

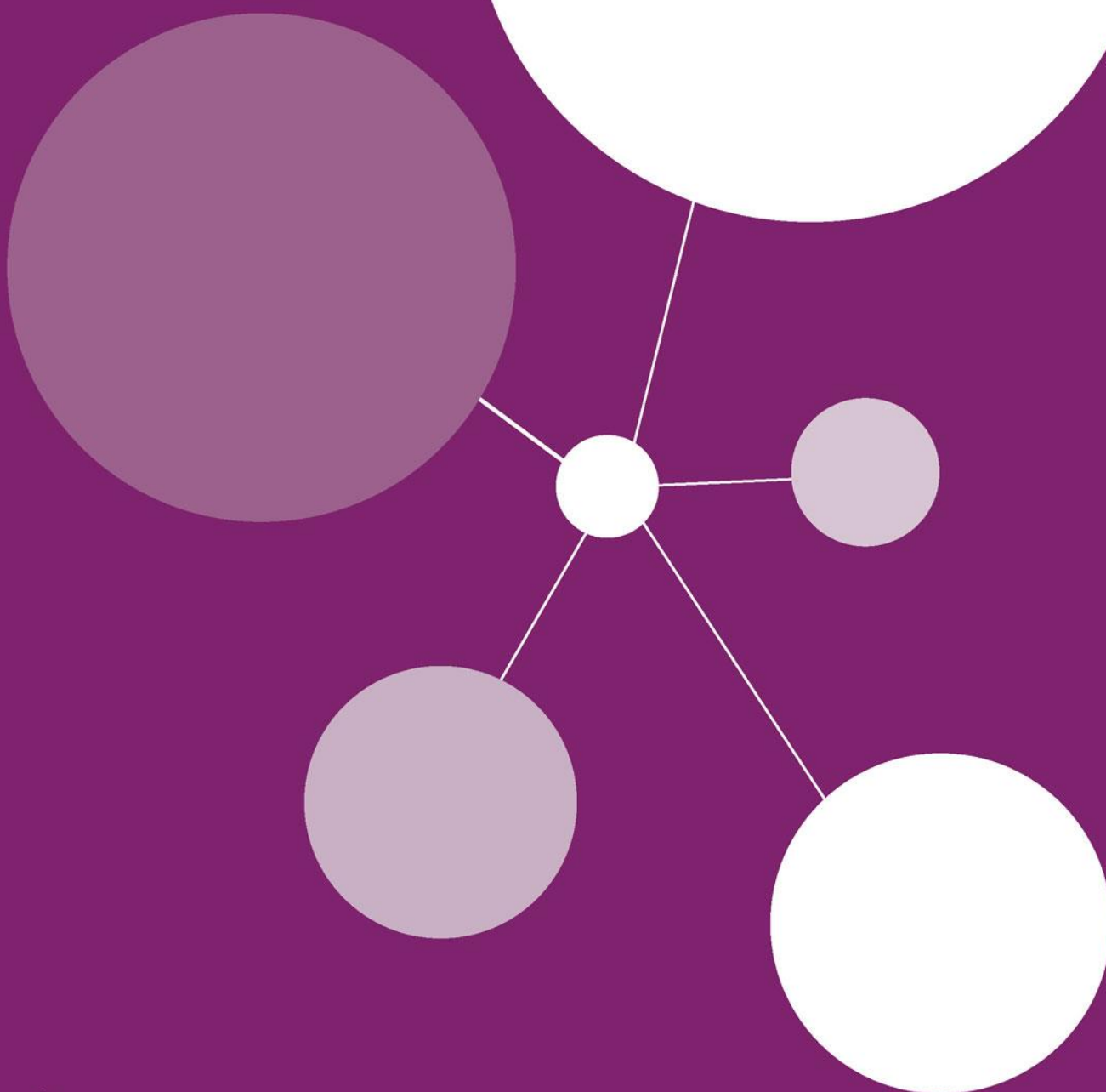


**NCRI**

National  
Cancer  
Research  
Institute

# **NCRI Skin Cancer Clinical Studies Group**

**Annual Report 2015-16**



Partners in cancer research

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## **NCRI Skin Cancer CSG Annual Report 2015-16**

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

The skin cancer portfolio contracted over the last year, following closure of major commercial sponsored registration studies evaluating molecular targeted agents and immune checkpoint inhibitors. While recruitment overall has been lean, recruitment to interventional studies – the main focus of CGS-led studies - has been maintained and a number of registration interventional trials have this year radically changed standard of care for advanced melanoma patients. At ASCO 2015, Dr James Larkin presented preliminary results of the landmark CHECKMATE 067 ipilimumab + nivolumab combination registration trial and the associated NEJM paper is now one of the most cited melanoma research publications\*. CSG members have acted as clinical experts for several key NICE appraisals this year resulting in commissioning of both anti-PD1 antibodies, pembrolizumab and nivolumab, for the treatment of advanced melanoma\*.

The CSG has worked to develop academic studies focusing on key questions regarding how to optimise use of these agents in clinical practice and two key studies were submitted to HTA (DiscoVal, CI S Danson) and RFPB (INTERIM, CI P Corrie) in 2015. Work on both studies began well in advance of their respective NICE appraisal outcomes and both passed the first of their two stage application processes. Final outcomes for each full application will be known in 2016/17. If successful, these studies provide the opportunity for all metastatic melanoma patients receiving standard of care to be entered into a clinical trial and DiscoVal is a large scale study: N=1,068 over five years. Because of the time frames for funding awards and setting up trials, realistically, the positive impact on skin cancer study recruitment is likely to be realised in 2017/18.

Our academic programme has meanwhile focused on 'niche' patient groups, but again due to administrative and regulatory issues, the set-up times of studies funded in 2013/4 has been slower than expected: PIANO and SELPAC opened their first sites at the end of 2015, while PERM has yet to open. The cutaneous melanoma trial, PACMEL, completed accrual and closed in March 2016.

A key goal for the CSG is to develop new studies in non-melanoma skin cancer. Dr Neil Steven was awarded a major EME grant of around £2M in March 2015\*, focusing on primary management of Merkel cell cancer (Rational MCC), and sites will start to open in 2016/17. Studies likely to recruit higher numbers of patients treated for SCC and BCC remain in development and will be submitted for funding in 2016/17.

