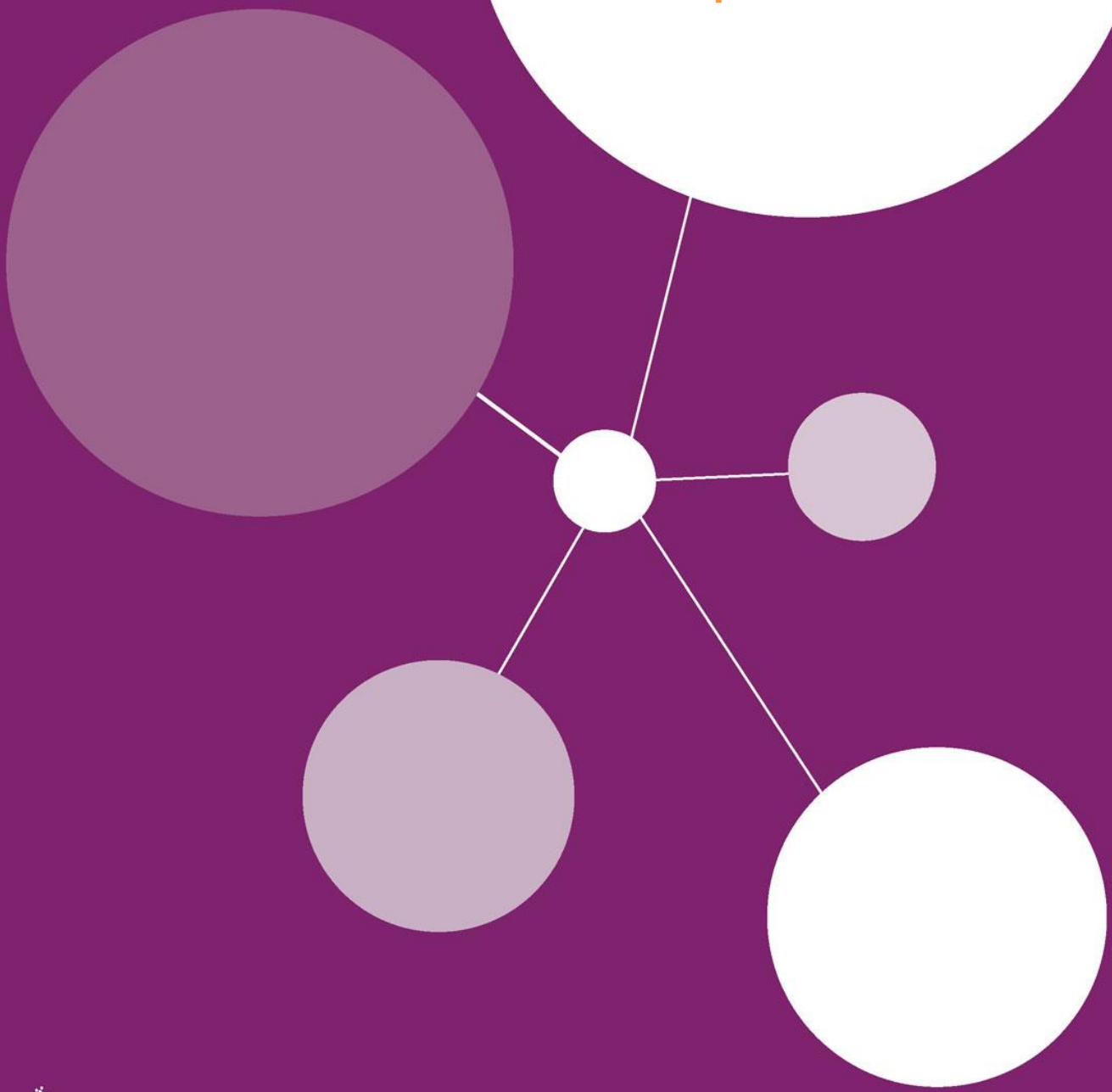
NCRI
National
Cancer
Research
Institute

NCRI Head & Neck Clinical Studies Group

Annual Report 2017-18



Partners in cancer research

NCRI Head & Neck Cancer CSG
Annual Report 2017-18

1. Top 3 achievements in the reporting year

Achievement 1 Opening the first investigator led window of opportunity trial, in head and neck cancer, in the UK.
Achievement 2 By rejuvenating the membership of the Thyroid Subgroup, four trial ideas and protocols have been developed for thyroid cancer – the highest activity in the last five years.
Achievement 3 Providing international leadership in head and neck cancer research by leading the head and neck cancer intergroup alongside increasing collaborations with European Organisation for Research and Treatment of Cancer (EORTC).

