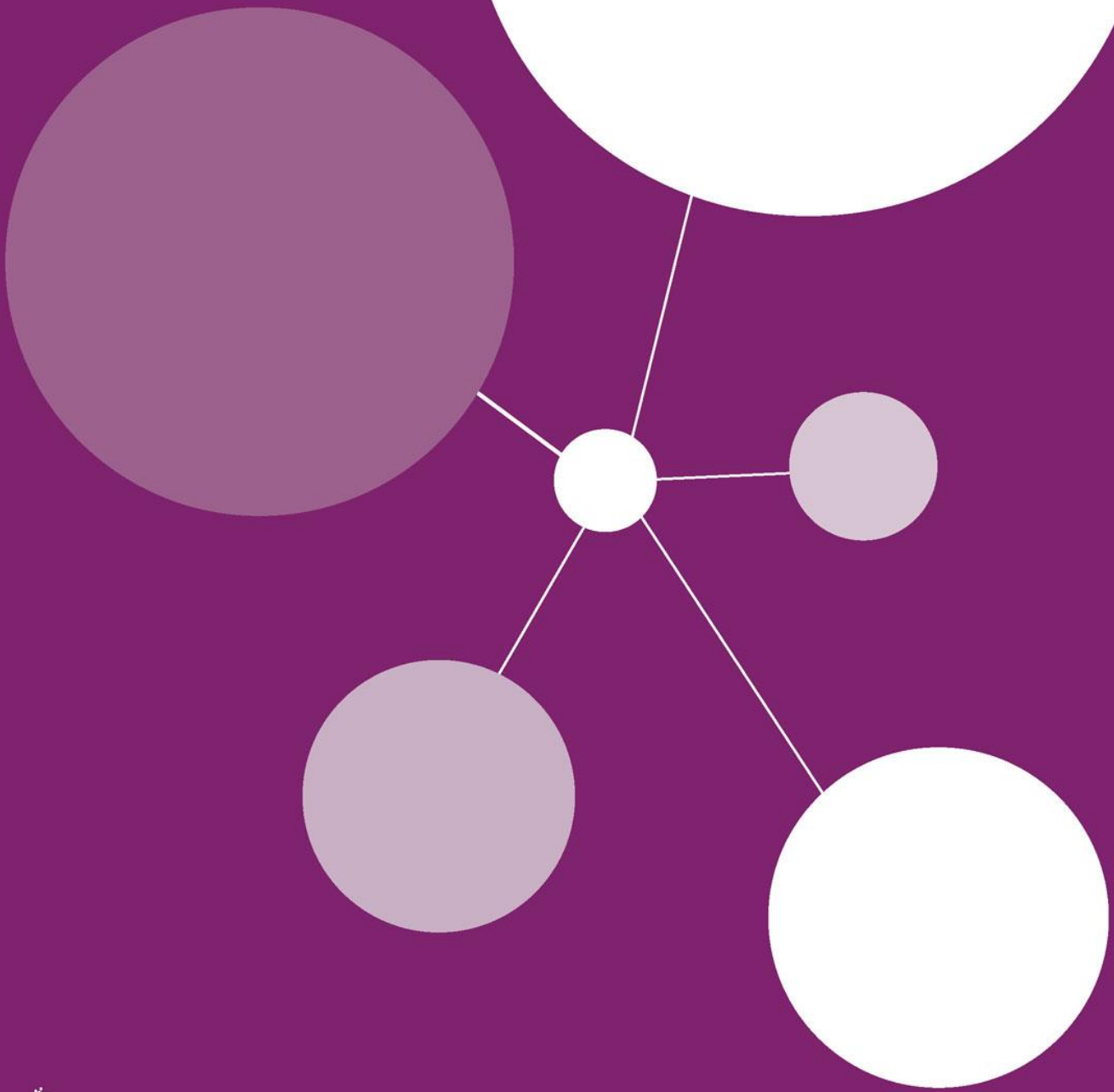
NCRI
National
Cancer
Research
Institute

NCRI Head & Neck Group

Annual Report 2018-19



Partners in cancer research

NCRI Head & Neck Cancer
CSG Annual Report 2018-19

1. Top 3 achievements in the reporting year

It has been an exciting year for the Head & Neck CSG!

1. The Group has had a leadership refresh, with a new CSG chair, 3 new SubGroup Chairs and several new members, including a new cohort of trainees, funded through the relevant colleges. These changes will assist with a new dynamic approach for the upcoming years, starting with a very successful strategy meeting in early 2019.
2. The Group has been successful in gaining funding for several new clinical trials within diseases ranging from premalignant disease, sentinel lymph node evaluation in early stage disease to immunotherapy studies for advanced disease and includes the first UK funding success for a Proton Beam Therapy study.
3. Several of the larger clinical studies have successfully established ambitious global collaborations including European and Australian sites joining into the PATHOS study and Indian sites within the ComPARE trial.