\*Top three achievements this year

## 2. Structure of the Group

Advice from last year's review panel has been acted upon and the need to continue to restructure the Group has been addressed in the recent 2016 membership application round. To this end, we have appointed two new clinical oncologists to the main CSG and two new dermatologists to the Non-melanoma Subgroup. We now have three clinical oncologists on the CSG with diverse expertise in melanoma and non-melanoma skin cancer, as well as brachytherapy and early phase trials.

Two new medical oncologists joined the CSG, replacing medical oncologists rotating off the Group. Professor Ottensmeier has been appointed (replacing Professor Middleton) with a view to providing leadership in translational research. He is working with Dr Danson to develop a translational research study associated with DiscoVal which will be submitted for funding if HTA support is confirmed for the main clinical trial.

Our first two trainees completed their attachment to the Group in May 2016 and were valued considerably. We hope to extend full membership to one of the trainees next year. The recent new round of trainee applications has been very impressive and included two surgeons. We plan to appoint one surgical and one medical oncology trainee to the Group.

## 3. CSG & Subgroup strategies

### Main CSG

The CSG benefitted this year from having our three yearly strategy day in November 2016, to which we also invited all LCRN skin cancer subspecialty leads. The meeting was particularly productive and we were fortunate to be able to follow this meeting with a further LCRN/NCRI combined meeting in March 2016 funded by the NIHR CRN. This enabled us to progress some new research ideas discussed in November. Interestingly, several LCRN subspecialty leads applied to become NCRI CSG members and two LCRN subspecialty leads are now taking forward new research study ideas to formal study proposals.

The CSG's key priority for this year was to establish national all-comer studies available to metastatic melanoma patients treated with either immune checkpoint inhibitors or molecular targeted therapies with the potential for high recruitment numbers and we have made good progress to achieve this priority. We submitted two studies for funding, each of which were successful at outline stage and they now await a final funding decision from HTA (DiscoVal: anti-PD1 antibody treatment for one year versus until progression) and RfPB (INTERIM: intermittent versus continuous dosing of BRAF/MEKi).

These trials in effect will be our 'bread and butter' activity, aimed at generating high, stable recruitment: DiscoVal = 1,068 over five years, INTERIM = 150 patients over two years. They will complement our ongoing programme of rare (uveal and ckit mutant) melanoma studies. In addition, we have a plan to expand the breadth of our portfolio in the coming one/two years, addressing screening and psychosocial studies as well as for patients with melanoma brain metastases.

Our second key priority is to develop studies in non-melanoma skin cancer. Our programme of work in Merkel cell cancer is established, but the need to develop studies in the far more common cohorts of SCC and BCC need to be addressed. The goal to submit an SCC study to a funding body was set but was not achieved as multidisciplinary agreement on study design has

proved difficult. This goal should be achieved in the first half of next year. Meanwhile, restructuring and refreshing the non-melanoma skin cancer subgroup with new dermatology and clinical oncology consultant membership is intended to facilitate new research opportunities.

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

The aim of the Subgroup is to promote and support high quality, multicentre clinical trials, translational research and other activities in the field of non-melanoma skin cancer including both common keratinocyte skin cancers (SCC and BCC) and rarer skin cancers (including Merkel cell carcinoma and dermatofibrosarcoma protuberans, DFSP)

Our portfolio currently includes SPOT (an RCT of SCC prevention in organ transplant recipients; NIHR RfPB, CI C Harwood) and the Gorlin Syndrome Study (a commercial RCT of a topical Hedgehog pathway inhibitor for BCC). We have also undertaken extensive preliminary work (submitted for publication) to establish the feasibility of an RCT for surgical management of primary DFSP. UKMCC1 (2<sup>nd</sup> line MCC interventional study) closed to recruitment this year, an abstract was submitted to ASCO 2016 and was accepted as a poster.

Our key strategic aims this year were:

1. Development of a clinical trial for management of MCC: now achieved with funding of Rational MCC (MRC EME, CI N Steven) which opened to recruitment in June 2016.
2. Development of a clinical trial in management of primary SCC: COMMISSAR - a multicentre RCT of conventional versus Mohs micrographic surgery and adjuvant radiotherapy in high risk primary SCC – after extensive preliminary work, this is now in the final stages of submission for funding before end of 2016.

We have additional trials in earlier stages of development for management of low risk BCC (CIRCLE, an RCT for surgical and non surgical management in primary and secondary care) and high risk BCC (an RCT comparing electrochemotherapy methodologies) and these studies will be a particular focus of our efforts over next year.

## **4. Task groups/Working parties**

The Skin Cancer CSG Early Diagnosis Task Group was established in May 2015 and is Chaired by Dr Fiona Walter (who also Chairs the NCRI Primary Care CSG Screening Subgroup) and is intended to function for three years in the first instance. The Task Group is exploring research opportunities in (1) primary population screening and (2) secondary screening (post-surgical surveillance) of patients at high risk of recurrence after primary resection of locoregional melanoma.

1. Primary population screening (Leads Dr Fiona Walter & Dr Pippa Corrie)

Dr Walter's current NIHR funded MelaTools programme is maturing and data from this work is being used to inform a potential screening pilot proposal. Within MelaTools, an instrument to identify those in the general population at higher risk of having melanoma has been validated and the health economics of various screening strategies is currently being modelled. Working also with a plastic surgeon with an interest and expertise in Telemedicine, we hope to crystallise a proposal during 16/17.

2. Secondary screening of patients at high risk of recurrence (Leads: Dr Girish Gupta & Dr Ewan Brown)

During the course of the year, various options for evaluating surveillance strategies in high risk resected melanoma patients have been explored. A survey of melanoma MDTs has generated some baseline data, which was recently published in BJD (Gupta et al, 2016) and other international surveillance studies were reviewed for the potential to collaborate. However, Drs Gupta and Brown have been unable to identify a credible research strategy to address currently. The possibility of a national audit was considered but the outcome of some locoregional audits will be awaited in the first instance.