2. Structure of the Group

The CSG membership was rejuvenated in 2017 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 year two new members have been added – Mr Paul Nankivell, an Ear, Nose and Throat (ENT) surgeon, and former trainee member, and Dr Jon Wadsley, a clinical oncologist to replace members who have rotated off.

3. CSG & Subgroup strategies

Main CSG

Identify key research areas

The key research areas of the CSG follow our strategy set in 2015. The priority areas include research in the treatment of high risk post-operative patients, research in advanced, recurrent and metastatic head and neck cancer along with the development of the thyroid cancer research portfolio.

Improving the UK head and neck phase I capability

Over the last year, the CSG have continued to consolidate and implement strategy. The Group has been successful in opening the first window of opportunity trial that is investigator led in the UK. This has significantly improved and strengthened the UK's phase 1 capability in head and neck cancer. Furthermore, the CSG has continued to collaborate with industry to deliver more phase 1 trials for patients in the UK.
The Head & Neck CSG have also successfully developed the protocol for a new adjuvant and post-operative immunotherapy trial – one of the key deliverables in our strategy.

Enhance international collaborations

The CSG has developed a strong leadership position internationally, especially within the Head and Neck Intergroup. The Group have also continued to develop our working relationship with the EORTC, and have successfully attracted funding for the “best of” trial, run by the EORTC.

Develop new PIs and ensure succession planning

The Group have successfully graduated a second group of clinical trials fellows via the CSG trainee scheme, with six fellows completing their 18-month fellowships. The group continue to develop the talent pool of the CSG, and have recently appointed our first clinical trials fellow as a core member of the Group, Mr Nankivell.

CSG structure and function

The CSG continues to function in a highly effective and collaborative manner.

Epidemiology & Survivorship Subgroup (Chair, Professor Steven Thomas)

Understanding the reasons behind late stage diagnosis

The complex factors that play a role in diagnostic delay are framed within the interaction that exists between the patient and the healthcare infrastructure. Delays are influenced by psychosocial, financial, structural and educational barriers at various stages throughout the diagnostic and treatment process. Diagnostic delay is also influenced by patient presentation in the clinic and patient management until definitive diagnosis. Delays in treatment can lead to further disease progression, increased morbidity and poor survival. It is planned to collaborate with international partners to investigate the socio-economic, logistic and biological predictors of late stage at diagnosis for head and neck cancer.

Improve detection of recurrent cancer in cancer survivors

Those with head and neck cancer tumours have a variable prognosis, nevertheless follow up protocols are similar. Recurrence typically occurs in the first three years and detection rate in routine clinical follow up is poor. Trials are planned to explore more efficient approaches such as the use of PET-CT guided surveillance at one year. In addition, earlier diagnosis of recurrence increases the potential of reducing the frequency of follow up for cancer survivors.

Improve lifestyle interventions in head and neck cancer survivors

Smoking and alcohol use are generally known to influence mortality. A prospective analysis of mortality risk adjusting for important prognostic factors in the H&N5000 cohort has shown current smokers have approximately a 70% higher all-cause mortality risk in comparison to those who had never smoked, whilst former smokers were over 40% more likely to die during follow-up. A diagnosis of head and neck cancer results in important changes in alcohol consumption and smoking prevalence which are dynamic in the first year after diagnosis and indicate opportunities for intervention. Only three trials have evaluated smoking cessation interventions in head and neck cancer survivors with new trials being evaluated.

The Epidemiology & Survivorship Subgroup aims to assess the association between Body Mass Index (BMI) and survival to determine if the association is causal. The Subgroup also aims to establish the route by which effect is exerted for development of therapeutic options.

Early palliative care for people with head and neck cancer

Applying the concept of introducing palliative care early after diagnosis on patient reported outcomes and end of life care in head and neck cancer survivors.

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

Develop interventional trials for laryngeal and hypopharyngeal cancer

The Surgery & Localised Therapies Subgroup continues to thrive, developing and running 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. Membership is being refreshed this spring. The Subgroup is involved in building a successful stream of opportunity trials in all head and neck cancers which are primarily surgically treated. (CRUK AMG319, INSPIRE [commercial -UK only site in Europe to recruit] and now NICO [Nivolumab as neoadjuvant therapy for stage 3 and 4 resectable oral cavity cancer]).

