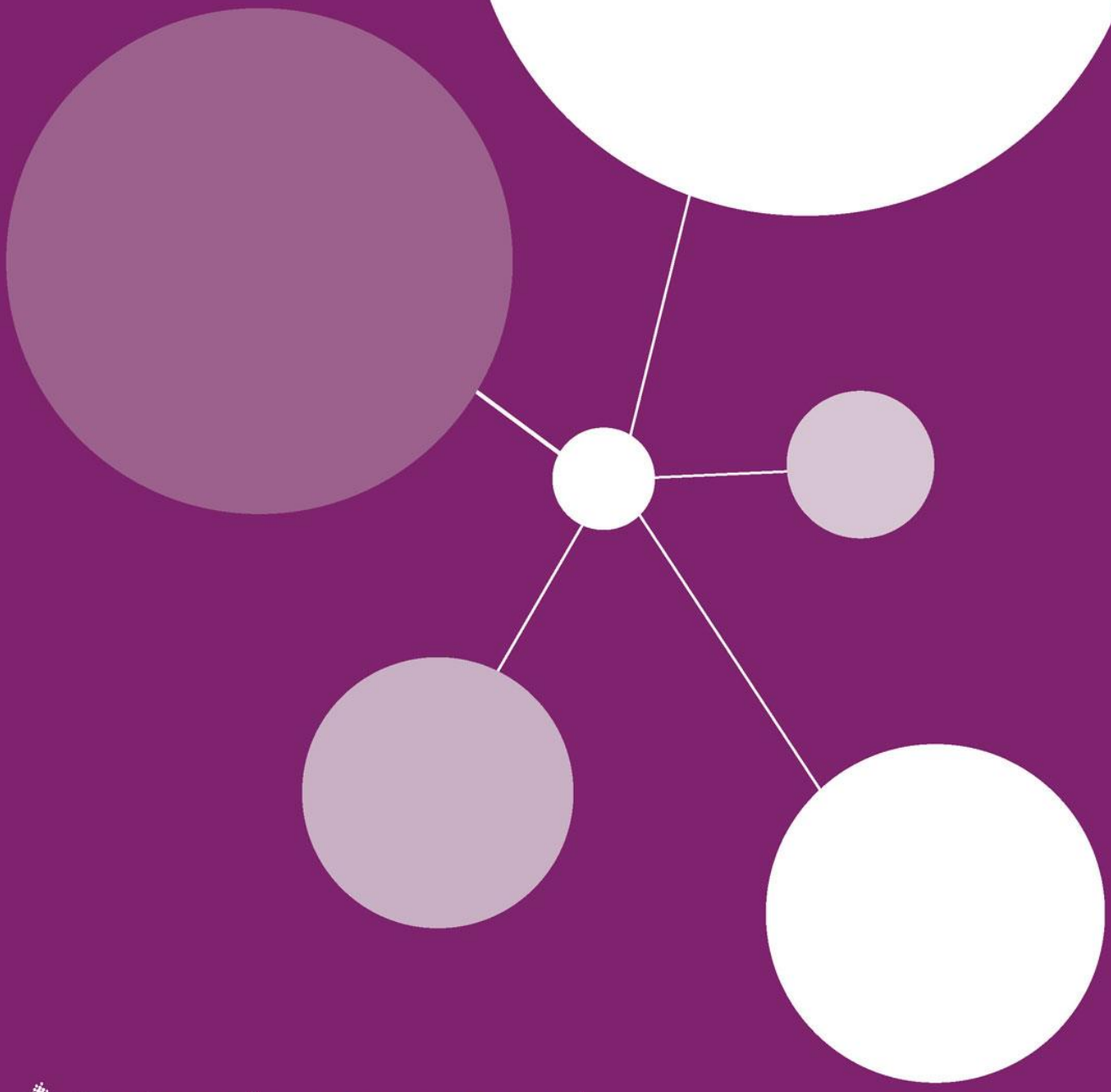
NCRI
National
Cancer
Research
Institute

NCRI Skin Cancer Clinical Studies Group

Annual Report 2016-17



Partners in cancer research

NCRI Skin Cancer CSG Annual Report 2016-17

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

The 2015-16 Annual Reports review feedback asked CSGs to focus on developing high recruiting trials, strengthen translational science and refresh CSG Subgroup membership. Specifically, the CSG was encouraged to focus on developing non-melanoma research studies and broaden the skin cancer portfolio to include screening and psychosocial studies.

In response, we have made good progress on most of these tasks: funding for the DANTE trial and INTERIM trial was secured from HTA and RfPB respectively. Both trials are due to open to recruitment in the next year. These trials each explore key clinical questions of international importance and provide the opportunity to recruit large numbers at all national specialist centres treating metastatic melanoma patients. Sample collections for each trial are planned (CRUK funding has been secured for the INTERIM sample collection), thereby building our translational research capability.

The CRUK outline submission to fund a randomised trial evaluating both surgery and radiotherapy in high risk resected squamous cell carcinoma was rejected in November 2016. However, the useful feedback has resulted in a revised, more focussed proposal to be submitted in the coming year.

Group membership diversified this year and acquired new dermatology and clinical oncology expertise (in both the main CSG and Non-Melanoma Skin Cancer Subgroup), a pathologist, a new statistician and a medical oncologist with a specific interest in psychosocial medicine. They have contributed to several research proposals now in development which should lead to funding applications in 2017-18.

Although a negative trial, the Group was rewarded with an oral presentation at ASCO 2017 for the final results of the national adjuvant melanoma trial, AVAST-M (CI: Pippa Corrie). AVAST-M included a translational programme (PROM, CI: Mark Middleton), from which first evidence that ctDNA may have useful prognostic value has been generated (ASCO 2017 abstract; manuscript submitted for publication).

2. Structure of the Group

Consistent with feedback from the 2015-16 report, the CSG membership has continued to evolve with the aim of facilitating new research avenues. This year, the Group has acquired new

dermatology and clinical oncology membership, a pathologist, a new statistician and a medical oncologist with a specific interest in psychosocial medicine. Several new research proposals are now in development, which should lead to funding applications in 2017-18.

The Non-Melanoma Skin Cancer Subgroup has also refreshed its membership with several new dermatologists being invited to join the Subgroup. Links with those experts rotating off the main Group remain in place and it is hoped that several new proposals for non-melanoma skin cancer studies will progress in the next year.

3. CSG & Subgroup strategies

Main CSG

The main aims of the Skin Cancer CSG for 2016-17 were: 1) to secure two high recruiting multicentre clinical trials for metastatic BRAF wild type and BRAF mutant melanoma patients in order to facilitate recruitment of patients receiving standard therapies to studies addressing questions of high international importance, 2) to fund a non-melanoma skin cancer clinical trial and 3) continue to diversify the skin cancer portfolio beyond interventional systemic therapy trials, with particular goals to generate new studies in screening and psychosocial medicine.