## 5. Patient recruitment summary for last 5 years

In the Skin Cancer CSG portfolio, 9 trials closed to recruitment and 7 opened this year.

**Table 1 Summary of patient recruitment by RCT/Non-RCT**

Year	All subjects		Cancer patients only		% of cancer patients relative to incidence	
	Non-RCT	RCT	Non-RCT	RCT	Non-RCT	RCT
2011/2012	705	505	691	505	8.3	6.1

**Table 2 Summary of patient recruitment by Interventional/Non-interventional**

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2012/2013	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	516	245	516	239	4.19	1.94

As demonstrated above, overall recruitment this year has fallen slightly, although recruitment to interventional trials has increased. Much of the non-interventional activity is not within the control of the CSG. The CSG primarily focuses on interventional studies, so the increase in interventional trial activity is in fact quite reassuring. The increase is in part due to the surgical excision margins study, MelMart, which is driven by our plastic surgeon CSG member, Mr M Moncrieff.

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

- Other CSGs

Linking through Dr Fiona Walter, we are working to develop a primary care screening strategy in 2016/17

Linking with the Brain Tumour CSG, Dr Jim Lester is working with Dr Gill Whitfield to develop an interventional randomised phase II study to evaluate pembrolizumab +/-SRS in patients with limited melanoma brain metastases. The study outline will be presented to CTRad in June 2016 and move forward to funding as a feasibility study later in the year.

- International groups

Dr Paul Lorigan is now a member of the EORTC Melanoma Group Steering Committee and he has agreed to provide a link to the CSG in the form of written reports. Three EORTC-led melanoma studies are currently active in our portfolio and the CSG is actively supporting recruitment to them (EORTC 1325, EORTC 18081, EORTC 1208 - Minitub). We have been communicating with the EORTC regarding the potential to collaborate with DiscoVal since international recruitment could enable a large study to be completed sooner and potentially address overall survival, as well as the current primary end point of progression-free survival. The EORTC has indicated it would prefer to run their own similar study but with the potential to combine datasets in due course. The two trial teams are in regular communication to ensure compatibility between protocols.

- ANZMTG

The UK actively contributes to ANZMTG-led trials in our portfolio: WBRT and MelMart.

Network subspecialty leads (SSLs):

Interaction with the SSLs has been particularly fruitful in the last six months, thanks to the opportunity to meet together in November 2015 – all SSLs were invited to and attended the Skin Cancer CSG strategy day - and March 2016, when the NIHR CC offered to fund an ad hoc meeting at short notice before the end of the financial year. This allowed us to take forward new study ideas proposed in November as well as review recruitment to our current portfolio.

SSL advice on the design of INTERIM was particularly helpful and the study outline proposal was modified prior to submission to RfPB in December 2015. The revision most likely contributed to the success of the study in reaching the second stage of the two stage application process. The skin cancer SSLs are clearly very engaged and in fact three applied for NCRI Skin Cancer CSG membership in the recent round of applications, two of whom were appointed. A new psychosocial study discussed at both meetings is now in development and led by the Thames Valley SSL, Dr M Payne).

## 7. Funding applications in last year

**Table 3 Funding submissions in the reporting year**

<b>Cancer Research UK Clinical Research Committee (CRUK CRC)</b>			
<b>Study</b>	<b>Application type</b>	<b>CI</b>	<b>Outcome</b>
<b>July 2015 (CTAAC)</b>			
None			
<b>December 2015</b>			
None			
<b>May 2016</b>			
None			
<b>Other committees</b>			
<b>Study</b>	<b>Committee &amp; application type</b>	<b>CI</b>	<b>Outcome</b>
DiscoVal: A randomised phase III discontinuation trial to evaluate optimal duration of anti-PD1 monoclonal antibody treatment in patients with metastatic melanoma - September 2015	HTA – Outline application	Dr Sarah Danson	Successful
DiscoVal: A randomised phase III discontinuation trial to evaluate optimal duration of anti-PD1 monoclonal antibody treatment in patients with	HTA – Full application	Dr Sarah Danson	Awaited

metastatic melanoma - February 2016			
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 - December 2015	RfPB – Outline application	Dr Pippa Corrie	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 - March 2016	RfPB – Full application	Dr Pippa Corrie	Awaited

## 8. Collaborative partnership studies with industry

Commercially sponsored studies have contracted this year: five closed, one adjuvant study is open and two studies are in set-up. The wave of major international registration trials evaluating immune checkpoint inhibitors and BRAF+MEK inhibitor combination regimens in metastatic melanoma has now come to an end. Although this represents a loss of trial and treatment access, subsequent commissioning of these new agents now allows for academic studies developing their use beyond their licensed indication. The weakness of awaiting new drug commissioning is the time frame between registration trial closure and positive NICE guidance being issued, as well as uncertainty regarding whether guidance will be positive. In the cases of DiscoVal and INTERIM, discussions with relevant drug manufacturers (BMS, Novartis and Roche) were started well before NICE appraisal meetings with a view to starting the trial application process underwritten by industry. In each case, outline proposals were submitted with ongoing industry negotiations ongoing. Since submitting full applications, NICE appraisals have been positive in each case. Depending on final funding outcomes, we are in a position to discuss with industry potential support for exploratory translational studies.

In terms of academic studies with industry collaboration, PACMEL finally closed in March 2016, SELPAC and PIANO have just opened and PERM is due to open imminently.

## 9. Impact of CSG activities

In the last five years, the skin cancer trial portfolio has made a spectacular impact on routine clinical practice, contributing to radical changes in survival for metastatic melanoma patients. In 2010, there were no systemic therapeutic agents with proven survival benefit. Within a five year time span, nine new treatments have been licensed based on survival gain shown in randomised clinical trials. CSG members played a key role in bringing international registration trials of both checkpoint inhibitors and MAPkinase inhibitors into the UK, giving our patients and clinicians early access to state of the art treatment and ensuring international recognition of the UK as a major player in the conduct of melanoma research. Several UK clinicians were co-authors on associated publications. CSG members have acted as clinical experts on behalf of the RCP and again been highly influential in converting research into clinical practice, by contributing to eight positive NICE technology appraisals. Three further appraisals are planned in 2016/17. The median overall survival of metastatic melanoma has been extended from median six-eight months, to around two years, with up to 20% of patients achieving long term remission.