Continued trial development

We have made significant progress in the following areas:

- Premalignancy – LISTER trial (Lugols iodine visualisation for excision vs control of dysplasia feasibility phase recruiting in four centres). SAVER trial (sodium valproate vs placebo for patients not suitable for surgical management) has overcome placebo cost issues and will open shortly (EME funded).
- LOOC; Sentinel node biopsy imaging and surgery in oropharynx cancer – through to final EME stage.
- Post-op trials in oral cancer – The Liteform trial (low level laser light therapy for patients with oral mucositis following adjuvant chemoradiotherapy or radiotherapy) recruiting in a number of sites. RaPTOR trial for medical therapy for osteoradionecrosis remains a placebo agent challenge for the group.
- Patient Concerns Inventory Trial funded by RfPb open in two centres (Liverpool and Leeds).

The Subgroup maintains two trainee members and has ongoing success with PATHOS, PATHOS T, Best-of (UK arm now funded by CRUK) and ComPARE; all oropharynx trials

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

Continue to recruit efficiently into current portfolio of open studies

2017 has been a productive year for the Systemic Therapy & Radiotherapy Subgroup, with particular emphasis on the generation of studies involving immunotherapy. Several studies are under development or are close to opening with immune checkpoint inhibitors within several clinical settings, matching gaps within the portfolio. The NICO study will explore the role of nivolumab in patients with operable oral cavity disease. The addition of a fifth arm with durvalumab into the ComPARE study aims to examine its role in high risk oropharnyngeal disease following chemoradiotherapy. Both the POPPY and EACH studies will respectively investigate pembrolizumab and avelumab with cetuximab in populations of patients with recurrent or metastatic HNSCC and OBERON will generate safety and activity signals for durvalumab and cetuximab in IO-pretreated recurrent disease.

Recently funding has also been agreed to support a basket study exploring the Pfizer IO portfolio in recurrent head and neck cancers, which also offers a great opportunity to improve understanding of the role for combination immunotherapies within this area of unmet need. In addition, a study of combination immune checkpoint inhibitors in metastatic salivary gland cancers is also in development.

These studies have tissue and blood sampling integral to their design, offering a great opportunity for translational research.

Consider new trial designs for areas of unmet need

These new studies will complement the current portfolio within the Systemic Therapy & Radiotherapy Subgroup, which involves a healthy mix of early and late phase trials. In HPV-driven oropharyngeal cancer, De-ESCALaTE recently completed recruitment, with PATHOS recruitment continuing.

CompARE continues to recruit well in patients with high risk orophayngeal disease, with ORCA2 exploring radio-sensitisation with olaparib in high risk pharyngeal or laryngeal SCC. NIMRAD continues to recruit in patients not suitable for dual modality therapy. Wisteria, a study looking at potentiation of post-operative CRT for oral cancer, with a second biological 'windows' arm to better under mechanisms of chemo-potentiation opened in 2017. The second 'windows' study explores the impact of PI3K-delta inhibition on the tumour immune environment which is already recruiting well.

Open studies currently set up and progress studies in development

Further consideration will be given to randomised studies in high risk oral cavity and first line recurrent or metastatic disease. A consortium is currently focusing on the development of a large phase III study in high risk hypopharyngeal or laryngeal cancer.

Thyroid Subgroup (Chair, Dr Jon Wadsley)

Develop a multi-centre trial for high risk differentiated thyroid cancer

Following work done to establish a network of UK centres capable of standardised I131 dosimetry to deliver the SELIMETRY trial, work is in progress to develop a protocol assessing a dosimetric approach to I131 therapy for patients with high risk differentiated thyroid cancer. A full proposal is to be brought to the next Thyroid Subgroup meeting.

Increase surgical trials on the portfolio

Several surgical studies are currently in development.
Following a successful preliminary application, a full application has been invited to the NIHR EME programme for 'Near Infrared Fluorescence (NIRF) Imaging to prevent Post-Surgical Hypoparathyroidism (PoSH) after Thyroid Surgery (NIFTy), a phase II/III pragmatic, multicentre randomised controlled trial'.
'Lobectomy vs Total Thyroidectomy for low risk well-differentiated thyroid cancer' has a national survey under way. The trial proposal will be discussed at the next Head & Neck CSG meeting.
'Lobectomy Surgery for Intermediate Cytology Thy3 and Ultrasound U3 Solitary Thyroid nodules less than 4 cm in size' is also to be discussed at the next CSG meeting.