2. Structure of the Group

There has been a natural succession within the Group over the last few years, with a number of more established members rotating off, leading to a membership rejuvenation ~3 years ago. Several of these newer members stepped up to becoming Subgroup Chairs in 2018, with Jon Wadsley, Anthony Kong and Ioanna Nixon becoming chairs for the Thyroid, STaR and Survivorship Subgroups respectively. Their enthusiasm is palpable in meetings, boding well for innovation and engagement in the upcoming years whilst retaining capacity and mentorship for the development of new studies.

The Group retains a good balance, comprising of seven clinical oncologists, five surgeons, three medical oncologists, two pathologists, one radiologist and one statistician as well as key input from two consumers. We also have five newly appointed trainees (surgery, oncology and pathology). The increase in Medical Oncology input and a new Medical Oncology Chair appropriately reflects the expansion of the testing of novel agents in Head & Neck research.

3. Head & Neck Group & Subgroup strategies

Head & Neck Group

Current key research areas

The current key research areas follow our strategy plans established in 2015, to be refreshed in 2019. The priority areas include research in the management of high risk post-operative patients, research in advanced head and neck cancer, the expansion of the thyroid cancer research portfolio and a general increase in early phase studies and international collaboration.

Identify key research areas

The CSG held a very productive strategy meeting in early 2019 which will refocus the strategy from 2019 onwards and has helped to identify key aims for the upcoming years including:

- Large observational study for pre-invasive disease
- Repeat HN5000 within newer treatment era
- A systematic approach to rarer Head & Neck cancers, including thyroid cancers and salivary gland cancers, initially observational with plan to evolve into interventional studies
- A focus on methods for earlier diagnosis of primary and recurrent disease and chemo-prevention strategies
- Trials in oral medicine, including management of fibrosis and dry mouth, including consideration about important PROMs data
- Closer liaison with CT-PAG and CM-Path to ensure consistent sample collection with relevant guidelines and QA
- Increase collaboration with International Groups including the EORTC and Head & Neck Intergroup
- Increase collaborations to attract more academic and commercial early phase drug and device trials
- Strengthen links and communication with NIHR CRN Head & Neck leads to ensure timely delivery of studies within the portfolio

This will involve the revised subgroups utilising current relationships and developing new ones with support from the core group. Improved understanding of basic science will underpin many of these approaches and a more strategic engagement with scientists will be undertaken over the upcoming years. Focus groups to develop specific trial objectives will continue to be developed, generating an atmosphere for collaborative working and mentorship. Active involvement of consumers within the sub-groups is key to this and an additional aim for the upcoming years.

Epidemiology & Survivorship Subgroup (Chair, Dr Ioanna Nixon)

The Epidemiology & Survivorship Subgroup has been incredibly successful under the leadership of Steven Thomas and in recent years has been focussed on maximising the delivery from the H&N5000 study. The Subgroup has recently appointed a new chair to continue these successes and inspire the Group to new activities.

Understanding the reasons behind late stage diagnosis

Existing interactions between patient and healthcare infrastructure is framing the complex factors that play a role in diagnostic delay. Delays are influenced by a wide range of factors such as psychosocial, financial, structural and educational at various stages throughout the diagnostic and treatment process. Treatment delays can lead to further disease progression, increased morbidity and poor survival. We are collaborating with international partners to investigate the socio-economic, logistic and biological predictors of late stage diagnosis for head and neck cancers.

The Headspace study is a collaborative case control study funded by Horizon 2020 between Europe and South Africa. The study is coordinated by IARC and aims to investigate multiple reasons for poor prognosis, individual and structural reasons for late diagnosis, the influence of life style, genetic factors on poor outcomes.

Improve detection of recurrent cancer in cancer survivors

Prognosis for patients with head and neck cancer is variable, nonetheless follow up protocols are similar. Recurrence typically occurs in the first three years and detection rate in routine follow up is poor. The use of PET –CT guided surveillance at one year is going to be evaluated in a study exploring more efficient approaches to follow up for head and neck cancer patients.

Improve lifestyle interventions in head and neck cancer survivors

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

Understanding "what matters to me" in head and neck cancer survivors to improve quality of life in this patient group.

Treatments for patients with Head and Neck cancers are morbid and can have a detrimental impact on basic functions including speech, swallowing and appearance. As a result, these can have a profound negative effect on emotional wellbeing. The Epidemiology and Survivorship Subgroup is aiming at promoting research in line with 'UK top 10 Living With and Beyond Cancer' research priorities to better understand issues around survivorship and inform interventions to enhance quality of life for these patients. The subgroup aims to look at mental health and wellbeing in patients with Head and Neck cancers, aiming to understand association between fear of recurrence, anxiety and depression, disease factors and socioeconomic factors.