We have made good progress regarding these aims, particularly the first and third aim:

1. Funding for the DANTE trial evaluating optimal duration of anti-PD1 antibody therapy (CI: Sarah Danson) was secured from HTA and funding for the INTERIM trial of intermittent versus continuous dosing of BRAF targeted therapy (CI: Pippa Corrie) was secured from RfPB. Both trials are due to open to recruitment in 2017-18. These trials each explore key clinical questions of international importance providing opportunity to recruit large numbers at national centres treating metastatic melanoma patients. CRUK funding has been secured for the INTERIM sample collection (CI: Mark Middleton) and an application for the DANTE-Trans sample collection will be submitted in June 2017.
2. Expanding the non-melanoma studies portfolio remains our biggest challenge. Refreshment of the main CSG, including appointment of a clinical oncologist and dermatologist each with an interest in non-melanoma skin cancer, as well as membership of the Non-Melanoma Skin Cancer Subgroup, will hopefully generate benefits in the coming year. New study proposals are discussed below.
3. Working with Professor Fiona Walter, who is a member of both the NCRI Primary Care CSG and SPED Advisory Group, the Group continues to work towards a proposal for an early detection pilot in a population defined as being at high risk for developing melanoma. Dr Miranda Payne initially began working with the CSG on a psychosocial medicine proposal in her capacity as an NIHR regional skin cancer Subspecialty Lead (SSL) and is now progressing this concept as a newly appointed CSG member.

Non-Melanoma Skin Cancer Subgroup (Chair, Dr Catherine Harwood)

The aim of the Non-Melanoma Skin Cancer Subgroup is to promote and support high quality, multicentre clinical trials, translational research and other activities in the field of non-melanoma skin cancer. In particular, the Subgroup aims to:

- Support initiatives in providing an evidence base for treatment of the common keratinocyte skin cancers (SCC and BCC).
- Support research for rarer non-melanoma skin cancers such as Merkel cell carcinoma and DFSP.

Key aims were defined at the last strategy day held in November 2016 and remain as follows:

1. Funding of a clinical trial in management of high risk primary SCC (COMMISSAR).
2. Development of a trial for low risk BCC (CIRCLE).
3. Development of one other study for rarer cancers.

Progress

1. The COMMISSAR outline proposal - a randomised trial evaluating both surgery and radiotherapy in high risk resected squamous cell carcinoma - was rejected by CRUK CRC in November 2016. However, the useful feedback has helped to generate a more focussed proposal based on the role of adjuvant radiotherapy to be submitted next year.
2. BCC projects remain in discussion, with the goal of generating at least one key study funding application next year.
3. Rational MCC (Merkel cell carcinoma, CI: Neil Steven) is now funded and sites are being opened across the country. Currently, patient registration is going well but the challenge is to ensure sufficient patients are randomised in order to secure ongoing support for this trial in a rare patient group.

4. Task groups/Working parties

An Early Diagnosis Task Group (TG) was set up two years ago in order to explore opportunities to develop studies in this area. The TG was able to contribute significantly to the final design of Dr Peter Murchie's funded feasibility RCT (ASICA) evaluating the role of a behaviour change intervention digitally delivered using a tablet computer designed to prompt and maintain skin self-examination in identifying new melanoma in those patients with a previously resected primary melanoma (stage 0-2C primary cutaneous melanoma within preceding 24 months). This study is in set-up and starts recruiting in limited UK sites in July 2017.

The main goal of the TG is to progress the concept of a national melanoma screening/surveillance study. Through Dr Fiona Walter's NIHR-funded MelaTools programme, it is apparent that screening the general population is not realistic. However, MelaTools has defined a higher risk group which can be self-identified via GP surgeries and health economic modelling of potential screening interventions for this population has commenced (manuscript submitted for publication). Further exploratory work is being undertaken within this programme which will inform the potential for a pilot study and focus on early detection of melanoma in a higher risk population. It is therefore anticipated that this TG will remain in place a further year to facilitate development of a research proposal.

5. Patient recruitment summary for last 5 years

In the Skin Cancer CSG portfolio, 10 trials closed to recruitment and 13 opened.

Total skin cancer recruitment fell this year, largely due to closure of several locally-led non-interventional studies. Virtually all of the non-interventional studies on the portfolio are out of the CSG's control. Reassuringly, recruitment to interventional trials increased compared with last year. Most CSG-led trials are interventional, but these tend to recruit much lower numbers compared with the non-interventional studies. The recruitment data demonstrates the importance of non-interventional research contributing to overall skin cancer activity.

As already described, the CSG has worked hard over the last two years to secure potentially high recruiting studies which should impact positively on interventional trial recruitment: DANTE target recruitment is 1,068 over five years and INTERIM target recruitment is 150 over two years. The time scale for securing funding and setting up trials means that this new activity will only be realised from 2017-18 onwards.

There is a need to develop non-interventional studies and the proposed DANTE-Trans sample collection may well enhance additional non-interventional activity, provided the funding application in 2017-18 is successful and consent to collect samples as part of registration in the DANTE trial prior to randomisation is allowed to 'count' as recruitment activity. Since DANTE will randomise patients who are progression-free at one year, double of the number of patients are likely to be registered in advance and could potentially be consented for translational sample collection.

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	534	140	534	140	4.3	1.1
2013/2014	534	403	530	403	4.3	3.3
2014/2015	622	217	609	175	4.9	1.4
2015/2016	504	234	504	228	4.09	1.85
2016/2017	182	320	182	312	1.48	2.53

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

The CSG has excellent links with NIHR Cancer: CRN SSLs. A Joint NCRI/NIHR meeting has been held annually for the last three years and has yielded both new study proposals and new CSG membership, as some SSLs have themselves got involved in study development. This close relationship helps as a means of also addressing barriers to current clinical trial recruitment.

The Skin Cancer CSG shares membership with the Primary Care CSG (Professor Fiona Walter) as a means of addressing opportunities for screening, prevention and early diagnosis studies. Dr Jim Lester (clinical oncologist) continues to work with the Brain CSG to explore brain metastasis clinical trials.

The CSG has close ties with the EORTC through Professor Paul Lorigan (University of Manchester and previous Chair of the Skin Cancer CSG) who chairs the EORTC Metastatic Melanoma Subgroup and he is currently exploring whether the EORTC may wish to contribute to recruiting to DANTE.

The CSG has also facilitated UK recruitment to several ANZMTG trials in difficult to recruit patient populations and several of their trials have been adopted onto the portfolio, e.g. the WBRT and RT2 trials.

Our surgeon, Professor Marc Moncrieff, has collaborations with the USA and has brought EAGLE FM into the portfolio. Very recently, SWOG (The Southwest Oncology Group), via Professor Toni

Ribas, has shared several metastatic melanoma study proposals with the CSG and we will take forward opportunities to work with this group in 2017-18.