Develop an open trial for systemic targeted therapy for anaplastic thyroid cancer

The international Anaplastic Thyroid Cancer tissue bank offers the subgroup a unique resource to undertake translational research in this rare and challenging disease. A number of projects are underway which investigate the potential for targeted or immunotherapies, with a view to developing a clinical trial. Given the rarity of this condition this is likely to require international collaboration and links are established through the International Thyroid Oncology Group (ITOG).

Coordinate molecular pathology studies through the group

The Subgroup benefits from the input of an expert in molecular pathology with an interest in circulating tumour DNA. This has allowed a co-ordinated approach for the development of molecular pathology specific studies and the incorporation of translational elements into other studies (e.g. SELIMETRY).
A full protocol regarding 'Multi-Centre Evaluation of Circulating Tumour DNA as a Potential Biomarker in Advanced Thyroid Cancer' is to be presented at the next CSG meeting.

Nurture links with pharma to increase opportunities for further commercial and investigator led studies

Following recent approval of a number of targeted therapies in thyroid cancer by The National Institute for Health and Care Excellence (NICE), negotiations are ongoing to develop investigator led studies to collect further data regarding the optimal use of these therapies. The Subgroup's well-established network of specialist thyroid centres facilitates cross referral of patients when commercial trials are open in a limited number of centres.

4. Task groups/Working parties

The Head & Neck CSG had no task groups or working parties during the reporting year.

5. Funding applications in last year

Table 2 Funding submissions in the reporting year

The Head & Neck CSG has spent this year consolidating the previous two years success in funding. Despite that there have been several successful outline applications, which are now progressing to full applications. There are also several projects currently being worked up for funding applications, including applications on new areas such as salivary gland disease, and long-term surveillance.

Cancer Research UK Clinical Research Committee (CRUK CRC)				
Study	**Application type**	**CI**	**Outcome**	**Level of CSG input**
May 2017				
CompARE Collect	Full application	Professor Hisham Mehanna	Supported	
Optimizing immunotherapy for head and neck cancer	Full application	Professor Christian Ottensmeier	Not supported	
November 2017				
TWEET: A randomised phase II Trial of WEE1 inhibitor (AZD1775) with Taxane chemotherapy (paclitaxel) versus paclitaxel in head and neck squamous cell carcinoma	Early Phase & Feasibility Study (Full Application)	Dr Anthony Kong	Preliminary	
PATHOS: Post-operative adjuvant treatment for HPV-positive tumours	Late Phase Study (Full Application)	Professor Mererid Evans	Deferred	
Other committees				
Study	**Committee & application type**	**CI**	**Outcome**	**Level of CSG input**

6. Consumer involvement

The Consumer members of the Head & Neck CSG, Ms Emma Kinloch and Dr Timothy Humphrey, have played a full role in the work of the Croup this year, including the development of new studies, contributing to the CSG review of proposals seeking funding, review and development of patient information material, membership of trial steering groups and input into the future strategy of the CSG.

Emma Kinloch

Emma Kinloch has been a member since 2015 and through her work running a head and neck cancer 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 an appointment on the ACCOI Board and a collaboration on the set up of a new UK wide network for salivary gland cancers with connections made through, and supported by, the CSG. The scientific mentoring relationship within the CSG has allowed the opportunity for support with and insight into CSG work when needed.

Timothy Humphrey

Timothy Humphrey became a member of the NCRI Head & Neck CSG in September 2017 and is also a member of the NCRI CTRad initiative. As a result of Tim's CSG membership, and as a cancer research scientist with experience in taking basic research into clinical trials, he has also become both a patient advocate and scientific advisor for several research and clinical trial applications. As a patient advocate, Tim is keen to ensure that clinical trials are based on high quality preclinical data.

7. Priorities and challenges for the forthcoming year

Priority 1 Recruit a new CSG Chair.
Priority 2 Recruit replacement clinical trials fellows.
Priority 3 Deliver the remaining objective of the strategic plan, mainly through developing a large observational study.
Challenge 1 Develop a new strategy for the next three years.
Challenge 2 Managing the transition of leadership as Chair of the CSG and one subgroup chair are rotating off the CSG.
Challenge 3 Increasing the number of new applications.

8. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies

A – Main CSG Strategy

B – Epidemiology & Survivorship Subgroup Strategy

C – Surgery & Localised Therapies Subgroup Strategy

D – Systemic Therapy & Radiotherapy Subgroup Strategy

E – Thyroid Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 – Top 5 publications in reporting year

Appendix 5 – Recruitment to the NIHR portfolio in the reporting year

Professor Hisham Mehanna (Head & Neck Cancer CSG Chair)

Appendix 1

Membership of the Head & Neck Cancer CSG

Name	Specialism	Location
Dr Olly Donnelly*	Clinical Oncologist	Southampton
Dr Bernadette Foran	Clinical Oncologist	Sheffield
Dr Anthony Kong	Clinical Oncologist	Birmingham
Dr Kate Newbold	Clinical Oncologist	London
Dr Ioanna Nixon	Clinical Oncologist	Glasgow
Dr Nachiappan Palaniappan	Clinical Oncologist	Cardiff
Dr Stefano Schipani	Clinical Oncologist	Glasgow
Dr David Thompson	Clinical Oncologist	Manchester
Dr Timothy Humphrey	Consumer	Oxford
Ms Emma Kinloch	Consumer	London
Dr Martin Forster	Medical Oncologist	London
Dr Joseph Sacco	Medical Oncologist	Liverpool
Dr Adel Samson*	Medical Oncologist	Leeds
Dr Stefano Fedele	Oral Medicine	London
Professor Stephen Porter	Oral Medicine	London
Dr Jacqueline James	Pathologist	Belfast
Dr Karwan Moutasim*	Pathologist	Southampton
Dr Max Robinson	Pathologist	Newcastle
Dr Wai Lup Wong	Radiologist	Stevenage
Dr Christina Yap	Statistician	Birmingham
Mr Jagtar Dhanda*	Surgeon	London
Mr John Biddlestone*	Surgeon	Glasgow
Dr Emma King	Surgeon	Southampton
Professor Jim McCaul	Surgeon	Bradford
Professor Hisham Mehanna (Chair)	Surgeon	Birmingham
Professor Steven Thomas	Surgeon	Bristol
Mr Stuart Winter	Surgeon	Oxford
Mr Oliver Dale*		Gloucestershire
Ms Clare Schilling*		London

* denotes trainee member

Membership of the Subgroups

Epidemiology & Survivorship Subgroup		
Name	**Specialism**	**Location**
Professor Gerry Humphris	Clinical Oncologist	St Andrews
Dr Charles Kelly	Clinical Oncologist	Newcastle
Mrs Christine Allmark	Consumer	Yorkshire
Professor Luc Bidaut	Medical Physicist	Lincoln
Professor Hisham Mehanna	Surgeon	Birmingham
Professor Simon Rogers	Surgeon	Liverpool
Professor Steven Thomas (Chair)	Surgeon	Bristol

Surgery & Localised Therapies Subgroup		
Name	**Specialism**	**Location**
Ms Clare Schilling *	Clinical Fellow	London
Dr Mererid Evans	Clinical Oncologist	Cardiff
Mr Max Robinson	Pathologist	Newcastle
Mr Jagtar Dhanda	Surgeon	Staffordshire
Professor Terry Jones	Surgeon	Liverpool
Mr Tas Kanatas	Surgeon	Leeds
Dr Emma King	Surgeon	Southampton
Dr Kim McCaul (Chair)	Surgeon	London
Professor Hisham Mehanna**	Surgeon	Birmingham
Mr Paul Nankivell	Surgeon	Birmingham
Mr Mike Nugent	Surgeon	Sunderland
Mr Vinidh Paleri	Surgeon	Newcastle
Mr Andrew Schache	Surgeon	Liverpool
Professor Richard Shaw**	Surgeon	Liverpool

Systemic Therapy and Radiotherapy Subgroup		
Name	**Specialism**	**Location**
Dr Shreerang Bhide	Clinical Oncologist	London
Dr Bernadette Foran	Clinical Oncologist	Sheffield
Dr Anthony Kong	Clinical Oncologist	Birmingham
Dr Stefano Schipani	Clinical Oncologist	Glasgow
Dr Ketan Shah	Clinical Oncologist	Oxford
Dr Martin Forster (Chair)	Medical Oncologist	London
Dr Joseph Sacco	Medical Oncologist	Liverpool
Professor Wim Oyen	Radiologist	Oxford
Dr Catharine West	Scientist	Manchester
Dr Emma King	Surgeon	Southampton
Professor Hisham Mehanna**	Surgeon	Birmingham