CSG members provide ad hoc peer review for a variety of CRUK and NIHR funding bodies. Following restructuring of the CRUK funding processes, Dr James Larkin was appointed as deputy Chair to the CRC and Dr Pippa Corrie was appointed as a member of CERP.

## 10. Consumer involvement

Simon Rodwell is a member of trial management groups for the portfolio Rational MCC and MelaTools studies as well as for the DiscoVal study under funding consideration. He has advised on various other protocols and patient leaflets including those for the INTERIM and PAUSE studies.

In his role as CEO of Melanoma Focus, Simon Rodwell is responsible for the charity's interaction with the CSG. Melanoma Focus has a membership of 230 that includes the UK's leading melanoma clinicians, scientists and specialist nurses. Examples of collaborative initiatives with the CSG include the joint nomination of Melanoma Focus members for NICE appraisals and collaboration in responding to Government decisions on the funding of BRAF+MEK inhibitor combinations.

During the year, Melanoma Focus's activities included: the selection of a guideline development group in preparation for a project to develop national clinical guidelines for mucosal melanoma; continuing to recruit NHS Trusts to the melanoma database project; the launch of a project to develop a patient decision aid for melanoma; the start of a third research study funded under the charity's patient impact programme, Validation of Ambra-1 and Loricrin as prognostic biomarkers for the early detection of high risk melanomas, at Newcastle University; and support for a small project to investigate various aspects of orbital melanoma.

The charity held its two annual study day meetings in 2015: in May at the Christie School of Oncology and in October at the Royal Society of Medicine, the latter attracting a record number of delegates.

Pat Fairbrother joined the CSG in October 2016 and brings with her considerable experience as a lead member of the Independent Cancer Patients Voice and lay member of the NHR England skin cancer clinical reference group. Her main interest is non-melanoma skin cancer and she has been welcomed to the Non-Melanoma Subgroup. She has provided advice on aspects of the INTERIM study qualitative assessment of treatment-related skin toxicities.

## 11. Open meetings/annual trials days/strategy days

NCRI Skin Cancer CSG Strategy Day, November 2015:

As already described, this was a productive day which benefitted greatly from having most LCRN SSLs in attendance. After this meeting, we were able to formalise our three year strategic plan (see attached document below).

LCRN/NCRI Meeting, March 2016:

As already described, this was a very useful opportunity to bring NCRI and LCRN colleagues back together to progress our research plans. This was an ad hoc meeting and it raises the question of how we arrange such meetings in the future.

The NCRI Skin Cancer CSG does not have an annual trials day. However, the trial portfolio is publicised at the annual Melanoma Focus Conference, where all delegates are provided with a clinical trials booklet generated by the NCRI Executive and clinical trials are addressed within the conference agenda.

## 12. Priorities and challenges for the forthcoming year

### Priorities:

- Secure funding for high recruiting national multicentre advanced melanoma clinical trials evaluating optimal use of checkpoint inhibitors (DiscoVal) and MAPkinase inhibitors (INTERIM).
- Submit squamous cell carcinoma study (COMMISSAR) for funding.
- Extend the breadth of the portfolio by developing studies in new areas: screening, radiotherapy, psychosocial, translational.

### Challenges:

- Securing funding for academic multicentre clinical trials.
- Maintaining recruitment activity across the skin cancer portfolio while new studies are being set up.
- Maintaining the momentum generated in the last six months and bring new initiatives to fruition.

## 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

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 Rebecca Lee*	Clinical Research Fellow	Manchester
Dr Mazhar Ajaz	Clinical Oncologist	Guildford
Dr Jim Lester	Clinical Oncologist	Sheffield
Dr Agata Rembielak	Clinical Oncologist	Oldham
Ms Patricia Fairbrother	Consumer	Derby
Mr Simon Rodwell	Consumer	Bury St Edmunds
Dr Girish Gupta	Dermatologist	Lanarkshire
Dr Catherine Harwood	Dermatologist	London
Dr Charlotte Proby	Dermatologist	Dundee
Dr Rubeta Matin*	Dermatologist	Oxford
Dr Fiona Walter	General Practitioner	Cambridge
Dr Ewan Brown	Medical Oncologist	Edinburgh
Dr Pippa Corrie (Chair)	Medical Oncologist	Cambridge
Dr Sarah Danson	Medical Oncologist	Sheffield
Dr James Larkin	Medical Oncologist	London
Professor Christian Ottensmeier	Medical Oncologist	Southampton
Dr Neil Steven	Medical Oncologist	Birmingham
Mr Marc Moncrieff	Surgeon	Norwich
Professor Keith Wheatley	Statistician	Birmingham

\*denotes trainee member

## Membership of the Subgroups

Non-melanoma Skin Cancer Subgroup		
Name	Specialism	Location
Dr Christina Yap	Biostatistician	Birmingham
Dr Carie Corner**	Clinical Oncologist	Hertfordshire
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	Medical 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 trainee member