7. 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**
May 2016			
None			
November 2016			
COMMISSAR: COnventional surgery versus Moh's Micrographic surgery for hIgh-risk primary cutaneous Squamous cell carcinoma and the role of Adjuvant Radiotherapy	Outline application	Professor Catherine Harwood	Not invited to full
INTERIM sample collection application: a randomised phase II feasibility study of INTERmittent versus continuous dosing of oral targeted therapy In patients with BRAF mutant unresectable or metastatic Melanoma	Full application submitted December 2016	Professor Mark Middleton	May 2016: Successful
Other committees			
Study	**Committee & application type**	**CI**	**Outcome**
A randomised phase III discontinuation trial to evaluate optimal duration of anti-PD1 monoclonal antibody treatment in patients with metastatic melanoma	HTA Full application Submitted February 2016	Professor Sarah Danson	November 2016: Successful
INTERIM: a randomised phase II feasibility study of INTERmittent versus continuous dosing of oral targeted therapy In patients with BRAF mutant unresectable or metastatic Melanoma	RfPB Full application Submitted March 2016	Dr Pippa Corrie	August 2016: Successful

8. Collaborative partnership studies with industry

A number of current academic interventional studies led by previous CSG members rely on industry support, for example SELPAC (Astra Zeneca combinations alliance, CI: Paul Nathan), PIANO (Plexxicon, CI: Paul Lorigan) and PERM (MSD, CIs: James Larkin and Paul Nathan). Each of these studies are recruiting below target and the primary reason given in each case is that these trials are recruiting rare patient populations, e.g. metastatic uveal melanoma, CKIT mutant acral/mucosal metastatic melanoma and metastatic melanoma with at least two accessible tumours for irradiation and measurement. The trial CIs have rotated off the CSG but the CSG remains committed to working with them and the SSLs to address barriers and facilitate recruitment.

It is worth noting that the two new metastatic melanoma trials, DANTE and INTERIM, have been designed to recruit patients receiving standards of care, thereby not being reliant on industry partnership. DANTE was designed with an expectation that PERM would have completed recruitment before opening. These two trials will now overlap but sites will be encouraged to prioritise PERM for those patients eligible for both studies.

Current and ex-CSG members continue to work with Pharma to bring new industry sponsored studies into the portfolio and function as national CIs for these multicentre trials.

9. Impact of CSG activities

The overall survival primary endpoint of the melanoma adjuvant trial, AVAST-M (CI: Pippa Corrie), was analysed in early 2017 and selected for presentation at ASCO 2017. The study showed that although adjuvant bevacizumab offered a significant improvement in disease free interval, this did not translate into an overall survival benefit. AVAST-M included an extensive blood and tumour sample collection (PROM, CI: Mark Middleton) and a programme of translational/biomarker initiatives may yet impact future patient management. For example, outcomes of both the observational and interventional arm were influenced by patient BRAF and NRAS mutation status; initial ctDNA studies undertaken by the Lorigan/Marais group (Manchester) suggest that measurement of ctDNA after surgery predicts for overall survival (ASCO 2017 abstract; manuscript submitted for publication).

CSG members (Agata Rembielak and Christian Ottensmeier) contributed to the NICE guidance BCC vismodegib scoping (ID 1102), although were not invited to be the clinical experts for this technology appraisal. Dr Neil Steven, is currently contributing to the NICE Merkel cell avelumab technology appraisal (ID1043).

Following restructuring of NHSE, the national chemotherapy CRG is developing tumour-specific working groups to provide specialist advice in drawing up and maintaining national systemic treatment algorithms which will inform commissioning. The group membership includes the relevant CSG Chair and four geographically based clinical experts. The Melanoma Working Group was established at the end of 2016. In addition to assisting with algorithm development, the Group (led by Pippa Corrie) was influential in challenging the new Blueteq access criteria introduced in December 2017 for dabrafenib+trametinib and ipilimumab+nivolumab, both of which had gained positive NICE guidance earlier in the year. While the NICE guidance was broad, based on drug licensing criteria for access, the Blueteq criteria significantly and inappropriately constricted access. The Melanoma Working Group was able to secure revisions to the Blue-teq access criteria, arguing from the evidence-base. Furthermore, Blueteq criteria will be put in place for all future NICE-approved high cost drugs and they have the potential to conflict with clinical trial recruitment. The Chair was able to secure confirmation from Peter Clark and David Thomson that they will ensure a process by which CIs of NIHR portfolio trials can request amendment(s) to the criteria in order to allow trial recruitment. For example, approval was secured to amend the criteria to allow clinicians to register patients in the Blueteq system when recruiting to INTERIM.

10. Consumer involvement

Patricia Fairbrother
During the year, my activities have included supporting my regional skin cancer clinical specialist group in terms of user involvement. This work included advising on the construction of a melanoma patient survey for the region, and currently, along with GPs with a special dermatology interest, constructing a non-melanoma cancer patient survey. This will include directing patients to links for research based websites. I have been involved in several teleconferences for clinical trials management including Commissar (in progress), INTERIM and the Primary Care CSG MelaTools programme.

I am on the point of starting up an online support group for non-melanoma patients, including former patients. This group will not only be used for support but also occasional comment and opinion for researchers who are looking for consumer input to patient information for funding applications and studies. I am also currently a lay member of the Skin Clinical Reference Group for NCRAS.

An initiative to make contacts internationally, started by a fellow member of the NCRI Consumer Forum, has culminated in me making connections with the ANZ Melanoma Trials Group. The trials group has a number of melanoma and non-melanoma trials running currently. It is of special interest to me to have this connection as I have lived in New Zealand and have close family there. I look forward to extending our interests in the future.

I am a member of the Non-Melanoma Skin Cancer Subgroup where I have attended face-to-face meetings plus several teleconferences. These meetings featured updates on several trials including Commissar, SPOT, and two new studies, ROSEBAC and CIRCLE (high risk BCC and low risk BCC). It is with the Subgroup that I came up with the idea of starting up an online support group for non-melanoma patients.

Simon Rodwell
As the consumer member of DANTE, INTERM and the Rational MCC trials management groups, I took part in meetings and advised on patient-related issues, edited documents such as lay narratives and patient information sheets. I also service on TMGs not in the CSG trials portfolio.

Via Melanoma Focus as an observer, my main patient-related activities include:

- Melanoma helpline – Established January 2017, based on a six person nurse specialist team via a call centre. Widely advertised with take-up gradually increasing. See: http://melanomafocus.com/support/helpline/.
- Melanoma patient decision aid – Launched May 2017, this online tool describes treatment options, helping patients participate more effectively in decision making with the aim of improving communication between melanoma specialists and their patients. See: http://melanomafocus.com/support/helpline/.
- National clinical guidelines for mucosal melanoma: funded by Melanoma Focus and almost complete, having begun in July 2016. This first project addresses ano-uro-genital melanoma, is due to go out to consultation imminently and will be published at the end of 2017/early 2018, with NICE approval. A future guideline for sino-nasal melanoma is planned. See: http://melanomafocus.com/activities/mucosal-guidelines/.