Thyroid Subgroup		
Name	**Specialism**	**Location**
Dr Laura Moss	Clinical Oncologist	Cardiff
Dr Kate Newbold (Chair)	Clinical Oncologist	London
Dr Jon Wadsley	Clinical Oncologist	Sheffield
Professor Mark Strachan	Endocrinologist	Edinburgh
Professor Allan Hackshaw	Epidemiologist	London
Dr Sarah Johnson	Pathologist	Newcastle
Dr David Poller	Pathologist	Portsmouth
Mr Radu Mihai	Surgeon	London

* 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	Increased number of trials opened in hospitals
	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	

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 – Epidemiology & 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/.

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

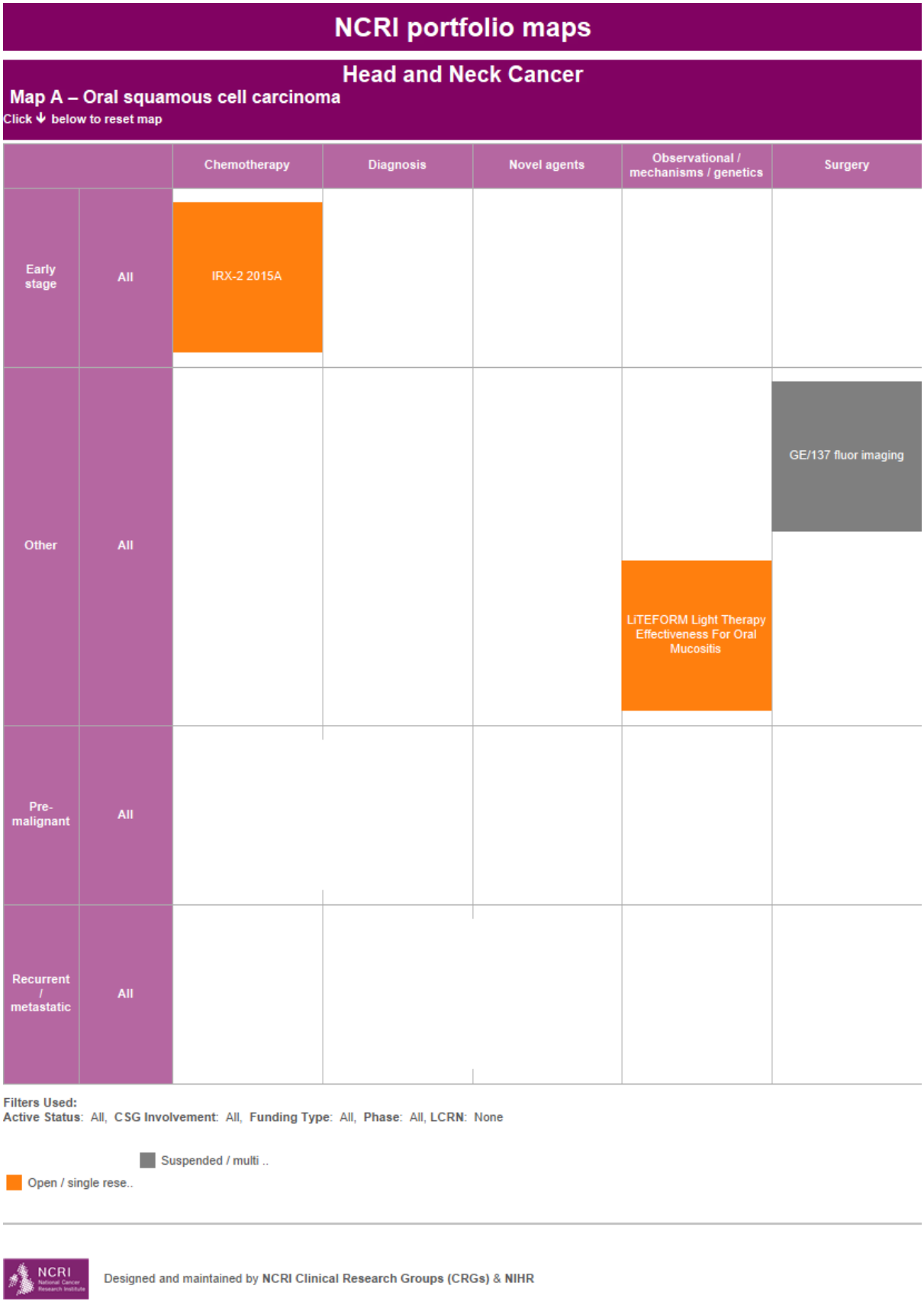
1. To continue to recruit efficiently into current portfolio of open studies, as outlined below
2. To open studies currently in set up, as outlined below.
3. To progress studies in development, as outlined below, including:
    - A randomised study in locally advanced hypopharyngeal/laryngeal cancer, 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 – Thyroid Subgroup Strategy