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

The Surgery & Localised Therapies Subgroup continues to focus on several important areas including premalignant disease and oral health, interventional studies in head and neck cancers which are primarily surgically treated, and post-operative trials. The CRUK AMG 319 'window of opportunity' study is now closed and in the write up with an aim to publication in 2019.

Develop interventional trials for laryngeal and hypopharyngeal cancer

These remain challenging disease subsites for trials, especially in the current environment of immunotherapy. The Wisteria trial (arms A and B) addresses these disease subsites to a degree (H Mehanna, University of Birmingham) and early work for a larger interventional study is in progress (V Paleri, ICR/RMH).

New Trials in Development

These are numerous and some highlights are listed below:

1. LOOC; sentinel node in oropharynx cancer; Clare Shilling & Mark McGurk, UCL. **Now funded through the NIHR EME stream.**
2. RaPTOR – Medical management of ORN; Funding applied for.
3. Resistance Training and Optimising Nutrition for Head and Neck Cancer Patients; Mike Nugent, Sunderland. PPI exercise complete; funding application RfPB
4. SPARTAN; Corticosteroids and post op pain in pts undergoing TORS resection of Head & Neck cancer. EME rejected; back to RDS; RfPB tier 3 application.
5. RESPECT trial; De-escalation of the elective neck in oropharynx cancer; Claire Paterson, Glasgow. In early development.

Continuing trial development

A brief summary of each is provided:

1. LISTER Feasibility Trial; Lugols for oral and oropharyngeal dysplasia surgical management. **Completed recruitment** – 47 Pts (aimed for 40). Data analysis ongoing – present in Rio at ICOMS Brazil May 2019. (ORACLE Trust and LNWH charitable funds).
2. LiTEFORM – M Nugent; A RCT of the clinical and cost effectiveness of Low Level Laser in the Management of Oral Mucositis in Head and Neck Cancer Irradiation. **80 patients recruited** – no extension to funding.
3. SAVER – Na valproate for non resectable oral dysplasia; **funding approved;** opening in 2019.
4. BEST-of study – EORTC / Mererid Evans and Terry Jones; Velindre NHS Trust CTU. 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.
5. DeFEND; Fibrin tissue adhesive in neck dissection surgery; recruiting well ahead of target; **phase 3 application planned** for in next HTA round (combined health economic & patient reported outcome)
6. MOSES trial – Vinidh Paleri; ICR CTU, London. TORs mucosectomy in the UKP and potential modifications to non-surgical treatment based on results. Currently **collecting preliminary data** prior to application.

Systemic Therapy & Radiotherapy Subgroup (Chair, Dr Anthony Kong)

Continue to recruit efficiently into current portfolio of open studies

Systemic Therapy & Radiotherapy Subgroup had a busy time over the last year. ComPARE trial is recruiting very well to target (the addition of a fifth arm with adjuvant durvalumab is recruiting well and the surgical arm is now closed). The EACH trial exploring avelumab and cetuximab combination in relapsed recurrent/metastatic SCCHN opened in July 2018 and continues to recruit well. The NIMRAD recruitment is on track and due to close in May 2019 with a revised target of 340 patients and a changed primary endpoint (locoregional control). ORCA2 is recruiting slowly and should complete recruitment in 2019. The PATHOS trial had funding awarded by CRUK to proceed to the phase III part and recruitment is going well, with the trial now opening in multiple sites worldwide. The Wisteria study has a slow recruitment and is behind the planned timeline, although new sites have been opened recently which may help recruitment. The RAPPER study had blood samples stored for 669 patients and the DNA was extracted from 312 patients with plans to genotype. The recruitment for PATRIOT, VocTox and HARE40 trials are ongoing.

Consider new trial designs for areas of unmet need

Many studies have been developed across different groups of patients and areas of unmet need over the last 2 years

- TORPEDO is evaluating proton beam therapy in HPV positive good prognosis OPSCC and recently had funding confirmed by CR-UK, with the first patient aiming for Oct 2019
- NICO study testing adjuvant Nivolumab in Oral SCC study has funding approved from BMS and the protocol is completed, with recruitment to start soon
- Oberon study testing durvalumab, tremelimumab + cetuximab in R/M SCCHN patients has funding approved and protocol is completed; sites currently being set up
- POPPY, a phase II study to assess the efficacy and safety profile of pembrolizumab in patients of a Performance Status of 2 with recurrent or metastatic HNSCC; Due to open in mid-2019
- INNOVATE trial testing novel plasma HPV DNA assay for treatment has MRC funding approved and is due to open in May 2019

Studies currently in development

In addition to the above studies that have recently received funding and are in set up, the following studies are in development and set up, a few of which are collaboration with International/European centres:

- Androgen deprivation therapy (ADT) for salivary cancers, an EORTC-led international multicentre, randomised phase II study aiming to evaluate the efficacy and safety of chemotherapy versus androgen deprivation therapy (ADT) in patients with recurrent and/or metastatic, androgen receptor (AR) expressing, salivary gland cancer (SGCs). Recruiting in Europe and aiming to open in UMK in 2019

- UPSTREAM: A pilot study of personalized biomarker-based treatment strategy or immunotherapy in patients with recurrent/metastatic SCCHN. Opened first centre in Q1 2019 with other centres to open in Q2 2019.
- TWEET, testing paclitaxel with the WEE1 inhibitor AZD1775 in recurrent/metastatic SCCHN had funding approved through CRUK/AZ but trial development is currently on hold pending AZ's decision on the future of AZD1775
- RADTVEC study (RT combined with TVEC) is being developed for SCCHN patients not suitable for concurrent chemotherapy or cetuximab and it is currently awaiting further decision from AMGEN due to company's uncertainty of the future direction of TVEC in SCCHN
- Prospero study was designed to test combination immunotherapy in salivary gland cancers and was in development although recently halted due to the discontinuation of MEDI9197 clinical development by AZ
- CUSTOM (high risk operable larynx / hypopharynx 'Michigan' approach) is currently being developed (Vin Paleri at ICR/RMH)

Thyroid Subgroup (Chair, Dr Jon Wadsley)

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

Building on the network of centres developed through the SELIMETRY trial capable of standardised dosimetry, the group have continued to work on a new trial design to test the benefits of dosimetrically guided radioiodine therapy compared with standard empirical therapy in patients with high risk disease. It is planned that a trial proposal will be taken to the CTRad Trials Proposals Meeting for further discussion in June 2019.

Increase surgical trials on the portfolio

This year funding has been secured from NIHR EME for the NIFTy trial, investigating the role of near-infrared fluorescence in aiding identification of parathyroid glands and avoiding postoperative hypoparathyroidism in patients undergoing thyroid surgery. The study is now in active set up.

A further surgical study, the HOT trial, aiming to randomise patients with low risk thyroid cancer to either lobectomy or total thyroidectomy has been submitted to NIHR HTA scheme. Extensive engagement with the thyroid surgical community has been undertaken. Whilst it is acknowledged that this will be a challenging trial to recruit to there is widespread support and it is agreed that this is the next important question to address in the management of low risk thyroid cancer.

BAETS are supporting a trainee led collaborative to undertake a national observational study of the epidemiology and initial management pathway of thyroid nodules (Thy3000). Apart from

generating valuable data it is hoped that this will encourage trainees to consider greater involvement in research and to become the CIs of the future.

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

The iNATT tissue bank continues to collect samples from patients with this rare and aggressive condition. Tissue has been released to allow a number of projects to be undertaken and NGS will soon have been undertaken on all current samples.
Engaging pharma to consider a study in this area has been challenging due to the extreme rarity of the condition, but discussions have been held about the possibility of accessing an ALK inhibitor and a BRAF inhibitor for patients with tumours demonstrating the relevant mutations. This continues to be actively pursued.

Coordinate molecular pathology studies through the group

The promising results of a pilot study testing the role of circulating tumour DNA as a biomarker for progression and response to treatment have been published this year. Work is now in progress for developing a larger multicentre study to further evaluate the role of this technology in assisting treatment decisions. Further expertise from molecular biologists to assist the group is being actively sought.

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

Links have been maintained with a number of companies developing new drugs in this field. A commercial trial of cabozantinib as second line therapy for advanced iodine refractory differentiated thyroid cancer is in set up in a number of UK centres and another study investigating a highly specific RET inhibitor in advanced medullary thyroid cancer hopes to open within the next year.

A very tight network of UK thyroid cancer centres facilitates cross referral of patients when studies are not available in their own centre.

Disappointingly an investigator led study proposal to investigate toxicity and quality of life issues for patients receiving lenvatinib was not supported by the company.

Develop studies addressing the risks of over diagnosis and over treatment in thyroid cancer

Given the significant increase in diagnosis of low risk, often incidentally discovered disease, this is becoming increasingly important. A series of trials (HiLo, IoN and now HOT) have investigated the possibility of de-escalating treatment for patients in these low risk groups. The group continues to support this work which has been internationally practice changing and has influenced international treatment guidelines.

It is increasingly recognised that trends to de-escalate treatment may have a significant and potentially adverse psychological impact on patients. The group is keen to further explore this

important aspect of patient management but is currently lacking the expertise in qualitative research methodologies to undertake this.