11. Open meetings/annual trials days/strategy days

The CSG does not have an annual trials meeting. However, the trial portfolio is publicised at the annual national (November) and regional (May) Melanoma Focus Conferences where all delegates are provided with a clinical trials booklet generated by the NCRI Executive and clinical trials are addressed within the conference agenda.

The CSG Chair has been invited to talk about how to access clinical trials at the forthcoming Melanoma Patient Conference, which was held for the first time in June 2017 and is likely to become a national annual event.

Following on from the very successful joint NCRI/NIHR meetings, the last one held in March 2016, a next joint meeting is planned for May 2017.

12. Priorities and challenges for the forthcoming year

Priorities

- To open DANTE and INTERIM to recruitment and secure funding for DANTE-Trans which would enhance both interventional and non-interventional activity.
- To revise, resubmit and secure funding for the non-melanoma skin cancer trial COMMISSAR.
- Develop new screening/early detection and psychosocial study proposals.
- Succession planning: Dr Harwood is due to leave the CSG in early 2018 and Dr Corrie is due to leave the CSG in May 2018.

Challenges

- Securing funding for academic multicentre clinical trials.
- Addressing recruitment to current non-commercial portfolio studies with important industry links in rarer patient groups (e.g. SELPAC, PIANO and PERM) which have CIs that are no longer members of the CSG.
- Maximising access to commercial sponsored trials. Current and ex-CSG members work with Pharma to bring new industry-sponsored studies into the portfolio and function as national CIs for them. A current challenge is that ex-CSG members closest to Pharma now work independently and we do not have a process by which these trials can be brought to the CSG early in their evolution in order to ensure NIHR portfolio adoption and negotiate maximum number of sites for the UK. The Chair has discussed this issue with several individuals and with Professor Poulam Patel, NIHR Specialty Lead for late phase trials, but the Group have not as yet found a reliable solution.
- Succession planning: Dr Harwood is due to rotate off the CSG in early 2018 and Dr Corrie is due to leave the CSG in May 2018.

13. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies
A – Main CSG Strategy
B – Non-Melanoma Skin Cancer Subgroup Strategy
C - Early Diagnosis Task Group Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous year

Dr Pippa Corrie (Skin Cancer CSG Chair)

Appendix 1

Membership of the Skin Cancer CSG

Name	Specialism	Location
Dr Mazhar Ajaz	Clinical Oncologist	Guildford
Dr Jim Lester	Clinical Oncologist	Sheffield
Dr Agata Rembielak	Clinical Oncologist	Manchester
Ms Patricia Fairbrother	Consumer	Derby
Mr Simon Rodwell	Consumer	Bury St Edmunds
Dr Catherine Harwood	Dermatologist	London
Dr Charlotte Proby	Dermatologist	Dundee
Dr Rubeta Matin	Dermatologist	Oxford
Dr Fiona Walter	General Practitioner	Cambridge
Dr Pippa Corrie (Chair)	Medical Oncologist	Cambridge
Professor Sarah Danson	Medical Oncologist	Sheffield
Professor Christian Ottensmeier	Medical Oncologist	Southampton
Dr Neil Steven	Medical Oncologist	Birmingham
Dr Miranda Payne	Medical Oncologist	Oxford
Dr Avinash Gupta*	Medical Oncologist	Oxford
Dr Paul Craig	Pathologist	Cheltenham
Mr Marc Moncrieff	Surgeon	Norwich
Dr Christina Yap	Statistician	Birmingham

* denotes trainee member

Membership of the Subgroups

Non-melanoma Skin Cancer Subgroup		
Name	**Specialism**	**Location**
Dr Christina Yap	Biostatistician	Birmingham
Dr Agata Rembielak	Clinical Oncologist	Manchester
Dr Pat Lawton	Clinical Oncologist	Nottingham
Ms Patricia Fairbrother	Consumer	Derby
Dr Girish Gupta**	Dermatologist	Lanarkshire
Dr Catherine Harwood (Chair)	Dermatologist	London
Dr John Lear	Dermatologist	Manchester
Dr Jack Mann	Dermatologist	Essex
Dr Rubeta Matin	Dermatologist	Oxford
Dr Andy Muinonen-Martin	Dermatologist	Leeds
Dr Charlotte Proby	Dermatologist	Dundee
Dr Jerry Marsden**	Dermatologist	Birmingham
Dr Neil Steven	Medical Oncologist	Birmingham
Dr Jenny Nobes**	Clinical Oncologist	Norwich
Professor Fiona Bath-Hextall**	Professor of Evidence Based Healthcare	Nottingham
Mr Marc Moncrieff	Surgeon	Norwich

Early Diagnosis Task Group		
Name	**Specialism**	**Location**
Dr Girish Gupta	Dermatologist	Glasgow
Dr Catherine Harwood	Dermatologist	London
Dr Rubeta Matin	Dermatologist	Oxford
Dr Charlotte Proby	Dermatologist	Dundee
Professor Peter Murchie	General practice	Aberdeen
Dr Fiona Walter (Chair)	General practice	Cambridge
Dr Ewan Brown	Medical Oncologist	Edinburgh
Dr Pippa Corrie	Medical Oncologist	Cambridge

**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

Skin Cancer CSG Strategy: December 2015 – December 2018

This strategy timeline has been produced to define the Skin Cancer Research Strategy Plan and its implementation. It runs from December 2015 until December 2018, and will be reviewed and updated at each CSG meeting (ND supported by All)
The document is composed of the following:

Page 2 – 7: NCRI Skin Cancer CSG Strategy: plan of implementation, containing agreed strategic objectives (1-6), specific actions, CSG leads and proposed deadlines.