1. Co-ordinate molecular pathologies studies through the group.
2. Develop a multicentre trial for high risk differentiated thyroid cancer, building of the dosimetry network developed for the SELIMETRY trial.
3. Increase surgical trials on the portfolio.
4. Develop a trial of systemic targeted therapy for anaplastic thyroid cancer.
5. Nurture links with pharma to increase opportunities for commercial and investigator led studies.

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	Observational / mechanisms / genetics	Quality of life
Early stage	HPV+/-	ORCA/2			
Locally advanced	Null				
	HPV-				
	HPV+/-			RAPPER ORCA/2	
	Other				
Pre-diagnosis	All				

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

Open / single rese..
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NCRI National Cancer Research Institute

Designed and maintained by **NCRI Clinical Research Groups (CRGs)** & **NIHR**

NCRI portfolio maps

Head and Neck Cancer

Map C – Thyroid-specific cancer

Click ↓ below to reset map

		Chemotherapy	Diagnosis / monitoring	Novel agents	Observational / mechanisms / genetics	Quality of life	Radiotherapy / radioisotope therapy	Surgery
Anaplastic	Locally advanced/ metastatic	E7080-M000-213 Anaplastic Thyroid Cancer						
Differenciated	Early stage		ElaTION				IoN CompARE Trial PATHOS	
	Locally advanced/ metastatic			Caprelsa in MTC			Evaluation of lancet blood sampling for radioiodine dosimetry	
Medullary	Early stage					Assessment of Quality of Life Tools in Medullary Thyroid Cancer (QaLM)		
	Locally advanced/ metastatic					Assessment of Quality of Life Tools in Medullary Thyroid Cancer (QaLM)		

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

Open / single rese..

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NCRI portfolio maps

Head and Neck Cancer

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

Click ↓ below to reset map

		1st line treatment	Chemotherapy..	Diagnosis	Novel agents	Observational / mechanisms / genetics	Quality of life	Radiotherapy	Surgery
Early stage	All		WEE1 inhibitor				ARTFORCE H&N		
Locally advanced	All	Lung Cancer,	Keynote- 412 WEE1 inhibitor Javelin Head and Neck OMO1.01.02 MK3475-689					Javelin Head and Neck	
	HPV-								
	HPV+				A Cancer Resear				
	HPV+/-		NIMRAD			RAPPER VoxTox		NIMRAD	
Other	All	B9991023	WO40242			Biological			
Recurrent / metastatic	All	CHECKMATE-65 Keynote 669	CANC - 5086 Checkmate 714 OMO1.01.02 CA017-063			Head and Neck C Head and Neck			