\*\*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

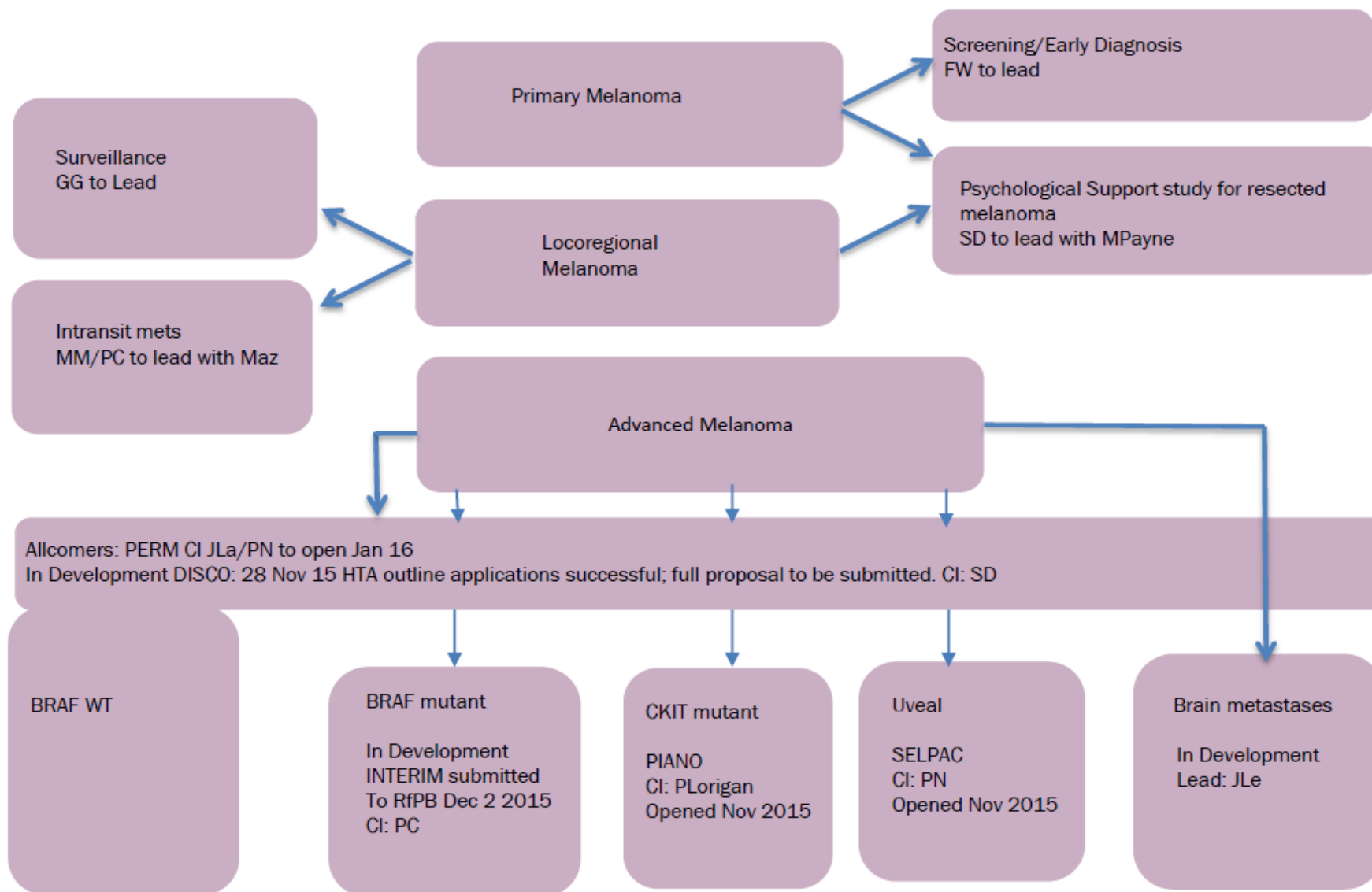
PC	Pippa Corrie	CSG chair
CH	Catherine Harwood	Non-melanoma skin cancer subgroup chair
JLa	James Larkin	Melanoma - cutaneous
SD	Sarah Danson	Melanoma – rare
CP	Charlotte Proby	SPED representative
MM	Marc Moncrieff	Surgical studies
JLe	Jim Lester	Radiotherapy – melanoma
FW	Fiona Walter	Primary care
EB	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