Page 8 – X: Overview and detailed breakdown of the entire strategy timeline

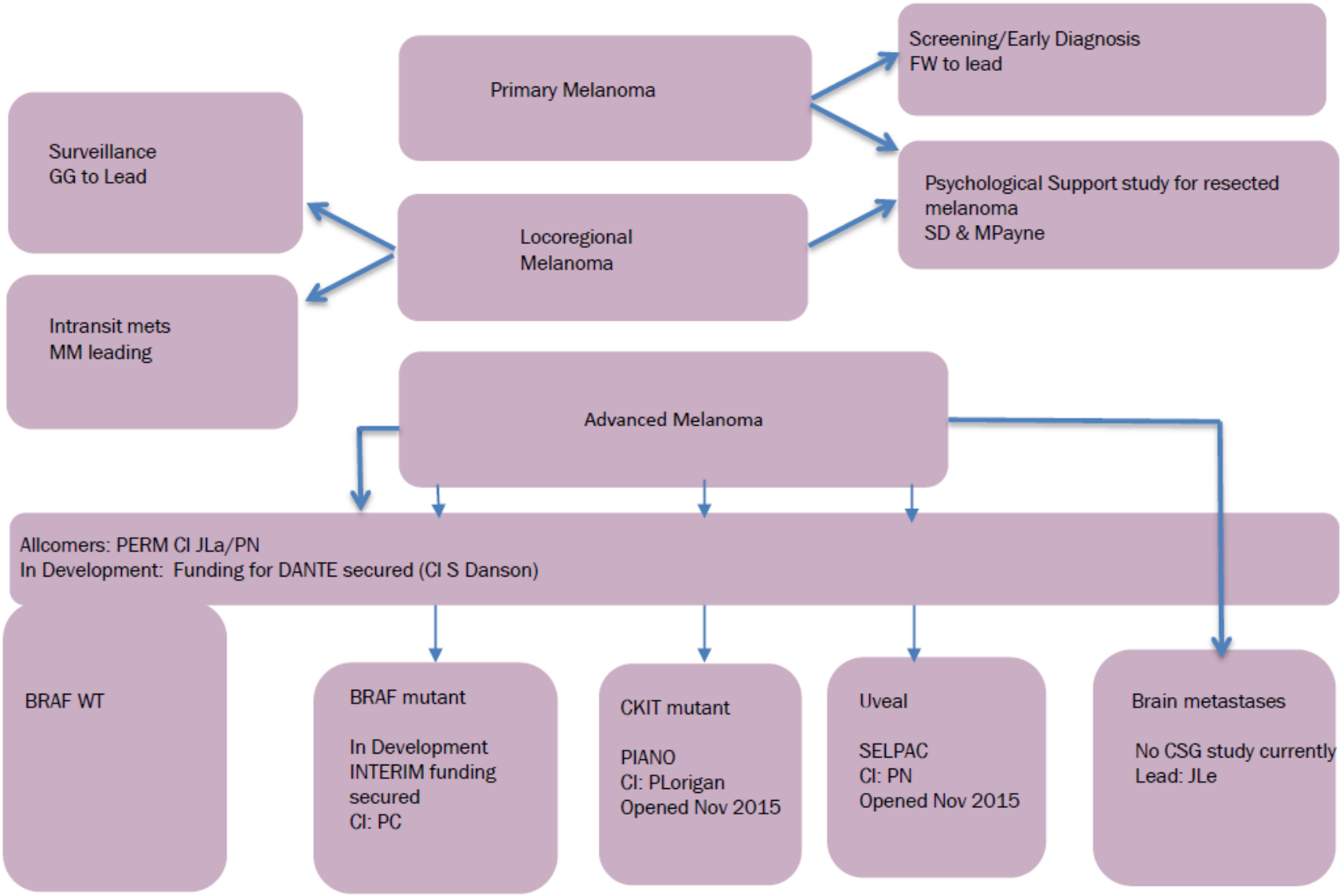
Skin Cancer CSG Members		Responsibility
PC	Pippa Corrie	CSG chair
CH	Catherine Harwood	Non-melanoma skin cancer subgroup chair
JLa	James Larkin	Melanoma - cutaneous
SD	Sarah Danson	Melanoma – rare
CP	Charlotte Proby	SPED representative
MM	Marc Moncrieff	Surgical studies
JLe	Jim Lester	Radiotherapy – melanoma
FW	Fiona Walter	Primary care
EB	Ewan Brown	Melanoma
GG	Girish Gupta	Dermatology
KW	Keith Wheatley	Statistics
SR	Simon Rodwell	PPI Lead - melanoma
PF	Patricia Fairbrother	PPI Lead – non-melanoma skin cancer
MA	Mazhar Ajaz	Radiotherapy
CO	Christian Ottensmeier	Translational research lead
AR	Agata Rembielak	Radiotherapy – non-melanoma
NS	Neil Steven	Non-melanoma - rare
ND	Nanita Dalal	PA
NK	Nicola Keat	NCRI Exec

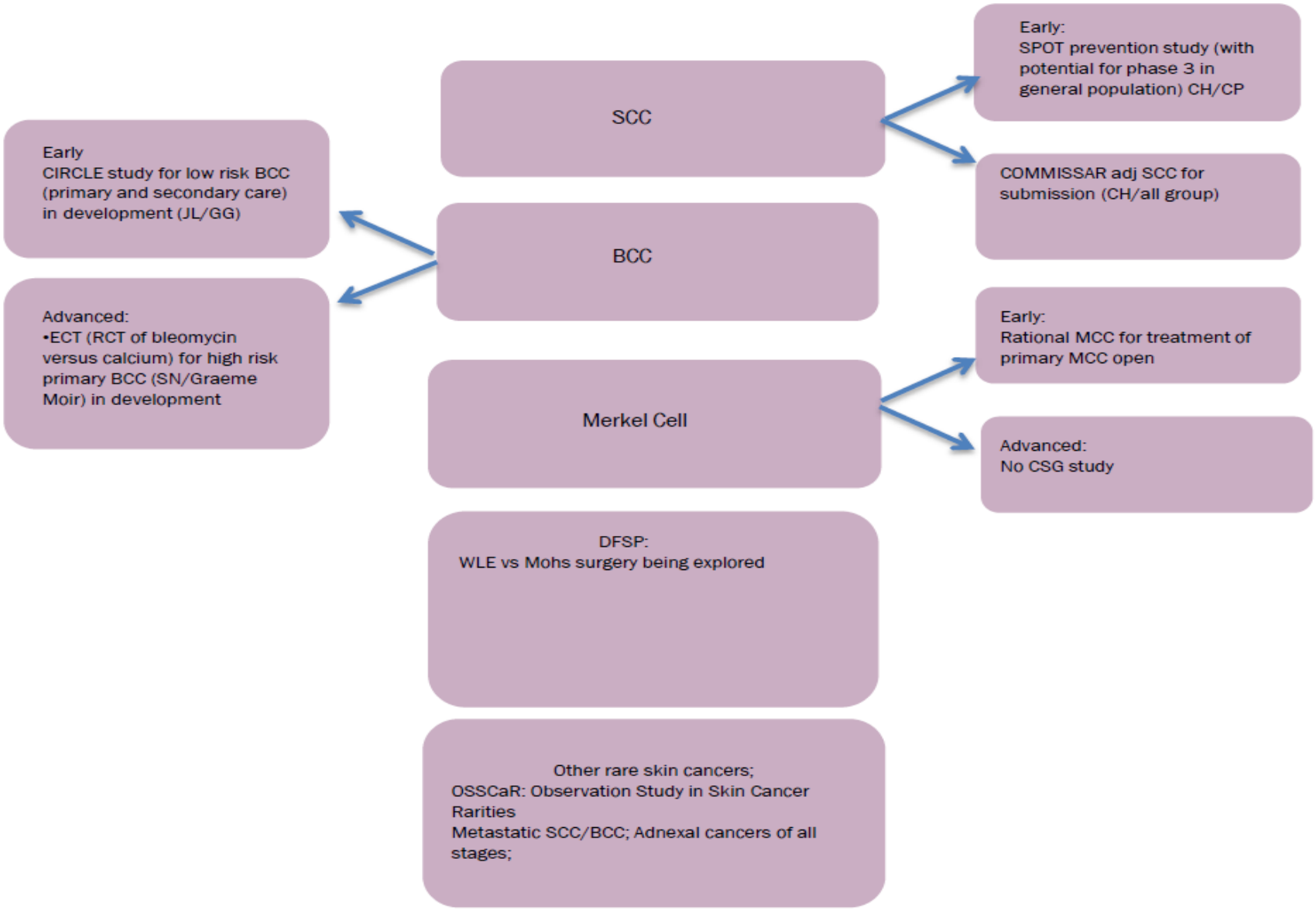
Strategic objective	Action	CSG Lead	Date	Outcomes
1a. Portfolio development (general)	Establish a set of priorities for the development and set up of studies that takes account of the NIHR portfolio, international agenda, available funding opportunities and clinical need	ALL	Document key priorities at Strategy Day 24 Nov15	Review Portfolio priorities 6-monthly at CSG meetings
1b. Portfolio development - melanoma	Ensure cohesive strategy of melanoma clinical trials, taking into account: - Opportunities within the international agenda, avoiding competition with key Pharma studies - The need for a high recruiting study studies - Balance between late and early phase studies - Multicentre studies with good regional coverage - All disease stages - All subgroups – rare forms & biomarker specific subgroups - Interaction with CRN subspecialty leads	ALL SD & PC leading on DANTE and INTERIM trials	Secure funding for 2 metastatic melanoma trials, DANTE and INTERIM in 2016	Funding for DANTE and INTERIM secured
1c. Portfolio development – non-melanoma skin cancer	Secure new studies for common and uncommon non-melanoma skin cancer •SCC •BCC •Merkel cell •Rarer non-melanoma skin cancers	CH/GG/CP/RM	Commissar funding application by May 2016; further development of CRICLE BCC study	Commissar funding application rejected; to revise and resubmit new study proposal; CIRCLE study to be submitted by end 2017
1d. Interaction with Cross Cutting groups	Identify leads within the CSG to link with the following cross cutting CSGs and advisory groups: •Primary Care •Screening, Prevention and Early Diagnosis (SPED) Advisory Group •TYA •CTRAD •CNS CSG	FW CP SD JLe JLe	Dec 2016	Proposal to work with other CSGs wrt immunotherapy toxicity management research opportunities – to take forward at May 2017 NCRI-NIHR meeting