4. Task groups/Working parties

The Head & Neck Group 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

Cancer Research UK Clinical Research Committee (CRUK CRC)					
Study	**Application type**	**CI**	**Outcome**	**Level of CSG input**	**Funding amount**
May 2018					
TWEET: A randomised phase II Trial of WEE1 inhibitor (AZD1775) with Taxane chemotherapy (paclitaxel) versus paclitaxel in HNSCC	Early Phase & Feasibility Study	Dr Anthony Kong	Supported	CSG developed	
PATHOS: Post-operative adjuvant treatment for HPV-positive tumours	Late Phase Study	Dr Mererid Evans	Supported	CSG developed	
November 2018					
TORPEdO: a phase III trial of intensity-modulated proton beam therapy versus intensity-modulated radiotherapy for multi-toxicity reduction in HPV related oropharyngeal cancer	Clinical Trial Award	Dr David Thomson	Conditionally Supported	CSG developed	
Circulating HPV DNA as a predictive biomarker in HPV positive head and neck cancer	Biomarker Project Award	Dr Shreerang Bhide	Not supported	CSG supported	
Neoadjuvant chemoselection for customised treatment versus standard of care for locally advanced laryngeal cancer: a randomised controlled trial	Clinical Trial Award Outline	Professor Vinidh Paleri	Not invited to full	CSG developed	
Other committees					
Study	**Committee & application type**	**CI**	**Outcome**	**Level of CSG input**	**Funding amount**
Circulating HPV DNA as a predictive biomarker in HPV positive head and neck cancer	MRC	Dr Shreerang Bhide	Supported	CSG supported	

Evaluation of the LightPath Imaging System in head and neck cancer surgery	Innovate UK	Joanne Oshea	Supported	CSG supported	

6. Consumer involvement

Emma Kinloch and Timothy Humphrey

The Consumer members of the CSG have played a full role in the work of the Group 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 inputting into the future strategy of the CSG.

Emma Kinloch has been a member since 2015. 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. Through her involvement with the NCRI Head and Neck CSG, she has collaborated with Dr Robert Metcalf, a medical oncologist from The Christie hospital in Manchester, to start a new UK charity focused on furthering research into rare salivary gland cancers.

The scientific mentoring relationship within the CSG has allowed the opportunity for support with and insight into, CSG work when needed.

Timothy Humphrey became a member of the NCRI Head and Neck CSG in September 2017 and is also a member of the NCRI CTRad. 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 **International Collaboration** Increase collaboration with International Groups, more specifically to develop a series of combined pan-European study proposals for challenging situations where a multinational approach will add value.
Priority 2 **Proton Beam Therapy (PBT) trials** Support the set up and opening of the TORPEdO study, which has recently become the first UK funded PBT study. This is a large complex study, randomising between IMRT, delivered locally, and IMPBT, delivered at two PBT Centres, and as such will require significant planning and extensive RTQA. In addition, there are other Head & Neck areas of need where PBT may be of value and studies to explore these will be developed within the CSG.
Priority 3 Explore the development of 1 or 2 observational studies. The current focus is on a follow on study to H&N5000 and a study of pre-malignant disease.
Challenge 1 Transition ideas from a very productive strategy meeting into a formal strategy and then into deliverable grant submissions and new applications.
Challenge 2 There are an increasing number of large pharma recognising the importance of Head & Neck cancer and whilst this interest is laudable, it means the Head & Neck clinical trial landscape is becoming competitive, increasing the challenge to recruit to academic studies, especially as commercial studies tend to be better funded than academic ones. In addition, the increased commercial interest and early success of immune checkpoint inhibitors in advanced disease means that the treatment landscape is changing quickly and difficult to predict / future proof academic randomised studies against.
Challenge 3 There is real pressure on Head & Neck clinical trials teams across the UK, with several big units on hold to new studies due to capacity issues and others setting recruitment caps. This

adds a huge challenge to the feasibility of delivering current studies and studies in development.

8. Collaborative partnership studies with industry

Several of the studies within the current trials portfolio and those in development are being developed in collaboration with industry. These include collaborations with AstraZeneca, BMS, Merck, MSD and Pfizer. These relationships are predominantly between investigators and their institutions and industry partners but the Group will explore ways of disseminating these relationships to maximise collaborative potential across UK.

9. Appendices

Appendix 1 - Membership of Head & Neck Group and Subgroups

Appendix 2 – Head & Neck Group and Subgroup strategies

- A – Head & Neck Group 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

Dr Martin Forster (Head & Neck Group Chair)