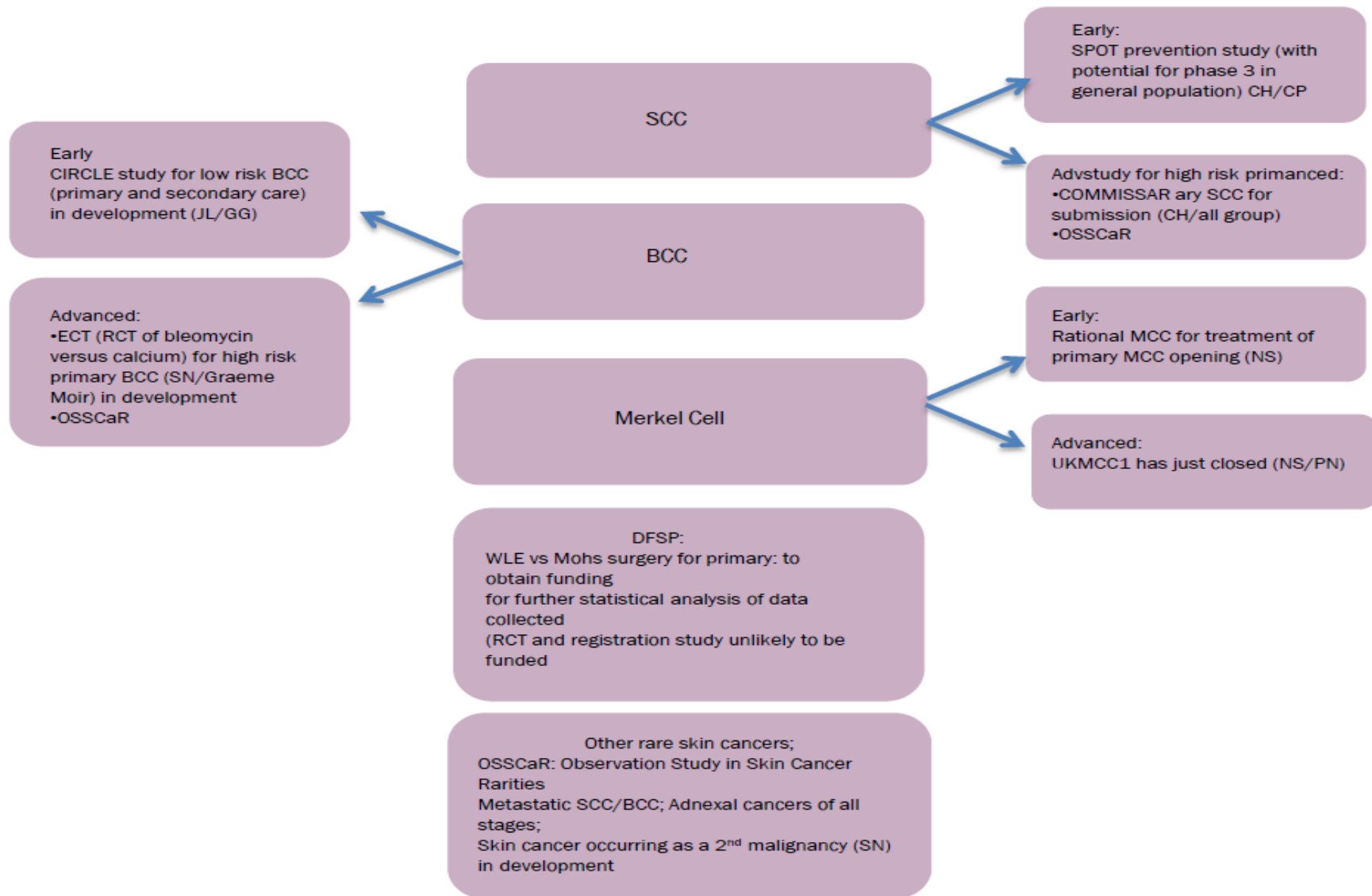
Strategic objective	Action	CSG Lead	Date	Outcomes
1a. Portfolio development (general)	Establish a set of priorities for the development and set up of studies that takes account of the NIHR portfolio, international agenda, available funding opportunities and clinical need	ALL	Document key priorities at Strategy Day 24 Nov15 Review May 2016	Review Portfolio priorities 6-monthly at CSG meetings
1b. Portfolio development - melanoma	Ensure cohesive strategy of melanoma clinical trials, taking into account: <ul style="list-style-type: none"> <li>- Opportunities within the international agenda, avoiding competition with key Pharma studies</li> <li>- The need for a high recruiting study open at all times</li> <li>- Balance between late and early phase studies</li> <li>- Multicentre studies with good regional coverage</li> <li>- All disease stages</li> <li>- All subgroups – rare forms &amp; biomarker specific subgroups</li> <li>- Interaction with CRN subspecialty leads</li> </ul>	PC/SD/JL/EB	Melanoma studies identified at Strategy Day 24 Nov 15  Progress review 6 monthly at CSG meetings	Timelines for current and planned studies agreed; leads for new studies identified and defined in strategy document
1c. Portfolio development – non-melanoma skin cancer	Secure new studies for common and uncommon non-melanoma skin cancer <ul style="list-style-type: none"> <li>•SCC</li> <li>•BCC</li> <li>•Merkel cell</li> <li>•Rarer non-melanoma skin cancers</li> </ul>	CH/GG/CP/RM	Non-melanoma priorities identified at Strategy Day 24 Nov 15 Commissar funding application by May 2016; further development of CRICLE study	Key priority to finalise Commissar and submit for funding before CSG meeting in May 2016; CIRCLE study to be submitted by end 2016
1d. Interaction with Cross Cutting groups	Identify leads within the CSG to link with the following cross cutting CSGs and advisory groups: <ul style="list-style-type: none"> <li>•Primary Care</li> <li>•Screening, Prevention and Early Diagnosis (SPED) Advisory Group</li> <li>•TYA</li> <li>•CTRAD</li> <li>•CNS CSG</li> </ul>	FW CP ? JLe JLe	Dec 2015	TYA not discussed – to keep under review Consider interaction with other CSGs: eg.H&N

Strategic objective	Action	CSG Lead	Date	Outcomes
1e. National Cancer Intelligence Network (NCIN)	<p>Establish clear link with skin cancer Clinical Reference Group (CTYA SSCRG)</p> <p>Explore with NCIN the use of data to inform study design and take over long term follow-up</p>	<p>??</p> <p>?? and ALL</p>	<p>November 2015</p> <p>Report 6 monthly at CSG meeting</p>	<p>NCIN Skin Cancer CRG</p> <p>Chair attended Strategy Day Nov 15</p>
2. Key research priority areas	<p><b>Surgery:</b> Working group to take forward new study for localised disease</p> <p><b>Early phase:</b> Increase the availability of NIHR adopted early phase studies for melanoma patients</p> <ul style="list-style-type: none"> <li>Liaise with CIs and study sponsors to request NIHR adoption</li> <li>Inform colleagues re opportunities re commercial early phase/ combinations alliance programmes</li> <li>Increase no. of melanoma study outline proposals being submitted for funding/endorsement</li> </ul> <p><b>Radiotherapy:</b> Establish new study for brain mets pts involving RT</p> <p><b>Translational:</b></p> <ul style="list-style-type: none"> <li>Work with key clinical and scientific groups to develop a translational research strategy: link with potential GeCIP</li> </ul> <p><b>Melanoma screening pilot study:</b> Working group to take new proposal forward</p>	<p>MM/PC</p> <p>JLa</p> <p>JLe</p> <p>JLa</p> <p>FW, CP, PC</p>	<p>May 2016</p> <p>Ongoing</p> <p>End 2016</p> <p>May 2016</p> <p>End 2016</p>	<p>Outline proposal to CSG May 16</p> <p>JLe to work with CNS MDT to explore potential RT+/-SRS study</p> <p>JLa to inform outcome of GeCIP submission</p> <p>FW to update on progress towards screening study May 201</p>
3a. Raising awareness and profile	<p>Regular dissemination of study recruitment activity and outcomes through newsletters, annual meetings and Annual Report to all stakeholders</p> <p>Consider dedicated annual NCRI skin cancer trials meeting</p> <p>Communications about new studies with CRN subspecialty leads</p> <p>Submission of abstracts to :</p> <ul style="list-style-type: none"> <li>NCRI Cancer Conference</li> <li>International cancer conferences: ESMO/ECC/ASCO/AACR/SMR</li> <li>NCIN Conference</li> </ul>	<p>PC/ND/SA</p> <p>All</p> <p>All</p>	<p>Ongoing</p> <p>2016?</p>	<p>PC to feedback to Subspecialty leads after CSG meetings</p> <p>ND to share strategy document with NCRI and LCRN skin cancer leads</p> <p>Discuss annual trials meeting at next CSG meeting May 2016</p>