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

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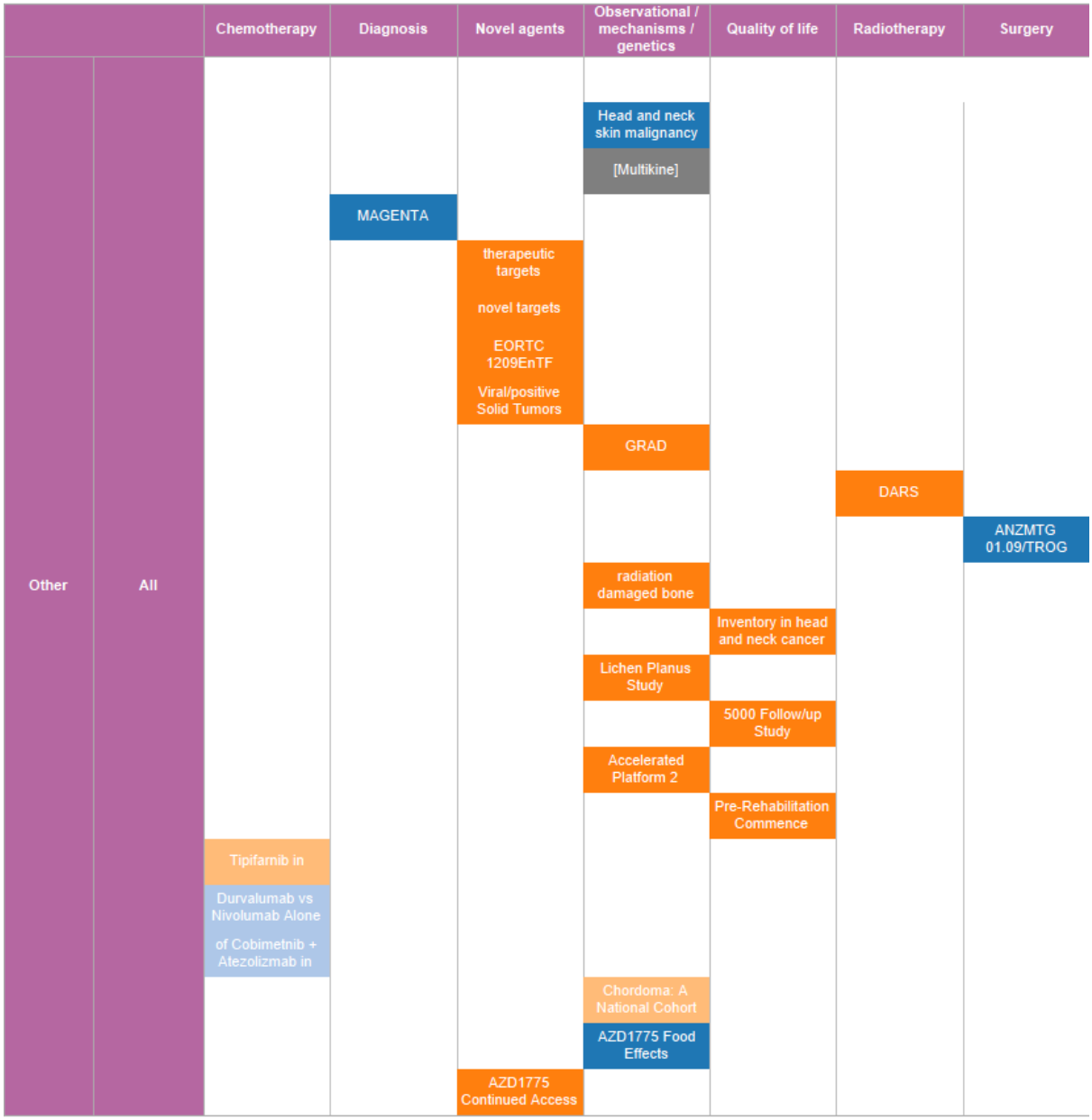
NCRI portfolio maps

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, **LCRN**: None

In Setup / single re.. Open / single rese..
In Setup / multi res.. Open / multi resea.. Suspended / singl..

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Appendix 4

Top 5 publications in the reporting year

Please note that the below section is incomplete

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1. Effect of Age on the Efficacy and Safety of Lenvatinib in Radioiodine-Refractory Differentiated Thyroid Cancer in the Phase III SELECT Trial. Brose MS et al, J Clin Oncol. 2017 Aug 10;35(23):2692-2699.	Select trial	Design and recruitment
2. Change in alcohol and tobacco consumption after a diagnosis of head and neck cancer: Findings from head and neck 5000. Head Neck. Penfold CM et al, 2018 Feb 27. doi: 10.1002/hed.25116. [Epub ahead of print]	Head Neck 5000	Design and execution
3. Early safety from phase 1b/3, multicenter, open-label, randomized trial of talimogene laherparepvec (T-VEC) + pembrolizumab (pembro) for recurrent or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN): MASTERKEY-232. ESMO 2017. Harrington K, Kong A, et al. Annals of Oncology, Volume 28, Issue suppl_5, 1 September 2017, mdx374.061.	Matserkey	Design, recruitment

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the Head & Neck Cancer CSG portfolio, 11 trials closed to recruitment and 20 opened.

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
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
2017/2018	2308	1403	2308	1399	24.25	14.7