Strategic objective	Action	CSG Lead	Date	Outcomes
1e. National Cancer Intelligence Network (NCIN)	Establish clear link with skin cancer Clinical Reference Group (CTYA SSCRG) Explore with NCIN the use of data to inform study design and take over long term follow-up	?? ?? and ALL	Report 6 monthly at CSG meeting	NCIN has restrutured, now NCRAS. Need to explore new ways of interacting
2. Key research priority areas	**Surgery**: Working group to take forward new study for localised disease **Early phase**: Increase the availability of NIHR adopted early phase studies for melanoma patients • Liaise with CIs and study sponsors to request NIHR adoption • Inform colleagues re opportunities re commercial early phase/ combinations alliance programmes • Increase no. of melanoma study outline proposals being submitted for funding/endorsement **Radiotherapy**: Establish new study for brain mets pts involving RT **Translational**: •Work with key clinical and scientific groups to develop a translational research strategy: link with potential GeCIP **Melanoma screening pilot study**: Working group to take new proposal forward	MM/PC Jla handing over to SD JLe Jla hading over to CO FW, CP, PC	May & Nov 2016 Ongoing Ongoing Early 2017 Ongoing	Outline proposal in advanced stage, to seek funding in 2017 JLe to work with CNS MDT to explore potential RT+/-SRS study Apply for INTERIM and DANTE sample collections FW to update on progress towards screening study May 2017
3a. Raising awareness and profile	Regular dissemination of study recruitment activity and outcomes through newsletters, annual meetings and Annual Report to all stakeholders Consider dedicated annual NCRI skin cancer trials meeting Communications about new studies with CRN subspecialty leads Submission of abstracts to : •NCRI Cancer Conference •International cancer conferences: ESMO/ECC/ASCO/AACR/SMR •NCIN Conference	PC/ND/SA All Annual NCRI-NIHR meeting ALL	Ongoing March 2016 May 2017 Ongoing	CSG trainee to be responsible for summarising CSG meetings to share with LCRH SSLs Current preference is to use the biannaul Melanoma Focus Meetings to share verbal clinical trials updates/portfolio trial summary booklet

Strategic objective	Action	CSG Lead	Date	Outcomes
3b. Ensuring successful delivery of studies through integration with NIHR CRN: Cancer	CSG members to commit to delivering studies developed by the CSG Interaction with LCRN Subspecialty Leads to determine placement of new studies and address barriers to actively recruiting patients Monitor recruitment to portfolio studies, esp those developed by the CSG to ensure delivery to time and target Contribute as far as possible to NIHR CRN: Cancer Speciality Objectives so they reflect what LCRNs need to deliver to ensure skin cancer patients can access the full portfolio of studies within England	ALL PC/ALL ALL ALL	Ongoing Ongoing Ongoing Ongoing	Recruit CSG-led studies to time and target Good regional placement of studies Meet NIHR CRN Speciality Objectives
3c. Maximise output from clinical trials	Establish working groups for new studies within 6 weeks of funding award to facilitate swift set up, including representation from CI, CRCTU, NIHR CRN: Cancer	CI/CTUs	Ongoing	
4. Strengthen UK wide and international working	Refine prioritisation process for international clinical trials to be submitted for funding to optimise the timing and success of applications Utilise IRCI for international studies of rare cancer types, where appropriate Work closely with UK representative on EORTC melanoma group steering committee Work closely with Melanoma Focus to integrate research and service	All ?? Invite representation at CSG meetings Invite representation at CSG meetings	Ongoing Ongoing May 2016 May 2016	Plorigan is EORTC link SRodwell continues currently as PPI and Melanoma Focus Lead

Strategic objective	Action	CSG Lead	Date	Outcomes
5. CSG structure and function	Establish Primary Melanoma Screening Working Party	FW	May 2016	Active
	Establish Secondary Melanoma Screening Working Party	GG	May 2016	Not taken forward
	Consider case for Translational Research Working Party	ALL	May 2016	Not taken forward
	Consider need for Working Party to develop brain mets strategy	JLe	May 2016	Not taken forward but needs prioritising
	Identify mentors for trainee registrars in the CSG	PC, MM	Nov 2016	
	Identify mentors for PPI members	PC & CH	Sept 2015	
6. Patient and Public Involvement and Impact	Ensure consumers are associated with the development of every new study at an early stage	All	Ongoing	CSG representative(s) invited to speak at the now annual Melanoma Patient Conference
	Consider developing research studies to address key questions of concern to PPI representatives and other consumers	SR/PF to bring new questions to the group	Ongoing	