Appendix 1

Membership of the Head & Neck Group

Name	Specialism	Location
Dr Rachel Brooker*	Clinical Oncologist	Liverpool
Dr Bernadette Foran	Clinical Oncologist	Sheffield
Dr Anthony Kong	Clinical Oncologist	Birmingham
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 Jon Wadsley	Clinical Oncologist	Sheffield
Dr Timothy Humphrey	Consumer	Oxford
Ms Emma Kinloch	Consumer	London
Dr Martin Forster (Chair)	Medical Oncologist	London
Dr Robert Metcalf	Medical Oncologist	Manchester
Dr Joseph Sacco	Medical Oncologist	Liverpool
Dr Jacqueline James	Pathologist	Belfast
Dr Lisette Martin*	Pathologist	Sheffield
Dr Max Robinson	Pathologist	Newcastle
Dr Wai Lup Wong	Radiologist	Stevenage
Dr Christina Yap	Statistician	Birmingham
Dr Emma King	Surgeon	Southampton
Mr Matt Lechner*	Surgeon	London
Mr Barry Main*	Surgeon	Bristol
Professor Jim McCaul	Surgeon	Bradford
Mr Paul Nankivell	Surgeon	Birmingham
Mr Andrew Schache	Surgeon	Liverpool
Mr Stuart Winter	Surgeon	Oxford

Membership of the Subgroups

Epidemiology & Survivorship Subgroup		
Name	**Specialism**	**Location**
Professor Gerry Humphris	Clinical Oncologist	St Andrews
Dr Charles Kelly	Clinical Oncologist	Newcastle
Dr Ioanna Nixon (Chair)	Clinical Oncologist	Glasgow
Dr Richard Simcock	Clinical Oncologist	Sussex
Mrs Christine Allmark	Consumer	Yorkshire
Professor Mary Wells	Health Services Researcher	London
Professor Luc Bidaut	Medical Physicist	Lincoln
Professor Hisham Mehanna	Surgeon	Birmingham
Professor Simon Rogers	Surgeon	Liverpool

Surgery & Localised Therapies Subgroup		
Name	**Specialism**	**Location**
Dr Claire Paterson	Clinical Oncologist	Glasgow
Mr Max Robinson	Pathologist	Newcastle
Mr Tas Kanatas	Surgeon	Leeds
Dr Emma King	Surgeon	Southampton
Dr Jim 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 (Chair)	Clinical Oncologist	Birmingham
Dr Stefano Schipani	Clinical Oncologist	Glasgow
Dr Ketan Shah	Clinical Oncologist	Oxford
Dr Joseph Sacco	Medical Oncologist	Liverpool
Dr Catharine West	Scientist	Manchester
Dr Emma King	Surgeon	Southampton
Professor Hisham Mehanna**	Surgeon	Birmingham

Thyroid Subgroup		
Name	**Specialism**	**Location**
Dr Matthew Beasley**	Clinical Oncologist	Bristol
Dr Kate Garcez**	Clinical Oncologist	Manchester
Dr Georgina Gerrard**	Clinical Oncologist	Leeds
Dr Laura Moss	Clinical Oncologist	Cardiff
Dr Jon Wadsley (Chair)	Clinical Oncologist	Sheffield
Ms Kate Farnell	Consumer	
Ms Helen Hobrough**	Consumer	
Dr Saba Balasubramanian**	Endocrinologist	Sheffield
Dr Kristien Boelaert	Endocrinologist	Birmingham
Professor Mark Strachan	Endocrinologist	Edinburgh
Professor Allan Hackshaw	Epidemiologist	London
Dr Glenn Flux**	Medical Physicist	London
Professor David Gonzalez-de-Castro	Molecular Oncologist	Belfast
Dr Sarah Johnson	Pathologist	Newcastle
Dr David Poller	Pathologist	Portsmouth
Professor Dae Kim	Surgeon	London
Mr Radu Mihai	Surgeon	London

* denotes trainee member

**denotes non-core member

Appendix 2

Head & Neck Group & Subgroup Strategies

A – Head & Neck Group 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

The Epidemiology and Survivorship Subgroup aspires to promote research on early diagnosis and early detection of recurrence in patients with head and neck cancers. In addition, it aims to support and develop research on survivorship for head and neck cancer patients.

The Subgroup will promote research in line with the 'UK top 10 Living With and Beyond Cancer' research priorities to better understand issues around survivorship and inform interventions to enhance quality of life for these patients.

The subgroup in its current form met on the 11th June 2019 in London. The focus of the meeting was on the following:

- Vision and narrative: Aims and focus of the subgroup
- Working better together and in agency with others
- Research in line with NCRI top 10 priorities and HN5000
- Funding avenues

In the meeting it was agreed the scope of work will focus on:

i. Using the patient reported outcomes collected in HN5000 to inform and shape the future research areas

ii. Support the ongoing clinical trials to ensure that they are successfully completed and more importantly their findings have the maximal opportunity to improve patient care.