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	ALL	Ongoing	Recruit CSG-led studies to time and target Good regional placement of studies  Meet NIHR CRN Speciality Objectives
	Interaction with LCRN Subspecialty Leads to determine placement of new studies and address barriers to actively recruiting patients	PC/CH	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 skin cancer patients can access the full portfolio of studies within England	ALL	Ongoing	
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	All	Ongoing	PC/NK to agree and take forward
	Utilise IRCI for international studies of rare cancer types, where appropriate	??	Ongoing	
	Work closely with UK representative on EORTC melanoma group steering committee	Invite representation at CSG meetings	May 2016	
	Work closely with Melanoma Focus to integrate research and service	Invite representation at CSG meetings	May 2016	

Strategic objective	Action	CSG Lead	Date	Outcomes
5. CSG structure and function	Establish Primary Melanoma Screening Working Party	FW	May 2016	
	Establish Secondary Melanoma Screening Working Party	GG	May 2016	
	Consider case for Translational Research Working Party	ALL	May 2016	
	Consider need for Working Party to develop brain mets strategy	JLe	May 2016	
	Identify mentors for trainee registrars in the CSG	CH & Jla	May 2015	
	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	
	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	





## **B – Non-Melanoma Skin Cancer Subgroup Strategy**

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

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## Appendix 3

### Portfolio maps

NCRI portfolio maps						
Skin Cancer						
Map A – Melanoma Click ↓ below to reset map						
		1st line metastatic	2nd line metastatic	Adjuvant	Non-interventional	Surgery
All melanomas	All	WBRT post local				
					CR UK Stratifie	
			PARP inhib...			
					Physical activ.	
					Vitamin D & Imm	
					UNITI	
					SC stem cells	
					Role of soluble	
					Talimog+ Laherp	
		Talimogene...				
Cutaneous - BRAF mutant	All cutaneous - BRAF mutant		Nivolumab			
					EktoTherixT	
		Pre-Op JX-594				
		The PERM Study				
					SerpinA12	
		BMS-936558				
					SCQOLIT	
					Peripheral Blood Transcriptome Study	
				Pegyl <sup>®</sup> IFN		
						MelMarT
Cutaneous - BRAF wt	Nras			Pegyl <sup>®</sup> IFN		
						MelMarT
	Other	PACMEL	PACMEL			
				Pegyl <sup>®</sup> IFN		
						MelMarT
Non - cutaneous	Mucosal ckit					
	Mucosal other	PIANO Study				
	Uveal					
		A Randomised th				
		Melphalan/HDS				

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

In Set-Up Pending ..
  Open Single CSG
  In Set-Up Pending ..
  Open Multi CSG

## NCRI portfolio maps

Map B – Non-melanoma  
Click ↓ below to reset map

Skin Cancer

		Adjuvant	Metastatic	Neoadjuvant	Non-intervention..	Pre-diagnosis	Surgery
All	All				CR UK Stratifie Head and neck s Physical activ. SC stem cells MEDI4736		
Basal cell carcinoma	All						
Merkel cell	All		UKMCC-01				
Other	All				Karposis Sarcom A study of selu		
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

Suspended Single ..

## Appendix 4

### Publications in the reporting year

#### SYMPTOM

Hall N, Birt L, Banks J, Emery J, Mills K, Johnson M, Rubin GP, Hamilton W, Walter FM. Symptom appraisal and healthcare-seeking for symptoms suggestive of colorectal cancer: a qualitative study. *BMJ Open* 2015;5(10):e008448. doi: 10.1136/bmjopen-2015-008448

Banks J, Hamilton W, Walter FM. The Discovery Programme and its impact on cancer diagnostics. *Br J Hosp Med*. 2015;76(10):558-9. doi: 10.12968/hmed.2015.76.10.558

Balasooriya-Smeekens C, Walter FM, Scott S. The role of emotions in time to presentation for symptoms suggestive of cancer: a systematic literature review of quantitative studies. *Psychooncology* 2015;24(12):1594-604. doi: 10.1002/pon.3833.

Rubin G, Berendsen A, Crawford SM, Dommett R, Earle C, Emery J, Fahey T, Grassi L, Grunfeld E, Gupta S, Hamilton W, Hiom S, Hunter D, Lyratzopoulos G, Macleod U, Mason R, Mitchell G, Neal RD, Peake M, Roland M, Seifert B, Sisler J, Sussman J, Taplin S, Vedsted P, Voruganti T, Walter FM, Wardle J, Watson E, Weller D, Wender R, Whelan J, Whitlock J, Wilkinson C, de Wit N, Zimmermann C. The expanding role of primary care in cancer control. *Lancet Oncol*. 2015 Sep;16(12):1231-72. doi: 10.1016/S1470-2045(15)00205-3

Walter FM, Rubin G, Bankhead C, Morris HC, Hall N, Mills K, Dobson C, Rintoul R, Hamilton W, Emery J. First symptoms and other factors associated with time to presentation and diagnosis and stage at diagnosis of lung cancer: a prospective cohort study. *Brit J Cancer*. 2015 Mar 31;112 Suppl:S6-S13. doi: 10.1038/bjc.2015.30. PMID: 25734397

#### ASICA

Murchie P, Allan JL, Brant W, Dennis M, Hall S, Masthoff J, Walter FM, Johnston M. Total skin self-examination at home for people treated for cutaneous melanoma: development and pilot of a digital intervention. *BMJ Open*, 2015; 6;5(8):e007993. doi: 10.1136/bmjopen-2015-007993

#### MelaTools programme

Walter FM, Abel G, Lyratzopoulos G, Melia J, Greenberg G, Brewster DH, Butler H, Corrie P, Campbell C. Seasonal variation in diagnosis of invasive cutaneous melanoma in Eastern England and Scotland. *Cancer Epidemiol*. 2015;39(4):554-61. doi: 10.1016/j.canep.2015.06.006.

Kassianos AP, Emery JD, Murchie P, Walter FM. Smartphone applications for melanoma detection by community, patient and generalist clinician users: a review. *Br J Dermatol*. 2015;172(6):1507-18. doi: 10.1111/bjd.13665

#### PROSPECTIV

Watson E, Shinkins B, Frith E, Neal D, Hamdy F, Walter FM, Weller D, Wilkinson C, Faithfull S, Wolstenholme J, Sooriakumaran P, Kastner C, Campbell C, Neal R, Butcher H, Matthews M, Perera R, Rose P. Symptoms, unmet needs, psychological well-being and health status in prostate cancer survivors: implications for redesigning follow-up. *BJU Int*. 2015 doi: 10.1111/bju.13122.