Primary Melanoma
Screening/Early Diagnosis
FW to lead
Surveillance
GG to Lead
Locoregional
Melanoma
Psychological Support study for resected melanoma
SD & MPayne
Intransit mets
MM leading
Advanced Melanoma
Allcomers: PERM CI JLa/PN
In Development: Funding for DANTE secured (CI S Danson)
BRAF WT
BRAF mutant
In Development
INTERIM funding secured
CI: PC
CKIT mutant
PIANO
CI: PLorigan
Opened Nov 2015
Uveal
SELPAC
CI: PN
Opened Nov 2015
Brain metastases
No CSG study currently
Lead: JLe

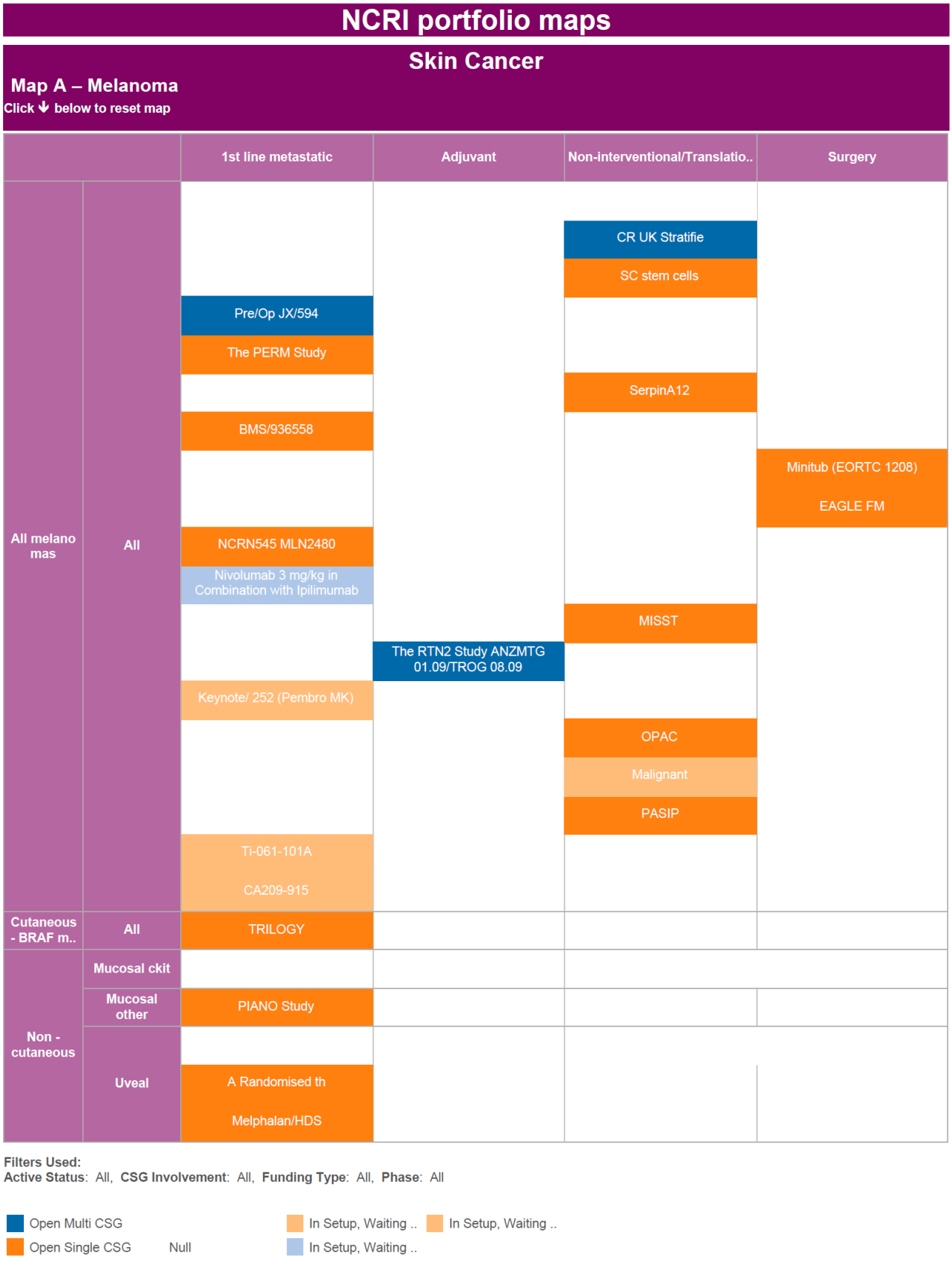

SCC
Early:
SPOT prevention study (with potential for phase 3 in general population) CH/CP
COMMISSAR adj SCC for submission (CH/all group)
Early
CIRCLE study for low risk BCC (primary and secondary care) in development (JL/GG)
BCC
Advanced:
•ECT (RCT of bleomycin versus calcium) for high risk primary BCC (SN/Graeme Moir) in development
Merkel Cell
Early:
Rational MCC for treatment of primary MCC open
Advanced:
No CSG study
DFSP:
WLE vs Mohs surgery being explored
Other rare skin cancers;
OSSCaR: Observation Study in Skin Cancer Rarities
Metastatic SCC/BCC; Adnexal cancers of all stages;

B – Non-Melanoma Skin Cancer Subgroup Strategy

This is incorporated into the main CSG strategy, see above.

Appendix 3

Portfolio maps



NCRI portfolio maps

Skin Cancer

Map B – Non-melanoma

Click ↓ below to reset map

		Adjuvant	Neoadjuvant	Non-interventional/other	Pre-diagnosis	Surgery
All	All			CR UK Stratifie Head and neck s SC stem cells MEDI4736 Patient Reported Outcome Measure In Skin Cancer Reconstruction Study		Skin marker device utility test
Basal cell carcinoma	All					
Merkel cell	All	Rational MCC				
Other	All			4SC AG -Advanced Stage (Stage IIB-IVB) MF or SS		
Squamous cell carcinoma	All				SPOT Trial	

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

Open Multi CSG
Open Single CSG
In Setup, Waiting ..