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
2. To open studies currently in set up, as outlined above.
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
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
6. Develop studies addressing the risks of over diagnosis and over treatment in thyroid cancer
7. Seek expertise in qualitative study design to facilitate eg work on impact of individualised decision making on patients

Appendix 3

Portfolio maps

NCRI Portfolio Maps

Head and Neck Cancer

Map A – Oral squamous cell carcinoma

ê below to reset map

		Chemotherapy	Diagnosis	Novel agents	Observational / mechanisms / genetics	Radiotherapy	Surgery
Early stage	All				Outcomes of neck surgery in oral cancer V1		
Locally advanced	2st line treatment				ADC for tissue factor, Tisotumab Vedotin		
Other	All	IDR-OM-02		NICO	Therapy Effectiveness For HPV Biomarkers in Head and Neck Cancer	IDR-OM-02	GE/137 fluor imaging
Pre-malignant	All						
Recurrent / metastatic	1st line treatment				Observational study in R/M SCCHN		
	2st line treatment				CANC - 5086		
	All		SAVER		OBERON TACTI-002 (P015); Keynote-PN798 LAG3 + pembro POPPY of KY1044 and atezolizumab in adv. treatments & survival for advanced		

Filters Used:
Active Status: All, **CSG Involvement**: Data collection in progress, **Funding Type**: All, **Phase**: All, **LCRN**: None

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

NCRI Portfolio Maps

Head and Neck Cancer

Map B – Pharynx-larynx squamous cell carcinoma

ê below to reset map

		Chemotherapy	Diagnosis	Observational / mechanisms / genetics	Quality of life	Radiotherapy	Surgery
Early stage	HPV+						PATHOS
	HPV+/-	ORCA/2					
Locally advanced	Null						
	HPV-						
	HPV+					PEARL: PET-BASED ADAPTIVE RADIOTHERAPY CLINICAL TRIAL	
	HPV+/-			RAPPER ORCA/2			
	Other						
Other	HPV+			Cempilimab with/without ISA101b in HPV16Positive Platin-Resistant OPC			
	Other			CompARE Trial			
Pre-diagnosis	All						
Recurrent / metastatic	Other			OBERON			

Filters Used:
Active Status: All, **CSG Involvement**: Data collection in progress, **Funding Type**: All, **Phase**: All, **LCRN**: None

Open / multi resea..
In Setup / single re..
Open / single rese..

NCRI Portfolio Maps

Head and Neck Cancer

Map C – Thyroid-specific cancer

ê below to reset map

		Chemotherapy	Diagnosis / monitoring	Novel agents	Observational / mechanisms / genetics	Quality of life	Radiotherapy / radioisotope therapy	Surgery
Anaplastic	Early stage							
	Locally advanced/ metastatic							
Differenciated	Early stage						IoN	
	Locally advanced/ metastatic			BLU-667 in Lung Cancer, Thyroid Cancer and Other Solid Tumours Cabozantinib in			SEL/I/METRY	
Medullary	Early stage							
	Locally advanced/ metastatic			Caprelsa in MTC BLU-667 in Lung Cancer, Thyroid Cancer and Other Solid Tumours				

Filters Used:
Active Status: All, **CSG Involvement**: Data collection in progress, **Funding Type**: All, **Phase**: All, **LCRN**: None

Open / single rese..

In Setup / single re..

NCRI Portfolio Maps

Head and Neck Cancer

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

ê below to reset map

		1st line treatment	2st line treatment	Chemothera..	Diagnosis	Novel agents	Observational / mechanisms / genetics	Quality of life	Radiotherapy	Surgery
Early stage	All			WEE1 IDO in head				ARTFORCE H&N		
Locally advanced	All			Keynote- 412 WEE1 OMO1.01.02 MK3475-689						
	HPV-									
	HPV+									
	HPV+/-			NIMRAD			RAPPER VoxTox		NIMRAD	
Other	All	B9991023		WO40242			Biological		Best-Of	
Recurrent / metastatic	All	EACH (EORTC	KO-TIP-007 Unresectable	OMO1.01.02		Investigation	Head and Neck C			

Filters Used:
Active Status: All, **CSG Involvement**: Data collection in progress, **Funding Type**: All, **Phase**: All, **LCRN**: None