### **The Melanoma Interview Study**

Scott SE, Birt L, Cavers D, Shah N, Campbell C, Walter FM. Patient drawings of their melanoma: A novel approach to understanding symptom perception and appraisal prior to healthcare consultation. *Psychol Health*. 2015;1-14. doi: 10.1080/08870446.2015.1016943.

### **wrt melanoma surveillance**

Parkins G, Brown E, Gupta G. Radiological imaging in all stage III melanoma - current practice in the United Kingdom. *Br J Dermatol* 2016 (in press)

### **Checkmate067**

J. Larkin, V. Chiarion-Sileni, R. Gonzalez, J.J. Grob, C.L. Cowey, C.D. Lao, D. Schadendorf, R. Dummer, M. Smylie, P. Rutkowski, P.F. Ferrucci, A. Hill, J. Wagstaff, M.S. Carlino, J.B. Haanen, M. Maio, I. Marquez-Rodas, G.A. McArthur, P.A. Ascierto, G.V. Long, M.K. Callahan, M.A. Postow, K. Grossmann, M. Sznol, B. Dreno, L. Bastholt, A. Yang, L.M. Rollin, C. Horak, F.S. Hodi, and J.D. Wolchok. Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma. *N Engl J Med*, May 31, 2015, DOI: 10.1056/NEJMoa1504030

### **MelMart**

Keith Wheatley, Jayne S. Wilson, Piers Gaunt, Jerry R. Marsden. Surgical excision margins in primary cutaneous melanoma: A meta-analysis and Bayesian probability evaluation *Cancer Treatment Reviews*, October 2015, 42 (2016) 73–81

### **PACMEL**

N Coupe, P Corrie, M Hategan, J Larkin, M Gore, A Gupta, A Wise, S Suter, C Ciria, S Love, L Collins, MR Middleton. PACMEL: a phase 1 dose escalation trial of trametinib (GSK1120212) in combination with paclitaxel. *Eur J Cancer* 2015;51:359-66.

### **IMAGE**

M Middleton, S Dalle, P Corrie, C Loquai, P Terheyden, KC Kahler, F Meiss, R Board, AM Arance, R Gutzmer, A Tarhini, D Dummer, S Ernst, E Richtig, P Wolter, K Bulger, S Kotapati, RK Le, J Brokaw, AP Abernethy. Initial safety results from a multinational, prospective, observational study in advanced melanoma (IMAGE). *Eur J Cancer* 2015;51 Suppl S3; S678 (3338).

### **Ipilimumab in the real world**

Ahmad A, Qian W, Ellis S, Mason E, Khattak MA, Gupta A, Shaw H, Quinton A, Kovarikova J, Thillai K, Rao A, Board R, Nobes J, Dalgleish A, Grumett S, Maraveyas A, Danson S, Talbot T, Harries M, Marples M, Plummer R, Kumar S, Nathan P, Middleton MR, Larkin J, Lorigan P, Wheeler M, Ottensmeier CH, & Corrie PG. Ipilimumab in the real world: the UK expanded access programme (EAP) experience in previously treated advanced melanoma patients. *Melanoma Res* 2015;25(5): 432-42.

### **Evolving treatment options for melanoma brain metastases**

Ajithkumar T, Parkinson C, Fife K, Corrie P, Jefferies S. *Lancet Oncology* 2015; 16 (13): e486-e497.

### **Treatment patterns in advanced melanoma: findings from a survey of European oncologists**

Jones C, Zhao Z, Barber B, Bagijn M, Corrie P, Saltman D. *Eur J Cancer Care* 2015;24 (6) 862-66.

### **Management of BRAF and MEK inhibitor toxicities in patients with metastatic melanoma**

SJ Welsh & PG Corrie. *Ther Adv Med Oncol* 2015;7:122-136.

**Unmet clinical needs in the management of advanced melanoma: findings from a survey of oncologists**

Jones C, Clapton G, Zhao Z, Barber B, Saltman D, Corrie P. Eur J Cancer Care 2015;24 (6) 867-72.

**ZeSS**

P Corrie, P Terheyden, AJ Tije, R Herbst, R Jansen, M Marples, D Debus, R Marconcini, M Blasinska-Morawiec, K Freivogel, MG Munson, G Goodman. A Prospective Observational Safety Study of Patients with BRAFV600 Mutation-positive Unresectable or Metastatic Melanoma Treated with Vemurafenib (Zelboraf® Safety Study [ZeSS]): Interim Results. EADO September 2015 oral presentation

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## Appendix 5

### Major international presentations in the reporting year

#### **The Melanoma Interview Study & MelaTools programme**

Mar 2016: Evolving Role of Primary Care in Cancer conference, Victorian Comprehensive Cancer Centre, Melbourne, Australia. Keynote: 'Supporting early diagnosis of melanoma in primary care.'

#### **DISCOVERY programme's Symptom study**

Mar 2016: Evolving Role of Primary Care in Cancer conference, Victorian Comprehensive Cancer Centre, Melbourne, Australia. Oral presentation: 'Patient factors associated with time to diagnosis for pancreatic cancer: findings from an English prospective cohort study.'

#### **MelaTools programme**

June 2015: NCIN cancer outcomes meeting, Belfast, N Ireland. Oral: melanoma seasonality study.

May 2015: 8<sup>th</sup> CaPRI annual meeting, Aarhus, Denmark. Oral: melanoma seasonality study.

#### **ZeSS**

P Corrie, P Terheyden, AJ Tije, R Herbst, R Jansen, M Marples, D Debus, R Marconcini, M Blasinska-Morawiec, K Freivogel, MG Munson, G Goodman. A Prospective Observational Safety Study of Patients with BRAFV600 Mutation-positive Unresectable or Metastatic Melanoma Treated with Vemurafenib (Zelboraf® Safety Study [ZeSS]): Interim Results. EADO September 2015, oral presentation.