Appendix 4

Publications in the reporting year

Study	Reference
The MELAMAG Trial	Anninga B, White SH, Moncrieff M, Dziewulski P, L C Geh J, Klaase J, Garmo H, Castro F, Pinder S, Pankhurst QA, Hall-Craggs MA, Douek M; MELAMAG MulticentreTrialists Group.. Magnetic Technique for Sentinel Lymph Node Biopsy in Melanoma: The MELAMAG Trial. Ann Surg Oncol. 2016 Jun;23(6):2070-8. doi:10.1245/s10434-016-5113-7. Epub 2016 Feb 19. PubMed PMID: 26895751
MelaTools Q	Usher-Smith JA, Kassianos A, Emery JD, Abel GA, Teoh Z, Hall S, Neal RD, Murchie P, Walter FM. Identifying people at higher risk of melanoma across the UK: a p[,;-primary care based electronic survey. Brit J Derm. 2016 Dec 23. doi: 10.1111/bjd.15181.
	Emery JD, Usher-Smith JA, Walter FM. Predicting the Risk of Melanoma. JAMA Dermatol. 2016 Aug 1;152(8):875-7. doi: 10.1001/jamadermatol.2016.1574.
RADVAN	Gupta A, Roberts C, Tysoe F, Goff M, Nobes J, Lester J, Marshall E, Corner C, Wolstenholme V, Kelly C, Wise A, Collins L, Love S, Woodward M, Salisbury A, Middleton MR. 0A randomised phase 2 trial of WBRT plus vandetanib for melanoma brain metastases - results and lessons learnt. Br J Cancer. 2016 Nov 8;115(10):1193-120
Utility of the Skin Cancer Quality of Life Impact Tool (SCQOLIT)	G. Wali, E. Gibbons, T. Mackenzie, W. Perkins, J. Reed, R.Turner and R. Matin. Utility of patient-reported outcome measures in non-melanoma skin cancers. PS14, British Journal of Dermatology (2016) 175 (Suppl. S1) pg 211
	G. Wali, E Gibbons, L Kelly, T Mackenzie and RN Matin. Feasibility of using patient reported outcome measures in non-melanoma skin cancers. 1033. Qual Life Res (2016) 25:1–196. Pg 77
LIMIT-1	Marsden JR, Fox R, Boota NM, Cook M, Wheatley K, Billingham L, Steven N. Effect of topical imiquimod as primary treatment for lentigo maligna - the LIMIT-1 study, NCRI Skin Cancer Clinical Studies Group the UK Dermatology Clinical Trials Network and the LIMIT-1 Collaborative Group, Br J Dermatol. October 2016, doi: 10.1111/bjd.15112. [Epub ahead of print]

Appendix 5

Major international presentations in the reporting year

Study	Conference details
MoleMate	Nov 2016, NIHR School for Primary Care Research Ten Year Anniversary Showcase. Oral: 'he MoleMate Trial: outcomes and impact
	Nov 2016, PRIME Centre Wales, Annual Event. Keynote: Supporting early diagnosis of melanoma in primary care
MelaTools Q	Oral presentation of the MelaTools Q study, July 2016, SAPC annual meeting, Dublin.
	The MelaTools Q study, Nov 2016, UICC- World Cancer Congress, Paris.
Rational MCC	Harwood, C, Results of an audit leading to the design of a new UK-wide trial (Rational MCC) comparing surgery versus radiotherapy as first definitive treatment for primary Merkel cell carcinoma. BAD - British Society for Dermatological Surgery Specialist session, 96th Annual Meeting of the British Association of Dermatologists. Oral and poster presentation of trial design, June 2016
	Cassell, O, Results of an audit leading to the design of a new UK-wide trial (Rational MCC) comparing surgery versus radiotherapy as first definitive treatment for primary Merkel cell carcinoma. BAPRAS - British Association of Plastic Reconstructive and Aesthetic Surgeons. Oral presentation of trial design, June 2016
	Steven, N, Results of an audit leading to the design of a new UK-wide trial (Rational MCC) comparing surgery versus radiotherapy as first definitive treatment for primary Merkel cell carcinoma. 2016 NCRI Cancer Conference. presentation of trial design, November 2016
UKMCC-01	Nathan PD, Gaunt P, Wheatley K, Bowden SJ, Savage J, Faust G, Nobes J, Goodman A, Ritchie D, Kumar S, Plummer ER, Lester JE, Ottensmeier CHH, Potter V, Barthakur U, Lorigan P, Marshall E,. Larkin JMG, Marsden J, Steven NM. A Phase II Study of Pazopanib (PAZ) in Metastatic Merkel Cell Carcinoma. J Clin Oncol 34, June 2016 (suppl; abstr 9542). Presented at ASCO 2016
UNITI	Bird J, Danson S & Nolan M, Melanoma, riding the rollercoaster: A longitudinal Grounded Theory study of the experience of melanoma patients and their carers. ECCO, Amsterdam 2017
IMAGE	Middleton MR, Corrie P, Dalle S, Lotem M, Board R, Arance AM, Meiss F, Terheyden F, Gutzmer R, Loquai C, Talbot T, Herbst R, Kähler K, Kotapati S, Le TK, Brokaw J, Abernethy

	AP. Real-world overall survival in advanced melanoma from the IMAGE Study. ASCO 2016
Phase 1b/2 Study of the Combination of IMCgp100 With Durvalumab and/or Tremelimumab in Cutaneous Melanoma	Middleton MR, Steven N, Evans J, Infante J, Sznol M, Mulatero C, Hamid O, Shoushtari AN Shingler W, Johnson W, Patel S, Parker D, Krige D, McAlpine C, Coughlin CM, Hassan NJ, Jakobsen BK & Corrie P. Safety, pharmacokinetics and efficacy of IMCgp100, a first-in-class soluble TCR anti-CD3 bispecific T cell redirector with solid tumour activity: results from the FIH study in melanoma. ASCO 2016
Phase 1b/2 Study of the Combination of IMCgp100 With Durvalumab and/or Tremelimumab in Cutaneous Melanoma	Middleton MR, Steven N, Evans J, Infante J, Sznol M, Mulatero C, Hamid O, Shoushtari AN Shingler W, Johnson W, Patel S, Parker D, Krige D, McAlpine C, Coughlin CM, Hassan NJ, Jakobsen BK & Corrie P. Safety, pharmacokinetics and efficacy of IMCgp100, a first-in-class soluble TCR anti-CD3 bispecific T cell redirector with solid tumour activity: results from the FIH study in melanoma. ASCO 2016
CheckMate 401	Dummer R, Gutzmer R, Corrie P, Millward M, Murzhenko A, Maio M. Clinical trial of nivolumabe combined with Ipilimumab followed by nivolumab monotherapy as frist-line therapy for patients with stage III unresectable or stage IV melanoma: CheckMate 401. EADO 2016
Efficacy of nivolumab plus ipilimumab (combination in patients with advanced melanoma and elevated serum lactate dehydrogenase	Larkin J, Ferrucci PF, Gonzalez R, Thomas L, Maio M, Hill A, Postow M, Savage KJ, Hassel JC, Corrie P, Wagstaff J, Mortier L, Schadendorf D, Hamid O, Long GV, Marquez-Rodas I, Rutkowski P, Walker D, Bhore R, Chiarion-Sileni V, Hogg D. Efficacy of nivolumab (NIVO) plus ipilimumab (IPI) combination in patients with advanced melanoma (MEL) and elevated serum lactate dehydrogenase (LDH): a pooled analysis SMR 2016
	Phase 1b/2 Study of the Combination of IMCgp100 With Durvalumab and/or Tremelimumab in Cutaneous Melanoma Shoushtari AN, Evans J, Corrie P, Steven N, Sznol M, Mulatero C, Infante J, Hamid O, Canestraro M, Coughlin CM., Shingler W, Krige D, Johnson A, Hassan NJ, Jakobsen BK & Middleton MR. A Phase 1 study of IMCgp100, a soluble HLA-A2 restricted gp100-specific T cell receptor-CD3 therapeutic with solid tumor activity in patients with advanced uveal melanoma (UM). SMR 2016