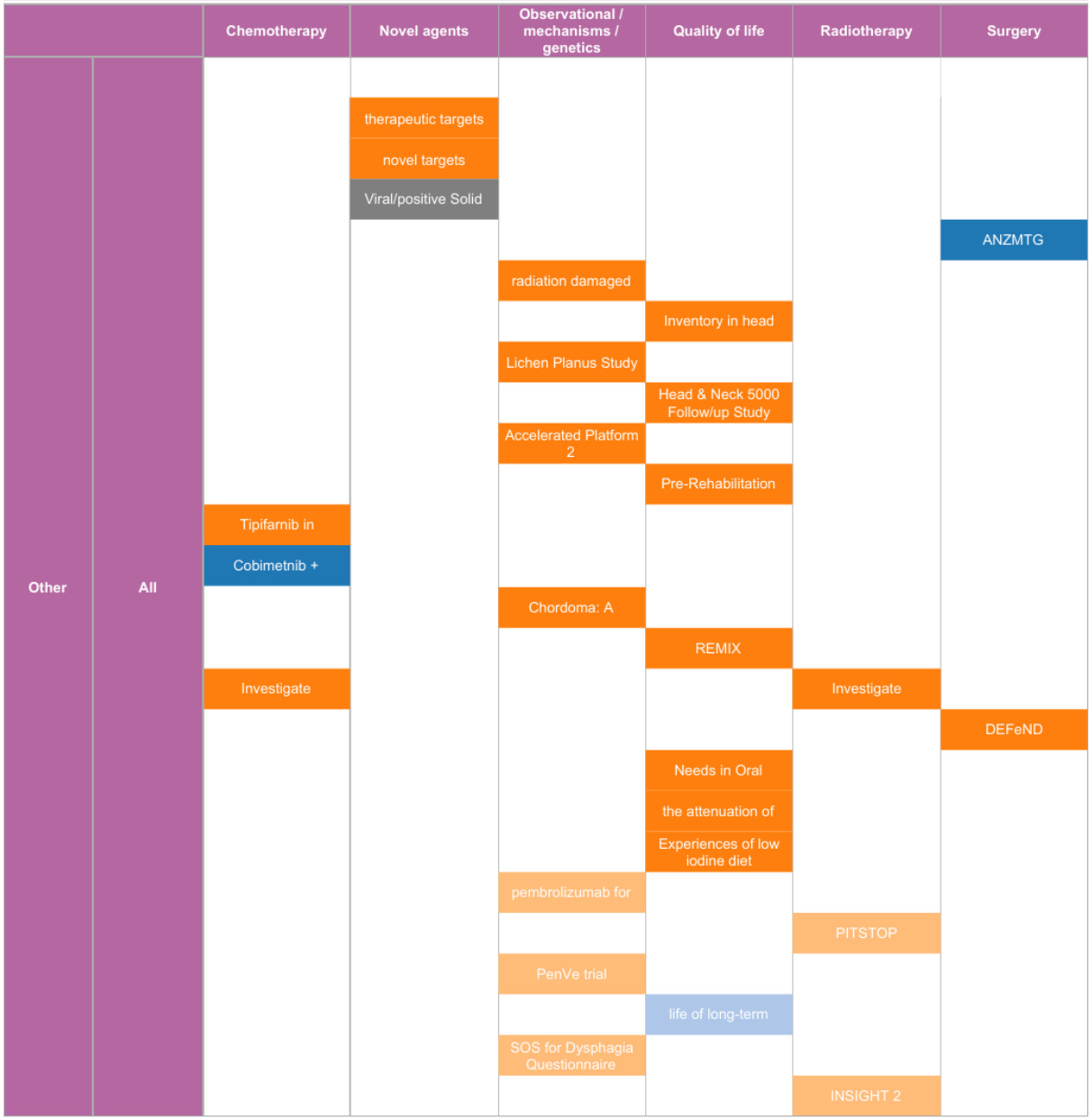
In Setup / single re.. Open / single rese..
In Setup / multi res.. Open / multi resea..

NCRI Portfolio Maps

Head and Neck Cancer

Map E – Cross-cutting: other

ê below to reset map



Filters Used:
Active Status: All, **CSG Involvement**: Data collection in progress, **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

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
Radiotherapy plus cisplatin or cetuximab in low-risk human papillomavirus-positive oropharyngeal cancer (De-ESCALaTE HPV): an open-label randomised controlled phase 3 trial. Mehanna et al. 2019 Lancet Vol.393 (10166), pp. 51-60.	Practice changing	Design, recruitment and delivery
Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study. Cohen et al. 2019 Lancet, Vol.393 (10167), pp. 156-167	Practice changing	Recruitment and delivery
Patritumab with Cetuximab plus Platinum-Containing Therapy in Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck: An Open-Label, Phase Ib Study. Dillon et al. (2018) Clin cancer res, Vol.25 (2), pp. 487-495	Progress to phase II/III	Design, recruitment and delivery

Results of a multicentre randomised controlled trial of cochlear-sparing intensity-modulated radiotherapy versus conventional radiotherapy in patients with parotid cancer (COSTAR; CRUK/08/004). Nutting et al. 2018 Eur j cancer, Vol.103, pp. 249-258.	Practice changing	Design, recruitment and delivery
'Association between comorbidity and survival in head and neck cancer: Results from Head and Neck 5000'. Schimansky et al. 2019 *Head and Neck*, vol 41., pp. 1053-1062	Informative and hypothesis generating	Design, recruitment and delivery

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the Head & Neck Group portfolio, 13 trials closed to recruitment and 21 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
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
2018/2019	436	994	413	980	3.42	8.13